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Effectiveness of an Innovative Home-Based Rehabilitation Program on Lower Limb Functions in Subjects with Chronic Stroke: A Randomized, Controlled Trial

Shamay Sheung-Mei Ng

A thesis submitted in partial fulfilment of the requirements for the Degree of Doctor of Philosophy

Department of Rehabilitation Sciences
The Hong Kong Polytechnic University
December 2004
STATEMENT OF SOURCES

The idea of the present investigation originated from my supervisor, Professor Christina W.Y. Hui-Chan, the design of the study and the planning of the experiment results from discussions between the author and Professor Hui-Chan. All experiments in the present investigations were completed solely by the author.

I, Shamay Sheung-Mei Ng, hereby declare that the work presented in this thesis is, to the best of the author's knowledge and belief, original, except as acknowledged in the text, and that the material has not been submitted, either in whole or in part, for a degree at this or any other University.

In addition, ethical approval from The Hong Kong Polytechnic University Human Ethics Committee was granted for the studies presented in this thesis. Subjects were required to read a subject information document and informed consent was gained prior to data collection.

Name: Shamay Sheung-Mei Ng
Signed:
Date: December 2004
Part of the work presented in this thesis have been published or presented in the following forums:

PUBLISHED PAPER

Ng SMS, Hui-Chan CWY (2004): The timed “Up & Go” test: Its reliability and association with the lower limb impairments and locomotor capacities in people with chronic stroke. *Archives of Physical Medicine and Rehabilitation* (in press)

CONFERENCE PRESENTATION

Ng SSM, Hui-Chan CWY (2004): Are timed “Up & Go” repeatable and associated with ankle muscle strength and walking abilities in people with chronic stroke. The Fourth Pan-Pacific Conference on Rehabilitation: Art and Science of Enablement, 2004 Sept 24-26; Hong Kong, China (SAR); p.57.

ABSTRACT

The aim of the work presented in this thesis was to develop an innovative home-based rehabilitation program in order to reduce spasticity, improve muscle strength of affected lower extremity and improve locomotor capacities in subjects with chronic stroke. Two series of studies were undertaken in this thesis. The pilot study sought to quantify the reliability of the 5 outcome measures used in the main study. The main study investigated the efficacy of 3 active home-based treatment programs versus no active treatment on the motor recovery of lower extremity functions in subjects with chronic stroke.

In the pilot study, 10 healthy elderly (mean age 63.5 ± 6.1 years) and 11 stroke subjects (mean age 61.1 ± 6.8 years) at least 1 year post-stroke (mean duration after stroke onset 5.6 ± 3.3 years) underwent 5 assessments: spasticity of ankle planarflexor by the Composite Spasticity Scale, ankle muscle strength by maximum isometric voluntary contraction (MIVC) of ankle dorsi- and plantar-flexors, gait performance by the GAITRite Walkway System, walking endurance by the 6-Minute Walk test (6 MW) and the functional mobility by the timed “Up & Go” test (TUG). High test-retest repeatability were found in the measurements for spasticity of ankle planarflexors (ICC=0.40 to 0.94), MIVC of ankle dorsi- and plantar-flexors (ICC=0.47 to 0.99), temporal spatial gait parameters (ICC=0.36 to 1.00), distance covered in 6 MW (ICC=0.91 to 0.98) and TUG scores (ICC=0.95 to 0.97). Our findings also showed that subjects with chronic stroke had a significantly higher level of spasticity in their affected ankle plantarflexors, weaker planarflexors, slower walking speed, poorer walking
endurance and decreased functional mobility when compared with those of the healthy elderly. Strong relationships were found between TUG scores on the one hand, and strength of plantarflexors ($r=-0.91, P<0.01$), gait velocity ($r=-0.86, P<0.01$), and walking endurance assessed by the 6 MW ($r=-0.93, P<0.01$) on the other. These findings make the TUG test particularly useful for assessing functional mobility in ambulant patients with chronic stroke.

For the main study evaluating the effectiveness of 3 home-based programs versus no active treatment in improving lower limb functions in subjects with stroke, a single-blinded placebo-controlled design was used. Eighty-eight subjects with chronic stroke (mean age 57.3 ± 8.1 years; mean duration after stroke onset 5.3 ± 3.5 years) were randomly allocated into 1 of 4 groups: TENS, TENS+TRT (task-related training), placebo-TENS (PLBO)+TRT, and control groups. Subjects in the 3 intervention group underwent the treatment program allotted once a day, 5 days a week for 4 weeks, while the control group received no active treatment. The 5 outcome measures mentioned above were assessed before ($T_0$) and after ($T_1$) treatment on Day 1; after 2 weeks ($T_2$) and 4 weeks of treatment ($T_3$); and at 4-weeks follow-up after treatment ended ($T_{FU}$).

The results showed no significant differences among the groups before treatment. The 2 TENS (TENS and TENS+TRT) groups produced significantly earlier reduction of plantarflexor spasticity (from $T_2$ on) and greater increase of peak dorsiflexion torque after 20 treatment sessions than the PLBO+TRT group, when compared with those of the control group ($P<0.05$). Only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the increase in peak dorsiflexor torque 4 weeks after treatment ended. For plantarflexion, only the 2 exercise
(TENS+TRT and PLBO+TRT) groups but not the TENS group had significant % increases in peak plantarflexion torque, IEMG of the MG muscle and reduction of EMG co-contraction ratio after 4 weeks of treatment, when compared with those of the control group. It is important to note that only the combined TENS+TRT group maintain most of the treatment effects 4 weeks after the treatment ended.

With regard to locomotor capacities, the combined TENS+TRT group demonstrated significantly greater % increase in gait velocity at the end of the 4-week treatment, when compared with that of the other 3 (TENS, PLBO+TRT and control) groups (all P<0.01). Accompanying the increase in gait velocity, significant among-group increases in cadence, step and stride length, stance time, single-leg support duration and decrease of double-leg support duration were found (P<0.05). The same combined TENS+TRT group also demonstrated significantly greater % increase of the distance covered in 6 MW and % decrease of the TUG time scores than those of the TENS and control groups (P<0.01).

To conclude, this thesis demonstrated that all 3 home-based rehabilitation programs involving TENS and/or task-related training is feasible and effective in reducing spasticity and in improving aspects of muscle functions in patients with stroke. The results further demonstrated that 20 sessions of combined TENS+TRT treatment was superior to either TENS alone or PLBO+TRT in enhancing the recovery of lower limb functions in chronic stroke survivors. Since the home program requires only minimal supervision from professional physiotherapists, it has the added benefit of being cost-effective to the patients and the society at large.
DEDICATION

I dedicate this work to my late father, Mr. Chuk-Kwong Ng (1916-2000), who taught me to be strong, patient and hard-working when I meet any difficulties.
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I am indebted to my chief supervisor, Professor Christina W.Y. Hui-Chan, for her enthusiasm, encouragement, support and guidance of the research and in the completion of this thesis. In addition, her kindness, her dedication to work, her demand for the acme of perfection and logical thinking in research have been inspiring to me, which will further propel me to strive for excellence in my future career.

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I am indebted to individuals who assisted with my data collection, especially Mr. Sik-Cheung Siu who wrote the computer programs for data collection and processing of the EMG data. I would also like to thank Ms. Anita K.Y. Wong, who was the physiotherapist providing treatment to the subjects in the present study. My thanks also go to Mr. Peggio Lam for his valuable advices on the statistical analysis in this thesis. I also thank Mr. Man Cheung and Mr. Ken Kan for their technical support.

I would like to extend my sincere thanks to Professor Roberta B. Shepherd, the supervisor of my Master Dissertation during my post-graduate study in the University of Sydney. She led my first step into the field of neurological rehabilitation which helped to develop my great interest in it.

I would like to thank all the subjects who participated in the present study. It is difficult to cope with the consequences of stroke, and I am grateful for their generosity and willingness to participate in the present study that required travel to the University several times over 8 weeks period.
I am most grateful to my mother and my late father, Mr. and Mrs. Chuk-Kwong Ng, for giving me the most precious gift of all - their endless love and support.

Finally, I express my deepest gratitude to my husband, Mr. Desmond Y.W. Lam, for giving me a wonderful family and his endless love, encouragement, support and patience throughout my post-graduate study, as well as our lovely son, Brian, who is such a good and strong boy that I was able to concentrate on the study during my candidature.

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LIST OF ABBREVIATIONS

ANOVA: analysis of variance
CSS: Composite Spasticity Scale
EMG: electromyography
ICC: intraclass correlation coefficient
IEMG: integrated electromyography
MG: medial gastrocnemius muscle
MIVC: maximum isometric voluntary contraction
Nm: Newton meter
PASS: Power Analysis and Sample Size
PLBO: placebo TENS
SPSS: Software Package of Social Statistics
TA: tibialis anterior muscle
TENS: transcutaneous electrical nerve stimulation
TRT: task-related training
TUG: timed "Up & Go" test
T₀: assessment before treatment
T₁: assessment immediately after first treatment on Day 1
T₂: assessment after 2 weeks of treatment
T₃: assessment after 4 weeks of treatment
Tᵢₙₐᵢₙ: assessment at follow-up
6 MW: 6-minute walk test
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Chapter 1

Introduction
1.1 Epidemiology of Stroke

1.1.1 Definition and Categories

Stroke is defined as “rapidly developing clinical signs of focal or global
disturbance of cerebral function lasting more than 24 hours (unless interrupted by
surgery or death) with no apparent non-vascular cause” (WHO MONICA Project
Principal Investigators 1988). There are three main categories of stroke:
ischaemic stroke (80% of cases), intracerebral haemorrhage (15%) and
subarachnoid haemorrhage (5%) (Warlow et al. 1996). Stroke most commonly
occurs in males in late middle to old age, usually in patients with hypertension,
atrial fibrillation, coronary artery disease, diabetes, hypercholesterolemia and
cigarette smoking (Benson and Sacco 2000).

1.1.2 Incidence

In the United States, approximately 750,000 subjects suffer a stroke each
year. The prevalence is 200-300 patients per 100,000 Americans (Williams et al.
1999); leaving 500,000 stroke survivors with disability annually (Heart Disease
and Stroke Statistics 2003). In the United Kingdom, about 130,000 people suffer
from stroke every year (Weir and Dennis 1997). In Mainland China, the
prevalence and incidence of stroke were 159.93 and 115.61 per 100,000 Chinese
(Li 1998). In Hong Kong, the stroke incidence was 100-200 per 100,000
inhabitants (Asian Acute Stroke Advisory Panel 2000). It was reported that a
total of 13,342 new cases of stroke occurred in Hong Kong which had a
population of 6.617 million in 1997 (Hospital Authority 1997).
1.1.3  Impact of Stroke on the Health Care System

Stroke is one of the leading causes of disability among the elderly population. The stroke-induced burden on the health care systems is enormous. It was estimated that there were 4.4 millions of stroke survivors in the United States. Forty percent had moderate functional impairments, and 15% to 30% had severe neurological deficits that led to impaired mobility and activities of daily living (American Heart Association 1999). The economic loss resulting from stroke approaches an estimated $51.2 billion annually (Heart Disease and Stroke Statistics 2003). The ratio of indirect to direct costs for stroke is approximately 1.3, which indicates that indirect costs resulting from compromised physical functioning and caregiver involvement are higher than the direct medical cost (Dobkin 1995). The high indirect cost of stroke makes the alleviation of disability in post-stroke patients a major interest of healthcare providers, researchers, and policy makers, and improving the independence of stroke survivors is the primary objective of post-stroke treatment.

1.2  Impairments of Motor Functions After Stroke

Lesions of central nervous system following stroke may result in impairments of cognitive, affective, sensory and motor functions. Motor impairments are common after stroke and some degree of recovery typically occurs in patients who survive. In a prospective study, Bonita and Beaglehole (1988) found that 88% of stroke patients had hemiparesis at stroke onset, with
equal numbers being graded mild, moderate or severe. However, by one month post-stroke, 26% had no impairment and 39% was graded as mild. At six months post-stroke 39% had no impairment and 36% had mild impairment. In other words, most recovery occurs relatively soon after stroke. Motor deficits observed after stroke include spasticity, muscle weakness and muscular incoordination (Bourbonnais et al. 1992).

1.2.1 Spasticity

The most widely accepted definition of spasticity to-date is a ‘motor disorder characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neurone syndrome’ (Lance 1980). Lance (1990) more recently reiterated this definition and added that ‘spasticity does not include impaired voluntary movement and abnormal posture’. The term spasticity is, however, widely used to describe the resistance to passive movement. There are increasingly more research findings showing that increased resistance to passive movement (hypertonus) is not solely due to hyperexcitability of stretch reflexes, but also to alternations in passive mechanical properties of muscles (Davies et al. 1996; Dietz et al. 1981; O’Dwyer et al. 1996).

It has been common in neurorehabilitation to consider spasticity as the major obstacle to improving motor function in patients with stroke (Bobath 1970, 1990). However, research has shown controversial results regarding the relationship between the level of spasticity and motor functions in patients with hemiplegia.
To elaborate, results of several recent studies showed that reducing spasticity could improve the functional capacities of hemiplegic patients (Hesse et al. 1994c, 1996; Hsu et al. 2003; Reiter et al. 1998). For example, several studies reported that injection of botulinum toxin type A into the spastic plantarflexors reduced the increased muscle tone and premature activity of these muscles during the terminal swing and early stance of a gait cycle, thus improving the gait velocity of patients with hemiparesis (Hesse et al. 1994c, 1996; Reiter et al. 1998). In contrast, low correlations between locomotor function and lower limb spasticity in ambulant individuals with chronic stroke have been found in many other studies (Bohannon et al. 1987; De Bujanda et al. 2003; Nadeau et al. 1997; Norton et al. 1975). Thus, the effect of velocity-dependent hyperactivity of stretch reflexes on strength and movement performance remains equivocal.

1.2.2 Muscle Weakness

Muscle weakness or paralysis is predominantly contralateral to the side of the lesion, although ipsilateral muscles are also affected (Colebatch & Gandevia 1989; Jones et al. 1989). Results of physiological and histochemical studies demonstrate that such weakness may be due to inadequate recruitment of motor units, loss of agonist motor units (McComas et al. 1973), reduced firing rates of agonist motor units (Rosenfalck and Andreassen 1980), atrophy of fast-contracting fibers (Dietz et al. 1986; Edstrom 1970), hypertrophy of slow-contracting fibers (Edstrom 1970), and prolonged contraction time of the affected muscles (McComas et al. 1973; Sahrmann and Norton 1977). Disuse atrophy (Duchateau and Hainaut 1987, 1990; Hachisuka et al. 1997; Rose and
Rothstein 1982) which is accompanied by adaptive changes in morphological and contractile properties of motor units and muscle fibers is also likely to contribute to the weakness observed following stroke (Bourbonnais and Vanden Noven 1989; Ng and Shepherd 2000).

Muscle weakness is now recognized as one of the major causes of motor impairments in patients with upper motor neuron lesion (Burke 1988; Carr et al. 1995; Landau 1980). Landau (1980) found that individuals complained of weakness and inability to perform tasks, not of having hyperexcitable knee jerks following stroke. Some clinical studies demonstrated that inadequate recruitment of agonist motor neurons, rather than the abnormally increased activity of antagonist motorneurons, is the major factor limiting voluntary movements in patients with stroke, but not spasticity (Fellows et al. 1994; Gowland et al. 1992).

1.2.3 Muscular Incoordination

Muscular incoordination is defined as the lack of ability to activate appropriate muscles for the execution of a purposeful movement in an accurate and effective manner (Bourbonnais et al. 1992). In stroke patients, it could result from a disruption of muscle activation patterns, including impaired activation of agonist and antagonist muscles (Hammond et al. 1988; Knutsson and Martensson 1980; Sahrmann and Norton 1977), impaired synergistic pattern of muscle activation (McLellan 1977), and synkineses which are involuntary movements that occur during the performance of voluntary movement (Brunnstrom 1970).
Some clinical studies demonstrated that muscular incoordination is one of the major factor limiting voluntary movements in patients with stroke (Hammond et al. 1988; Knutsson and Martensson 1980; Sahrmann and Norton 1977). For example, Sahrmann and Norton (1977) found that the primary impairment during rapid voluntary elbow flexion and extension was prolonged recruitment of agonist motor units and their delayed cessation at the end of movement.

1.2.4 Adaptation of Motor Performance

Disability following stroke may arise not only from the motor impairments caused by the neural lesion, such as weakness and loss of coordinated movement, but also from the tendency to altered motor behavior (Carr & Shepherd 1998; Shepherd 1992). Compensatory motor patterns or adaptive motor behaviors illustrate the ability of the remaining intact brain and its neural, musculo-skeletal and cardiovascular sub-systems to adapt. Shepherd (1992) suggested that compensatory or adaptive motor patterns seem to emerge as a result of several factors: the effects of lesion on movement control, the mechanical characteristics of the musculoskeletal linkage, and the environmental context in which the action is performed.

Adaptive motor behavior following stroke could also involve learning not to use the affected limbs. The concept of learned non-use has been proposed by Taub (1980) based on experiments with monkeys. Taub (1980) reported that, following somatosensory deafferentation of one upper limb, monkeys recovered function by using their unaffected arm. He suggested that since early attempts to
use the affected limb were unsuccessful, the monkey learned not to use it over time. Wolf and colleagues (1989) demonstrated that learned non-use is a factor contributing to poor function of the affected upper limb following stroke and head injury. Taub (1980) and colleagues (1993, 1994) further demonstrated in monkeys and in humans following stroke that restraint of the intact upper limb (i.e. prevention of the adaptive behavior) led to substantial improvement in function of the affected upper limb.

1.2.5 Locomotor Deficits in Patients with Stroke

Improved mobility, particularly in walking, is the goal of rehabilitation most often stated by patients with stroke (Bohannon et al. 1988; deWeerdt and Harrison 1985; Mumma 1986;). Locomotor ability is an important factor in determining the degree of physical ability after stroke (Perry et al. 1995) and has great impact on post-stroke functional outcome. Impairments from stroke could cause a compromised gait pattern, which could result in accidents, inability to care for oneself, and inability to work (Platz et al. 1994). In a study of 804 stroke survivors, Jorgensen et al. (1995) reported that at the time of admission to rehabilitation, 51% had no walking function and another 12% needed assistance to ambulate. After rehabilitation, 18% of the participants still had no walking ability, and 11% required assistance. Though the researchers reported that improvement in walking could not be expected beyond 11 weeks after stroke, retraining of walking remains a major goal in a rehabilitation program for persons with stroke.
Abnormal gait patterns had been observed in patients with stroke. Compared with able-bodied subjects, patients with stroke walked significantly slower, with decreased cadence, step and stride length, and increased duration of double-leg support (von Schroeder et al. 1995). These results are in agreement with the observations of other investigators (Bohannon 1987; Cozean et al. 1988; Dettman et al. 1987). Variations in the magnitude of these parameters are due to the wide variability of gait disorders after stroke (Knutsson and Richards 1979; Wall and Turnbull 1986), as reflected by the high standard deviations of these gait parameters.

The average gait velocity reported for subjects with stroke is lower than the values for able-bodied subjects. In studies reporting spatio-temporal characteristics, gait velocity ranged from 0.23 m/s (± SD 0.11 m/s) (Burdett et al. 1988) to 0.73 m/s (± SD 0.38 m/s) (von Schroeder et al. 1995). Consistent with the decrease in gait velocity, the values of cadence, step and stride length are lower in subjects with stroke than those for able-bodied subjects. Nakamura et al. (1988) reported the relationship between cadence and velocity to be linear up to a speed of about 0.33 m/s and a cadence of about 90 steps/min, with further gains primarily attributable to an increase in stride length.

There are 3 differences in the stance and swing phases between patients with stroke and able-bodied subjects. First, the stance phase of both affected and unaffected sides is longer in duration and occupies a greater proportion of the full gait cycle in subjects with stroke than in able-bodied walking at normal speed (Olney et al. 1991). Second, the stance phase is both longer and occupies a greater proportion of the gait cycle on the unaffected side than on the affected side
(Olney et al. 1991; von Schroeder et al. 1995). However, if the stroke data are compared to those of the able-bodied walking at similar speeds, the proportion of the stance phase on the unaffected side varies little from that of the able-bodied (von Schroeder et al. 1995), and is significantly shorter on the affected side. The third difference is that a greater proportion of the gait cycle in subjects with stroke is spent in double support than that of able-bodied walking at normal speeds (von Schroeder et al. 1995). However, when compared with able-bodied subjects walking at comparable speeds, the total double support of hemiparetic subjects is significantly lower (49% compared to 53%) than that of the able-bodied (Lehmann et al. 1987).

1.3 Long-Term Rehabilitation After Stroke

1.3.1 Long-Term Rehabilitation in Subjects with Chronic Stroke

In the past, many investigators believed that most recovery of function occurs in the first 3 months following stroke (Duncan et al. 1992; Kelly-Hayes et al. 1989; Wade et al. 1985). However, a growing body of evidence demonstrated that with appropriate training, individuals at 6 months or more after stroke can still improve their performance of functional tasks (Dean and Shepherd 1997; Lehmann et al. 1975; Rodriguez et al. 1996; Tangeman et al 1990; Taub et al. 1993; Werner and Kessler 1996; Yekutiel and Guttman 1993), and their aerobic capacity (Potempa et al. 1995). Despite this evidence, rehabilitation programs appear to be available only to patients during their stay in the hospital or
at out-patients units in Hong Kong. Extended therapy in terms of home-based programs are far from being developed.

The absence of ongoing rehabilitation programs after discharge from acute hospitals and out-patients units may be a major oversight of the society in Hong Kong, an oversight that could exacerbate disability and handicap. Many individuals with stroke are significantly disabled and handicapped upon hospital discharge (Dean and Mackey 1992; Harwood et al. 1997; Hill et al. 1997). A recent study (Hill et al. 1997) showed that only 7% of stroke patients discharged from rehabilitation met all 4 criteria defined for independent community ambulation. These criteria included: independent gait (Functional Independence Measure in locomotion > 5), ability to negotiate uneven terrain and kerb (Functional Ambulation Classification = 6), gait velocity ≥ 48 m/min (speed necessary to cross an average Melbourne intersection controlled by traffic lights), and gait endurance > 500 m (approximate distance of two suburban street blocks).

Previous studies have demonstrated that there is deterioration in the functional status of stroke survivors during the first few years (Davidoff et al. 1991; Dombovy et al. 1987). Several investigators have reported that stroke patients did not maintain their functional gains (Engardt 1994; Lindmark and Hamrin 1995; Richards et al. 1993), and had low levels of physical activities after rehabilitation stopped (Corr and Bayer 1992).

It appears that the persistent disability and handicap experienced by many individuals after stroke arise not only from the impairments resulting from stroke, but also from the deleterious neural, muscular, psychological, and cardiovascular adaptations that accompany disuse and use of maladaptive behavior (Hachisuka et
al. 1997; Ryan et al. 2000). It is essential for rehabilitation professionals to address the long-term needs of stroke survivors. However, few studies have examined the effectiveness of long-term rehabilitation programs for stroke survivors. Most of the studies that did involve highly selected patient samples and the use of expensive specialized training equipment, therefore limiting the applicability of their findings. As it will emerge below, home rehabilitation programs are one way to provide ongoing and cost effective treatment for patients with stroke to maintain and/or improve their performance.

1.3.2 Home-Based Stroke Rehabilitation Programs

Reducing the cost of health care has been increasingly important in the advent of rising costs, and the treatment of stroke is no exception. The high morbidity associated with stroke contributes to the economic burden of this condition worldwide (Adams et al. 1994; Bergman et al. 1995; Grieve et al. 2001). Home-based rehabilitation for neurological patients has been receiving increasing interest in recent years, because they not only provide the opportunity for rehabilitation after hospital discharge, but are also cost effective and offer better potential for community and family integration (Freeman 1997; Pace et al. 1999; Stonnington 1997).

Previous reports have described a variety of home-based programs for patients with stroke. Most of them were targeted at acute or subacute stroke survivors who were 7 to 90 days after stroke onset, and who had just completed inpatient rehabilitation (Anderson et al. 2000a, 2000b; Baskett et al. 1999; Ducan et al. 2003; Lijungberg et al. 2003; Mayo et al. 2000; Ozdemir et al. 2001;
Roderick et al. 2001; Teng et al. 2003; Widen Holmqvist et al. 1998). The development of these home-based programs was based on the concept of supported discharge that commences as soon as the patient is medically stable to leave the hospital, and comprises home-based rehabilitation and medical services. Evidence for the effectiveness of home-based stroke rehabilitation is available from several randomized controlled trials carried out over the past decade (Anderson et al. 2000b; Baskett et al. 1999; Ducan et al. 2003; Gladman et al. 1994; Mayo et al. 2000; Roderick et al. 2001; Rodgers et al. 1997; Rudd et al. 1997; Teng et al. 2003; Young and Forster 1992; Widen Holmqvist et al. 1998). These trials were carried out in patients with stroke who received either conventional rehabilitation program immediately upon discharge (Baskett et al. 1999; Duncan et al. 2003; Gladman et al. 1994; Gilbertson et al. 2000; Roderick et al. 2001; Young and Forster 1992), or early supported discharge from hospital with home rehabilitation (Anderson et al. 2000b; Mayo et al. 2000; Rodgers et al. 1997; Rudd et al. 1997; Teng et al. 2003; Widen Holmqvist et al. 1998). All have concluded that early supported discharge reduced the length of hospital stay, and home-based rehabilitation after stroke is feasible, acceptable to patients, and as effective as or not less beneficial than routine inpatient care and rehabilitation, without comprising patient safety or functional outcomes. However, such home programs or supported discharge services varied from an “as-needed” basis to routine care, and from primarily rehabilitation to nursing or medical interventions provided in a variety of settings, including inpatient, day-hospitals, outpatient and home environment. The choice of activities and setting depended on the level of the care required and patients’ preferences.
For patients with sub-acute stroke, a recent Cochrane Database review (Outpatient Service Trialists 2004) assessed the effects of rehabilitation services targeted at stroke patients resident in their community or home within 1 year of stroke onset or upon discharge from hospital. The authors identified a heterogeneous group of 14 properly randomized and controlled trials that compared the effectiveness of a community or home-based program with that of a conventional program or no care. The results indicated that community or home-based rehabilitation services appear to improve patients’ independence in their activities of daily living. As the evidence is derived from a review of heterogeneous interventions, the authors suggested that further exploration of intervention strategies is needed.

There are only few home-based rehabilitation programs specially designed for individuals with more than 1 year after stroke onset (Green et al. 2002; Monger et al. 2002; Rodriguez et al. 1996; Wade et al. 1992). Unlike discharge supported services for patients with acute stroke, the efficacy of home-based rehabilitation program for chronic stroke survivors has been controversial. Two uncontrolled clinical studies utilizing pre-test and post-test designs (Monger et al. 2002; Rodriguez et al. 1996) demonstrate that home-based rehabilitation program may enhance the motor recovery of stroke survivors. Rodriguez and colleagues (1996) investigated the efficacy of a home program for gait training in 18 patients at least 1 year after stroke. Home-based training was individualized with the goal of normalizing movement patterns and minimizing compensatory strategies in walking. Total physical therapy contact time averaged 35 (range, 9.5 to 62.5) hours, and training period covered a mean of 22 (range, 10 to 65) months.
Results showed that such individualized home-based training can significantly improve gait performance in terms of Winconsin Gait Scale and the subjective perception of well-being in terms of Health Status Questionnaire. In another uncontrolled clinical trial, Monger and colleagues (2002) investigated the efficacy of a 3-week task-specific home-based exercise protocol for improving sit-to-stand, with additional exercises to strengthen lower limb extensor muscles in 6 patients more than one year after stroke. The training protocol was supervised by a physical therapist who visited the subjects in their homes 3 times weekly, and subjects were asked to practise on their own each day for approximately 20 minutes. Results demonstrated that a home-based task-specific exercises and training protocol for sit-to-stand can improve the performance of sit-to-stand and increase walking speed in patients more than one year after stroke (Monger et al. 2002). However, there were some inherent limitations in the two uncontrolled clinical trials mentioned above (Monger et al. 2002; Rodriguez et al. 1996), such as the absence of a control group, small sample size and long-term effects of the intervention not being addressed. More robust studies such as randomized controlled trials were needed to validate the efficacy of these interventions.

In contrast to the positive findings mentioned above, two randomized controlled trials (Green et al. 2002; Wade et al. 1992) demonstrated that their home-based rehabilitation program did not enhance the motor recovery of stroke survivors. Green and associates (2002) randomized 170 patients one year after stroke to 2 groups. The treatment group received a community-based physiotherapy program carried out at home or in outpatient rehabilitation centers, and the control group received no treatment. The maximum contact period of
the program was 13 weeks with a minimum of 3 contacts per patient for the
treatment group. Their results showed that community or home-based
physiotherapy treatment led to significant, but clinically small, improvements in
mobility and gait speed that were not sustained after the treatment ended. In a
randomized, crossover clinical trial, Wade et al. (1992) randomized 94 patients
who were more than one year after stroke to 2 groups. One group received
individualized home-based treatment supervised by physiotherapists immediately
upon entry into the trial, whilst the other group received the same treatment after a
delay of 3 months. At 3 months, the "early" treatment group showed an
improvement, whereas the "delayed" treatment group had declined in their gait
speed. Between 3 and 6 months, the "delayed" treatment group showed
improvement and the previously "early" treatment group declined in their gait
speed. Wade and colleagues (1992) thus concluded that the increase in walking
speed was transient and small (8%) and did not improve patients' mobility.
However, these 2 studies suffered from some methodological problems that limit
the generalizability and validity of their results. None of them adequately
described the randomization procedure. In both studies, treatments were not
standardized in the intervention groups as a "problem-oriented" approach based
on the decision of the physiotherapist-in-charge was adopted. Thus, subjects in
the intervention group received unequal therapy times and huge variations in the
type, intensity and frequency of treatment. Besides, the outcome measures in
both studies were based on more global functions (e.g. Barthel index, Rivermead
mobility index), and more specific impairments were not measured.
Furthermore, the evaluations were not blinded, allowing the possibility of
investigator bias. Therefore, the effectiveness of a home-based rehabilitation program for subjects with stroke remains unclear, and no study so far has examined the optimal strategy for home-based rehabilitation in chronic stroke survivors.

1.4 Physiotherapeutic Treatment for Promoting Motor Recovery After Stroke

Studies have shown that comprehensive stroke rehabilitation programs can reduce short- and long-term disability (Indredavik et al. 1997; Stroke Unit Trialists' Collaboration 1997). Unfortunately, an optimal rehabilitative strategy still cannot be identified, and our understanding of specifically what therapy approach best promotes recovery remains limited.

1.4.1 Movement Rehabilitation After Stroke

To address the motor impairments which occur after stroke, several approaches to stroke rehabilitation have been developed in the last century. Based on different underlying assumptions, these approaches include proprioceptive neuromuscular facilitation (PNF) by Knott and Voss (1968), Brunnstrom approach by Brunnstrom (1970), and neurodevelopmental (NDT) approach by Bobath (1970). The PNF and Brunnstrom approaches involve the use of nonaffected or less paretic muscle groups to generate irradiation effects in the more paretic synergistic or contralateral muscles groups. The Bobath concept emphasizes the reduction of enhanced muscle tone in the affected limb.
Active movement of the affected limb is discouraged, as any exertion during movement could increase co-contraction of the spastic muscles and reduce coordination, which could lead to a reduction in the ability to perform functional activities (Bobath 1978). However, a number of studies have conclusively demonstrated that these traditional physiotherapeutic approaches do not differ with respect to their influence on the recovery of motor function in stroke patients (Ashburn 1993; Ernst 1990; Wagenaar et al. 1991).

Nowadays, the dominant approach to stroke rehabilitation in most countries is based on the NDT approach (Carr et al. 1994; Lennon et al. 2001; Nilsson & Nordholm 1992). However, the theoretical validity and practical effectiveness of this approach have been questioned (Gordon 1987), and there is little experimental evidence to support this approach. For example, Palisano (1991) failed to find conclusive evidence in support of NDT when he attempted to review the research on its effectiveness. Lincoln et al. (1999) found no significant differences in the time course of recovery or in the functional outcome, when they investigated the influence of an enhanced physiotherapeutic program derived from the Bobath concept on arm function and the degree of independence in activities of daily living in 282 patients with stroke. Recently, there have been challenges to the NDT approach which encourages active training of the affected limb as detailed below (Carr and Shepherd 1982; Butefisch et al. 1995; Sunderland et al. 1992; Taub et al. 1993).

Although there is evidence that rehabilitation after stroke can improve outcome (Ernst 1990) and reduce long-term disability (Indredavik et al 1997; Stroke Unit Trialists' Collaboration 1997), there are surprisingly few controlled
studies to compare the efficacy of different strategies. Langhammer and Stanghelle (2000) compared the traditional Bobath approach to the motor relearning programme for patients with acute stroke. The motor relearning programme is a task-oriented approach that encourages patients to be active learners and practice the skills of functional movements in different environmental context with maximum number of repetitions (Carr and Shepherd 1982). Langhammer and Stanghelle (2000) found that patients treated with the motor relearning program had better motor outcomes, more independent in the activities of daily living and shorter duration of hospitalization when compared with those treated according to the Bobath approach. Hesse and colleagues (1994) investigated the effects of a 4-week Bobath therapy program on gait performance in patients with chronic stroke. They found that there were minimal changes in patients’ functional performance assessed by maximal walking speed, walking endurance and stair climbing ability. Hesse and colleagues (1994) suggested that the lack of improvement in function may be due to the fact that Bobath approach emphasized static exercises during therapy, and patients were encouraged not to walk by themselves for fear of stereotyped abnormal synergies. Butefisch and colleagues (1995) also found that repetitive training of hand and finger movements was effective in improving hand function, while there was no improvement in hand function after Bobath therapy.

One active training approach, "constraint-induced therapy", was developed by Taub et al. (1993) to force stroke patients to use their affected extremities in natural motor activities (Taub et al. 1993). Taub et al. (1994) developed the theory of "learned non-use" to explain long lasting movement deficits in
deafferented monkeys, which could be overcome if animals were forced to use the affected arm by restraining their unimpaired limb. These concepts have been successfully introduced to the clinic in the rehabilitation of limb movements after stroke, by restraint of the less impaired limb accompanied by a programme of exercise for the affected limb (Kunkel et al. 1999; Miltner et al. 1999; Taub et al. 1993, 1999). Improved function after constraint-induced therapy has been attributed to altered patterns of movement-related cortical activities (Kopp et al. 1999; Liepert et al. 1998, 2000).

Physiotherapists adopt multiple interventions in their attempts to improve the motor recovery of patients following stroke, but an optimal form of physiotherapy strategy remains elusive (Ashburn et al. 1993; Hummelsheim 1999). However, having reviewed clinical trials of various therapeutic interventions for patients with stroke, Duncan (1997) found that interventions that have been shown to be effective involved active participation of patients, repetitive training, maximal practice, and strength training with resistance.

1.4.2 Transectaneous Electrical Nerve Stimulation (TENS) in Stroke Rehabilitation

1.4.2.1 Definitions and Categories

For over 3 decades, transectaneous electrical nerve stimulation (TENS), a type of peripheral nerve stimulation, has been used successfully for pain relief particularly that of musculoskeletal origin (Milne et al. 2001; Walsh 1997a, 1997b). TENS is a safe and well-established electrical modality that can be delivered over peripheral nerves, trigger points, acupuncture points or
dermatomes related to the painful segments, via cutaneous electrodes glued to the skin. Two different forms of TENS stimulation are commonly used in clinical situations:

(i) Conventional TENS at low intensity (2 to 3 times the sensory threshold) and high frequency (60 to 100 Hz).

(ii) Acupuncture-like TENS at high intensity (more than 3 times the sensory threshold) and low frequency (2 to 4 Hz).

Levin and Hui-Chan (1993) investigated the physiological mechanisms underlying the pain relief obtained by conventional TENS and acupuncture-like TENS. Electrical stimulation was delivered to the median nerve at the wrist of 17 healthy subjects and conduction velocities of the afferent fibers per type of stimulation were recorded over the median nerve in the cubital fossa. These investigators found that both types of TENS activated similar peripheral afferent fibers, predominantly in the A-beta range.

1.4.2.2 TENS and Motor Recovery in Subjects with Stroke

Afferent stimulation has been used to improve motor function in patients with stroke. In theory, increased inflow of signals from sensory and motor fibers could enhance the brain's ability to recover from injuries, which could partly explain the beneficial effects of this form of treatment (Pascual-Leone and Torres 1993). As aforementioned, selective stimulation of large afferent fibers can be achieved with transcutaneous electrical stimulation (TENS) (Levin and Hui-Chan 1993). Recent research shows that TENS can reduce excessive spasticity (hyperreflexia) (Afier 1984; Levin and Hui-Chan 1992; Seib et al. 1994;
Tekeoolu et al. 1998), decrease passive resistive torque during passive mobilization (Potisk et al. 1995), increase the strength of paralyzed muscle (Levin and Hui-Chan 1992), and improve the performance in activities of daily living (Tekeoolu et al. 1998) in subjects with chronic stroke. The effect is usually short-lasting from minutes to a few hours. However, Alfieri (1984) noted not only an immediate but also a permanent reduction of spasticity for 4 to 16 weeks after a number of treatment sessions. Regretfully, the investigator had not included a control group in his study, and they varied the number of treatment sessions for individual patients according to the initial level of tonic reflex activity and the antispastic effect of the electrical stimulation.

Two randomized controlled trials suggested that TENS is an effective adjunct in recovery of motor functions and activities of daily living in chronic hemiplegic patients (Levin and Hui-Chan 1992; Tekeoolu et al. 1998). Levin and Hui-Chan (1992) studied the effects of 3 weeks of high-frequency (99Hz) TENS applied over the peroneal nerve in 13 subjects with chronic stroke. In contrast to placebo stimulation which produced no significant effects in the control group, they found that repeated applications of TENS over 3 weeks decreased clinical spasticity, stretch reflexes in the spastic ankle plantarflexors and EMG co-contraction ratios. The treatment also increased vibratory inhibition of the soleus H reflex and voluntary ankle dorsiflexing force up to 820%. Tekeoolu et al. (1998) studied the effect of 8 weeks of high-frequency (100 Hz) TENS on activities of daily living in a group of 60 hemiparetic subjects who were 30 to 240 days following stroke. All subjects had mild to moderate motor deficits from stroke. In the group receiving TENS, a significant decrease in the spasticity of the leg and a
significant improvement in Barthel Index scores were found, when compared with those of the placebo TENS group. Although the results of these 2 randomized trials are encouraging, neither study did follow-up beyond the end of treatment, so that the long-term effects of the intervention remained unclear. In the study of Levin and Hui-Chan (1992), the sample size was small, which could have limited the generalizability and success of randomization. In the study of Tekeoolu and associates (1998), the combination of acute and chronic survivors added an additional confounding variable of spontaneous recovery.

Exploratory studies utilizing pre-test and post-test designs demonstrated that TENS over acupuncture point or sural nerve may also enhance the motor functions in patients with stroke (Potisk et al. 1995; Sonde et al. 2000). Potisk and colleagues (1995) reported the effect of applying high-frequency (100 Hz) TENS for 20 minutes over the sural nerve of the affected limb in 20 patients with hemiplegia. These authors found a mild but statistically significant decrease in the resistive torques at all frequencies of passive sinusoidal ankle movements, accompanied by a decrease in the reflex EMG activity of ankle muscles. The effect of TENS persisted up to 45 minutes. In a study with 16 hemiparetic subjects who had a stroke at least 5 months earlier, Sonde and colleagues (2000) found that stimulation of acupuncture point ST 36 with high-frequency (100 HZ) TENS for 30 minutes daily over a period of 3 months could reduce the spasticity of knee extensors and ankle plantarflexors in patients with stroke. Balogun et al. (1998) suggested that electrical stimulation of acupuncture points with surface electrodes could probably elicit the same physiological and therapeutic effects as those produced by acupuncture and electro-needling techniques. However, the
result of these 2 studies provided only preliminary encouraging results on the
efficacy of the intervention protocol, because of the absence of a placebo or
control group and the small sample size. Double-blinded or single-blinded
randomized controlled trials with larger patient sample size to ensure adequate
statistical power would be needed to provide more stringent and vigorous
evidence for the efficacy of TENS in patients with chronic stroke.

In summary, the majority of studies showing positive effects on spasticity had
used high frequency electrical stimulation. High frequency TENS may also be a
valuable modality in improving motor functions in subjects with chronic stroke.
However, the methodological problems of most studies have limited the
generalizability and validity of their results. There are large variations in the
skin area being stimulated, as well as in the treatment type, intensity and duration
which made comparisons among the different studies difficult. Therefore, the
effectiveness of TENS in enhancing motor recovery in patients with stroke
remains to be clarified, and no study so far has examined the optimal dosage of
TENS application in chronic stroke survivors, in terms of frequency and duration
of treatment period that could produce carry-over effects.

1.4.3 Task-Related Training (TRT) in Stroke Rehabilitation

1.4.3.1 Task-Related Training (TRT)

It has been suggested that task specificity is central to skill acquisition
(Gentile 1987), muscle strengthening (Jones et al. 1989; Sale 1988), and postural
control (Bouisset and Zattara 1987), and is thus an important consideration when
designing an effective and appropriate physical rehabilitation program (Carr and
Shepherd 1987, 1990, 1998). In a task-related training (TRT) program, patient is required to work in a task-specific activity or a self-directed, goal-driven activity, while being put in a position in which the weakened muscle would normally function. Assessment and training of functional ability should not be separated from those of the particular task. To improve walking, TRT involves strategies to increase muscle strength, coordination, and weight-bearing capacity of the affected lower limb, and to maintain a flexible musculo-skeletal system with opportunity for intensive practice (Carr and Shepherd 1998).

1.4.3.2 Task-Related Training (TRT) and Motor Recovery in Subjects with Stroke

The TRT is gaining theoretical (Carr and Shepherd 1987, 1998, 2000; Gordon 1987; Weinstein and Knecht 1990) and experimental support as a means of improving walking after stroke (Ada et al. 2003; Dean et al. 2000; Hesse et al. 1994, 1995, 1997; Macko et al. 1997; Malouin et al. 1992; Richards et al. 1993; Visintin et al. 1998). Several studies have provided evidence for the efficacy of task-related training in walking, although few have rigorously controlled experimental designs. In a randomized, placebo-controlled clinical trial, Ada et al. (2003) examined the effects of a treadmill and overground walking program on the ambulatory ability of 29 chronic stroke patients. The experimental group participated in a 30-minute treadmill and overground walking program 3 times a week for 4 weeks. The control group received a “placebo” program consisting of low-intensity home exercises and regular telephone contacts. The 4-week experimental program significantly increased walking speed and walking capacity,
but did not decrease the handicap measured by Sickness Impact Profile
(SA-SIP30) when compared with that of the placebo program. Nevertheless, the
gains were largely maintained 3 months after cessation of training. In a
randomized pilot trial, Richards and colleagues (1993) examined the effects of
early, intensive, gait-focused physical therapy on the ambulatory ability of acute
stroke patients. The experimental group received early, intensive gait-focused
therapy involving strengthening exercises and treadmill walking. A second
group received early, intensive conventional physical therapy. A third group
received conventional physical therapy similar to the second group but
commenced later and was not as intense. At 6 weeks, the group receiving
intensive gait-focused therapy walked significantly faster than the other two
groups receiving conventional physical therapy, whose walking velocities were
similar to each other. These findings suggest that it was the specific gait-focused
activity and not the timing or intensity of the intervention which was responsible
for the faster recovery of locomotor function in the experimental group. As the
study was conducted on patients with acute stroke, the efficacy of such program
on patients with chronic stroke were still unclear.

It has been suggested that modification of the task may be necessary if a
patient’s motor impairments preclude effective practice of the whole task, so that
he/she can practice the task in the presence of relatively poor muscle function
without using adaptive movements (Carr and Shepherd 1989). Several studies
suggest that partial body-weight-support treadmill training with a harness is useful
in improving gait following stroke (Hesse et al. 1994a, 1994b, 1997; Malouin et
al. 1992; Visintin & Barbeau 1989; Waagfjord et al. 1990). This technique
allows stroke patients with poor balance or motor control to practice walking repetitively at an early stage without using any adaptive or compensatory movements. For example, Hesse and colleagues (1994a) found that individuals, who had received regular physiotherapy based on the Bobath approach for at least 3 weeks without marked improvement in gait, showed significant improvements in gait velocity, cadence and stride length after 25 sessions of partial body-weight-support treadmill training.

Given the contribution of muscle weakness to the disability of stroke subjects, specific strengthening exercises are a critical component of task-related training after stroke (Dean et al. 2000; Malouin et al. 1992; Monger et al. 2002; Richards et al. 1993). In a randomized controlled pilot trial with 12 chronic stroke subjects, Dean et al. (2000) found that a 4-week TRT in walking that included task-related closed-chained lower limb strengthening exercises and gait re-education, improved locomotor functions in chronic stroke subjects. However, the findings of this study need to be interpreted with caution, as the results of only 9 of 12 eligible patients were reported and a selection bias may exist. Nugent et al. (1994) reported that the number of repetitions of closed-chained lower limb extensor strengthening exercises was correlated with an improvement in gait outcome in 54 patients with acute stroke. The question of whether a dose-response relationship existed in patients with chronic stroke was unanswered.

There is evidence that TRT following stroke is useful to improve the performance of functional movements other than walking. In a randomized controlled trial conducted in 20 subjects with chronic stroke, Dean and Shepherd
(1997) demonstrated that a TRT program designed to improve sitting balance control was effective in increasing speed of reaching, distance reached by the affected hand, and performance of sit-to-stand when compared with those of the control group receiving cognitive-manipulative tasks using the unaffected hand. In uncontrolled trials of patients with chronic stroke, TRT with or without specific strengthening exercises has been found to improve hand functions (Butefisch et al. 1995), performance of sit-to stand (Monger et al. 2002), and visual neglect with associated improvements in function in subjects with stroke (Rode et al. 2003).

In summary, the compendium of evidence from randomized controlled trials, uncontrolled clinical trials, single- and multiple-case studies consistently suggests that TRT is beneficial for regaining motor functions in subjects with chronic stroke. However, vigorous research studies are sparse and often involve only small patient sample size. The findings of these studies must be interpreted critically in light of such methodological limitations. Future research of double-blinded or single-blinded randomized controlled trials can provide more stringent and vigorous evidence for the efficacy of TRT in enhancing motor recovery in chronic stroke survivors.

1.5 Possible Mechanisms Mediating Recovery of Functions After Stroke

Rehabilitation which aims to reduce disability assumes that there is capacity within the nervous system to recover its function. Recovery of function following stroke has been demonstrated, yet specific underlying mechanisms are not well understood, but can be broadly classified into: resolution of pathology,
neuroplasticity and behavioral compensation.

1.5.1 Resolution of pathology

Early recovery during the first few days following stroke is likely due to factors such as resorption of edema and necrotic tissue, or opening of collateral circulatory channels for circulation to the damaged region, opening of latent synapses and synaptic reorganization (Lee & van Donkelaar 1995). Resolution of diachisis is also likely to play a role in functional recovery (Feeney & Baron 1986; Seitz et al. 1999). Diachisis is the process that function of remote cortical tissue is temporarily suppressed after focal cortical injury. It is found to persist for a long period of time after cortical injury, that is, after significant recovery has occurred (Infeld et al. 1995).

1.5.2 Neuroplasticity

1.5.2.1 Basic Mechanisms of Neuroplasticity

Recovery that occurs later probably reflects some plastic changes within the nervous system, with some areas of the brain being able to take on new functions previously performed by the damaged region before injury (Johansson 2000; Lee & van Donkelaar 1995). Motor plasticity is possible as the motor system is organized as a distributed network, and there is substantial functional overlap between different motor areas which are functionally specialized. There are 4 potential mechanisms which may cause such plastic changes: (1) unmasking - which implies opening up, possibly by release from tonic inhibition, of pathways
which exist anatomically but which have been functionally inactive prior to injury (Jacobs and Donoghue 1991); (2) collateral sprouting of fibers from surviving neurons with formation of new synapses (Ng et al. 1988; Stroemer et al. 1995); (3) redundancy in the CNS circuitry - a concept which suggests that there are multiple parallel pathways subserving similar functions and that an alternative pathway may take over the damaged one (Davidoff 1990; Lee & van Donkelaar 1995), and (4) altered synaptic strength in the existing local networks (Hagemann et al. 1998; Ivanco et al. 2000). However, details of the relative contributions of the various mechanisms to recovery of function following stroke await further elucidation.

There is a growing body of animal and human research demonstrating that there are a number of processes that may contribute to the recovery of motor functions following stroke. These research studies include: (1) reorganization of representation and function in the sensory and motor cortices following localized lesions; (2) use of alternate descending pathways on the lesioned side; and (3) use of uncrossed motor pathways and ipsilateral motor centers. Besides, there is some evidence suggesting that sensory and motor experiences after cortical lesion will influence the reorganization either positively or negatively (Held 1987; Nudo et al. 1996b). Lee and van Donkelaar (1995) also suggested that skill acquisition may undergo similar neurophysiological changes that accompany recovery of function after stroke. The challenge for neurorehabilitation experts is to take advantage of the potential of the nervous system for plastic changes, to shape functional reorganization in order to maximize recovery.
1.5.2.2 Reorganization of Representation and Function in Sensory and Motor Cortices

A growing body of animal and human research showed that there are considerable potentials for reorganization of representation and function in the sensory and motor cortices following localized lesions. Jenkins and Merzenich (1987) delineated the changes in cortical sensory maps in monkeys following ablation of an area of the sensory cortex representing one finger. Skin surfaces formerly represented at the site of lesion came to be represented in the surrounding intact cortical tissues. Doetsch et al. (1990) also found that adjacent areas of cortex began responding to sensory stimulation of the affected digit after lesions to the representation of a single digit in the somatosensory cortex of monkeys. Castro-Alamancos and colleagues (1992) demonstrated similar functional reorganization of the motor cortex following localized lesions in rats. Rats were trained to avoid electric shocks by pressing a bar with their forelimb. The forelimb area of the motor cortex was then excised. Following excision, there was deterioration in performance, but with further training, some rats reacquired the ability to use their forelimb. In these animals, there were alternations in the hindlimb area of the motor cortex. Interestingly, if a second lesion to the hindlimb motor cortex was made, then the original deficit reappeared. These findings suggest that functional recovery had occurred as a result of transfer of forelimb control to the hindlimb area. Nudo and Milliken (1996) made small lesions of the digit representation in monkey’s motor cortex. After 3-4 months of spontaneous recovery, intracortical microstimulation of
primary motor cortex revealed that stimulation of areas adjacent to the lesion, which had previously evoked elbow or shoulder movements, now produced movements of digits. A second study demonstrated that this local remapping could be enhanced by rehabilitative training (Nudo et al. 1996b).

Alternations in functional cortical representation have been demonstrated in individuals following stroke. In a positron emission tomography (PET) study, Weiller et al. (1993) found a ventral extension of activation during hand movement into the face area of motor cortex in some patients after capsular stroke. In a fMRI study, Pineiro and colleagues (2001) found a posterior shift in the location of motor cortical activity in patients with stroke, which could reflect increased recruitment of corticospinal projections from somatosensory areas.

1.5.2.3 Use of Alternate Descending Pathways on the Lesioned Side

Use of alternate descending pathways on the lesioned side is another possible mechanism underlying recovery of functions following stroke. This mechanism is feasible because of the existence of functional overlap within the sensorimotor network. For example, although the majority of corticospinal projections arise from the primary motor cortex, there are also direct projections from premotor and supplementary motor areas (SMA).

Previous studies provided evidence that the SMA of the cortex may take on new functions following damage to the primary motor cortex. For example, Aizawa and colleagues (1991) measured neuronal activities in the SMA of a monkey during an overlearned keypress task before and after lesion to the primary
motor cortex. Task-related activities in the SMA were found during the learning period but they disappeared after extensive training. However, the SMA became active again during task performance after the brain lesion. This finding demonstrates that there would be potentials for motor commands to reach the spinal cord from the SMA via alternate pathways, if the primary motor cortex and its descending projections were extensively damaged (Lee & van Donkelaar 1995). This is consistent with the finding from some brain imaging studies of differentially increased activation in the SMA in stroke patients (Cramer et al. 1997; Weiller et al. 1993). Altered SMA activities could reflect increased recruitment of non-primary motor corticospinal projections, or the need to “relearn” previously automatic or effortless movements after damage. In a PET study of stroke patients, Seitz et al. (1998) showed that movement of the recovered hand activated dorsolateral premotor cortex and SMA in both hemispheres, but not the primary sensorimotor cortex in either hemisphere. There have also been reports of increased activities in the prefrontal cortex (Marshall et al. 2000) and posterior parietal cortex (Nelles et al. 1999) associated with recovered movements in patients with stroke.

1.5.2.4 Use of Uncrossed Motor Pathways and Ipsilateral Motor Centres

Uncrossed motor pathways and ipsilateral motor centers may also play an important role in the recovery of function following stroke. Nathan and Smith (1973) found that 70-90% of the pyramidal fibers decussate to form the lateral corticospinal tract, and 10-30% of them remain uncrossed to form the ventral
corticospinal tract. The uncrossed corticospinal tract fibers play a role in controlling movements of the body on the same side as that of the cerebral hemisphere from which they originate (Davidoff 1990). There is thus potential for these uncrossed pathways and the ipsilateral hemisphere to take over new functions after unilateral lesions (Lee & van Donkelaar 1995).

There is some evidence to support the role of the ipsilateral hemisphere in the recovery of function following stroke. In a small group of patients having a second stroke who had recovered movement of the initially affected limb, Fisher (1992) found that a second stroke in the previously undamaged hemisphere resulted not only in new hemiparesis on the contralateral side, but also a reappearance of the original motor deficits in the limb ipsilateral to the second stroke. This suggests that the original recovery was mediated by the initially undamaged hemisphere. Other functional imaging studies have shown increased activation of the ipsilateral motor areas during movement of the affected limb after stroke (Chollet et al. 1991; Turton et al. 1996). For example, Chollet et al. (1991) found that there were significant increases in regional blood flow in both contralateral and ipsilateral primary sensorimotor cortices and in both cerebellar hemispheres, when subjects with stroke moved the fingers of their affected hand. Turton et al. (1996) further reported increased incidence of ipsilateral motor evoked potentials to primary motor cortex stimulation after stroke.

1.5.2.5 Factors Affecting Neuroplasticity

Results from both animal and human studies suggest that behavioral
experience after injury is a major factor affecting neuroplasticity during recovery of motor function after brain injury. It could influence the reorganization processes either positively or negatively. For example, following brain lesions, rats placed in an enriched environment in the presence of other animals, exercise equipment and accessible food, recovered function better than those placed in an impoverished environment (Held 1987). In another animal study by Nudo et al. (1996b), 4 squirrel monkeys were trained in skilled hand movements required to retrieve food pellets from small wells. After completion of the training, motor cortical maps were derived by intracortical microstimulation techniques. A focal ischemic infarct was induced in the hand area of the motor cortex. An intensive behavioral retraining protocol identical to that preceding infarct began within 5 days of surgery. Mapping of the motor cortex was repeated after 3-4 weeks of retraining. Results indicated that retraining after infarct was able to prevent loss of the hand territory in the cortical area adjacent to the infarct, which would have occurred if no training was given (Nudo & Milliken 1996). In addition, cortical hand representations had invaded adjacent areas formerly representing elbow and shoulders, and such cortical expansion was matched with the improvement of hand function. Results of these studies showed that cortical reorganization with beneficial consequences can be induced by training after experimentally induced cortical infarct. This is an important area of stroke research for promoting optimal recovery through rehabilitation.

1.5.3 Behavioral Compensation

Motor recovery after cortical injury could have occurred through behavioral
compensation, rather than via "true recovery" or restitution of "normal" motor strategies (Finger and Stein 1982; Friel and Nudo 1998; Stein 1998; Whishaw 2000). For example, by analyzing the kinematic data from arm and trunk of 9 stroke patients, Cirstea and Levin (2000) found that all subjects, even those with severe motor impairments, could finish arm pointing tasks in a sitting position. However, some of the stroke patients tended to compensate for their poor distal arm muscle control by increasing their trunk movement to finish the task. The degree of adoption of compensatory strategies thus appeared related to the degree of motor impairment. It has also been reported that rats with unilateral sensorimotor cortex lesions employed postural compensation to retrieve food, rather than establishing normal motor strategies (Whishaw 2000).

1.6 Rationale and Objectives of the Study

1.6.1 Rationale and Hypotheses

Although TENS has been used in stroke rehabilitation, only 7 clinical trials of high frequency TENS in hemiplegic patients were reported between 1966 and 2003 (Afiieri 1984; Levin and Hui-Chan 1992; Potisk et al. 1995; Seib et al. 1994; Sonde et al. 2000; Tekeoolu et al. 1998; Yan and Hui-Chan 2002). Among these, only 2 single-blinded randomized clinical trials with placebo groups (Levin and Hui-Chan 1992; Yan and Hui-Chan 2002) were found. In the study of Levin and Hui-Chan (1992), the outcome measures addressed motor impairments only, and follow-up data beyond the completion of treatment were not pursued. Although a concerted effort was made to address the problems of prior randomized clinical trials, Yan and Hui-Chan (2002) examined the efficacy of TENS in subjects with
acute stroke only, and the effects of intervention in subjects with chronic stroke need to be further investigated.

Yan and Hui-Chan (2002) demonstrated that a 60-min of daily TENS, begun within 2 weeks from stroke onset, and applied to 4 acupuncture points of the affected lower extremity (St 36, Lv 3, GB 34, UB 60) for 3 weeks, enhanced motor recovery in 56 subjects with acute stroke. In contrast to placebo stimulation, they showed that repeated application of TENS significantly slowed the development of spasticity of the affected ankle plantarflexors, improved motor recovery in the lower leg in terms of increased torque generated by the affected ankle dorsiflexors, and decreased EMG co-contraction during ankle dorsiflexion. Taken together with the findings from previous studies, Yan and Hui-Chan (2002) suggested that TENS may enhance the motor recovery of acute stroke patients through excitation of large diameter sensory and motor fibers (Levin and Hui-Chan 1993), enhancement of presynaptic inhibition of the spastic muscles (Levin and Hui-Chan 1992), and disinhibition of descending voluntary commands to the motoneurons of the paretic muscles (Levin and Hui-Chan 1992). Other authors (Asanuma and Keller 1991; Chae and David 1999) suggested that the proprioceptive and cutaneous impulses associated with stimulation-induced repetitive movements may have induced plastic changes e.g. long-term potentiations in the motor cortex, to modify the latter's excitability and to facilitate motor relearning.

The process of motor recovery in stroke survivors is thought to be completed by some 6 months from stroke onset (Duncan et al. 1994). In view of the positive findings on chronic stroke patients by Levin and Hui-Chan (1992), our
objective in the present thesis was to investigate if a home-based rehabilitation combining with TENS could further promote motor recovery in subjects at least 1 year after stroke. More specifically, this thesis set out to determine if a 4-week treatment period with TENS and other appropriate rehabilitation strategy could produce further recovery in motor function and functional mobility. Another objective was to find out whether these functional gains could be maintained after treatment stopped.

Muscle weakness is now recognized as one of the major causes of impairments of motor control in patients with stroke (Burke 1988; Fellows et al. 1994; Gowland et al. 1992; Sahrmann and Norton 1977). Training to improve muscle strength and control of motor and mobility function is an integral part of rehabilitation in subjects with stroke. Results of animal studies showed that cortical reorganization with beneficial consequences can be induced by task-specific training after experimentally induced cortical infarcts (Nudo and Milliken 1996; Nudo et al. 1996b). Successful achievement of the task was found to strengthen existing and potential neural connections. Task-related training is thus gaining theoretical and experimental support from animal studies, and has been used in physiotherapeutic clinics as a means of improving walking after stroke in man. However, few properly designed studies had been conducted to validate such a treatment approach.

For a review of task-related training in man, MEDLINE databases were searched using the text words “task-specific”, “task-related” or “task-orientated training”. This search identified 17 articles published in the English language between January 1966 and July 2004, of which only 4 single-blinded randomized
clinical trials assessing the efficacy of task-related training for patients with stroke were identified (Ada et al. 2003; Dean et al. 2000; Dean and Shepherd 1997; Richards et al. 1993). Most of these studies involved the use of expensive specialized training equipment such as Kinetron or treadmill, which may limit the applicability of their findings to a home environment. Moreover, there is still little consensus for the most optimal exercise protocol for stroke patients.

No study has examined the combined use of TENS and contemporary task-related training in a home-based rehabilitation program for subjects with chronic stroke hitherto. According to the available evidence reviewed in this Chapter, we summarised that neuroplasticity could be the scientific basis through which appropriate rehabilitation strategy could promote motor recovery even in chronic stroke. As TENS and task-related training appear to be capable of improving motor function separately in stroke subjects, we purport that their combined applications, when given with appropriate frequency and duration, could probably augment motor recovery even in subjects with chronic stroke. Our first hypothesis is, therefore, that subjects with first stroke at least one year ago, receiving home-based TENS in combination with task-related training at an appropriate treatment “dosage”, would experience earlier and/or greater motor recovery of lower limb muscle strength and locomotor abilities than those without any active treatment. (N.B. The treatment “dosage” examined in this thesis is based in part on our previous studies (Levin and Hui-Chan 1992; Yan and Hui-Chan 2002), and consisted of 60 minutes of TENS and 60 minutes of task-related training in the form of closed-chained lower limb strengthening exercises, once a day, 5 days a week for 4 weeks, making a total treatment period
of 20 sessions.) Our second hypothesis is that the combined effects of TENS and task-related training on the recovery of motor function and functional mobility after stroke would be significantly earlier and/or greater than those of TENS or task-related training alone.

1.6.2 Objectives

The present thesis consists of 3 studies: 1 pilot and 2 main studies.

The objectives of the pilot study are:

1. To quantify the reliability of the 5 outcome measures used in the main study. The outcome measurements included spasticity of ankle plantarflexors by the Composite Spasticity Scale, muscle functions in terms of maximum isometric voluntary contraction of ankle dorsi- and plantar-flexors recorded by load cell and surface electromyography, temporal-spatial gait parameters by GAITRite walkway system, walking endurance by the 6-minute walk (6 MW) test and functional mobility by the timed “Up & Go” (TUG) test.

2. To examine the differences of the 5 outcome measures between healthy elderly and subjects with chronic stroke.

3. To delineate possible associations between the timed “Up & Go” test and the other outcome measures in subjects with chronic stroke.

The objectives of the main studies are:

1. To compare the relative effectiveness of 4 treatment protocols on spasticity of ankle plantarflexors and ankle muscle functions over a 4-week treatment period in subjects with chronic stroke. The 4 treatment protocols include
TENS, TENS with task-related training (TRT), placebo-TENS (PLBO) with TRT and control without any active treatment.

2. To compare the relative effectiveness of the above treatment protocols on gait performance, walking endurance and functional mobility over a 4-week treatment period in subjects with chronic stroke.

1.7 Outline of the Thesis

The work presented in this thesis is concerned with rehabilitation aimed at reducing the disability associated with walking after stroke. Chapter 1 reviews the literature which highlights the epidemiology of stroke, its clinical pictures and treatment strategies in light of the findings from clinical trials and the fields of motor control, motor learning, biomechanics, and neural plasticity. Since translation from science to clinical service involves the process of deriving implications from broad areas of research to formulate interventions, hypotheses that can be clinically tested will be presented at the end of the chapter with clear statement of thesis objectives for the one pilot and two main studies.

Chapter 2 describes the methodology, including study design, subject inclusion and exclusion criteria, treatment protocols, measurement procedures, as well as statistical methods for data analyses. Chapter 3 reports the results of a pilot study that evaluated the reproducibility of all measurement protocols in both healthy elderly and subjects with chronic stroke. This chapter also reports the results of comparisons between healthy elderly and patients with chronic stroke in motor performance.

Chapter 4 compares the effects of 3 home-based programs (TENS,
TENS+TRT and PLBO+TRT) on the level of spasticity in the affected ankle plantarflexors and the performance of ankle dorsi- and plantar-flexors in subjects with chronic stroke, with those of the control subjects receiving no treatment. Chapter 5 examines the relative effectiveness of the same 3 home-based programs on gait performance, walking endurance and functional mobility in subjects with chronic stroke with those of the control subjects receiving no treatment. Chapter 6 summarizes the findings of this thesis and presents the overall conclusions as well as some recommendations for future research.
Chapter 2

Methodology
2.1 Summary

This study is a single-blinded, randomized, placebo controlled clinical trial. The subjects were between 45 to 74 years old who had experienced stroke (including both cerebral ischaemia and haemorrhage) at least one year ago, had moderate to severe level of spasticity in the affected ankle plantarflexors, and were able to walk independently for 10 m with or without walking aids. The sample size and study power were calculated a priori using power analysis of sample size (PASS). Stratified randomization was applied to achieve a nearly even distribution of some important parameters among the groups in terms of age, gender, type of stroke, side and level of spasticity. After giving their informed consent, subjects were randomly assigned to 1 of 4 groups: TENS, TENS + task-related training (TRT), placebo TENS (PLBO) + TRT, and control receiving no active treatment.

All subjects received a 4 weeks home-based rehabilitation program. In the TENS group, electrodes were applied to the acupuncture points of the affected lower extremity including ST 36, LV 3, GB 34 and UB 60. The parameters were 0.2 ms pulses at 100 Hz with an intensity of 2-3 times the sensory threshold. In the TENS+TRT group, subjects practiced task-related training which consisted of 6 different weight-bearing exercises specially designed to strength the lower limb extensors and improve gait performance following TENS treatment. In the PLBO+TRT group, the treatment protocol was the same as in the TENS+TRT group except that the electrical circuit in the TENS machine was disconnected. In the control group, subjects did not receive any active treatment. Treatment intervention lasted for 4 weeks, once a day, 5 days a week for 4 weeks. TENS
was applied continuously for 60 minutes per session, while task-related training lasted for 60 minutes following the application of TENS or placebo TENS.

Outcome measurements included the level of spasticity in the affected ankle plantarflexors, muscle strength in terms of the peak torque generated by maximum isometric voluntary contraction of the ankle muscles, and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion, plus temporal-spatial gait parameters, walking endurance assessed by the 6-minute walk test, and functional mobility evaluated by the timed "Up & Go" test. Reproducibility of the measurement protocols was tested in a pilot study (Chapter 3). The assessments were then conducted before treatment, immediately after the first treatment, bi-weekly during the 4-week treatment protocol, and at 4 weeks during follow-up.

Descriptive statistics were used for comparing subjects' baseline values across groups. Repeated measures of analysis of variance (ANOVA) were chosen to compare treatment effects on the outcome variables at the time intervals indicated above. The between-subjects factor was the "4 groups", and the within-subjects factor was the "5 time intervals". Correlation analyses were also conducted to determine the relationships between some of the outcome measurements.

The study was designed to provide answers to two main questions: (1) whether 3 treatment programs were more effective than control without any active treatment; and (2) whether TENS in combination with task-related training was more effective than TENS alone or placebo TENS with TRT in regard to motor and functional recovery from chronic stroke.
2.2 Introduction

This chapter describes the methodology and instrumentation used in the thesis. Its scope includes selection criteria of subjects, sample size calculation, randomization procedures, detailed descriptions of each treatment protocol, and strategies employed to enhance treatment compliance. Besides, rationale in choosing the outcome measures in this thesis is discussed. In order to ensure that the outcome measures used in the present study were repeatable, reliability of measurements of spasticity, muscle strength of ankle dorsiflexors and plantarflexors, temporal-spatial gait parameters, walking endurance and functional mobility, were examined in a pilot study. The testing procedures describe below are identical to the studies presented in the subsequent chapters of this thesis.

2.3 Subjects

2.3.1 Inclusion Criteria

Subjects were recruited into this study if they were:

1) Hong Kong citizens between 45 and 74 years old;
2) diagnosed with first stroke resulting in hemiplegia at least 1 year ago;
3) suffering from moderate to severe spasticity in the lower extremity and a minimum of $10^8$ of passive ankle dorsiflexion;
4) discharged from all rehabilitation services at least 3 months before the program commenced;
5) able to understand instructions;
6) able to give informed consent;
7) able to walk 10 meters independently with or without an assistive device; and
8) independent in daily activities prior to the stroke.

2.3.2 Exclusion Criteria

Subjects were excluded if they were:

1) having major unstable cardiopulmonary diseases such as acute myocardial infarction, wearing a cardiac pacemaker, unaccustomed shortness of breath, shortness of breath with mild exertion, tachycardia, claudiation, or severe pitting ankle edema;

2) known to have pre-existing neurological disorders, such as multiple sclerosis, Parkinson’s disease or dementia;

3) showing communication problems such as receptive dysphasia;

4) exhibiting cognitive disorders either through misunderstanding or through scoring less than 7 on the Abbreviated Mental Test (Hodkinson 1972);

5) with no prior neurosurgery or orthopaedic surgery in the lower extremity;

6) with no orthopaedic or arthritic problem which would interfere with their ability to undergo the assessment or exercise program;

7) unable to give informed consent;

8) unable to speak either Cantonese or English.
2.3.3 Sample Size and Study Power

The sample size was calculated using PASS (version 6.0) statistical software package, with the minimal effect size on the recovery of muscle force set at 0.38, as calculated from a previous study of the effects of TENS on the recovery of ankle dorsiflexion force (Levin and Hui-Chan 1992). This effect size was found to be the lowest, according to a meta-analysis performed by Glanz et al (1996) on 4 randomized controlled trials in post-stroke rehabilitation using electrical stimulation, by employing muscle force recovery as a common end point in all 4 studies, including that of Levin and Hui-Chan (1992). Presuming a dropout rate of 10% during treatment, the sample size was 88 (= 80 + 8), with 22 for each of the 4 groups. The statistical significance was set at 5% (alpha level = 0.05) and the power at 80% (beta level = 0.2).

2.3.4 Randomization Procedure

Randomization procedures were done by a computer program of stratified randomization written by Jensen (1991), called "Minimize" in order to avoid imbalance in the distribution of prognostic factors and to control the variables which had known effects on outcome measures. The stratification in this study included 2 age ranges (45-59 and 60-74 years), gender (male and female), side of hemiplegia (left and right side), and level of plantarflexor spasticity (moderate and severe, according to the Composite Spasticity Scale, Chan 1986). By using this computer program, the first patient was allocated at random and then an imbalance score based on distribution of patients already allocated was computed.
for the next patient. All factors for stratification were equally weighted by the program. Subjects were randomly allocated into 4 groups:

1. TENS
2. TENS + task-related training (TRT)
3. Placebo-TENS + task-related training (PLBO+TRT)
4. Control

Subjects in the present study were stratified according to age, gender, side of hemiplegia and level of plantarflexor spasticity, because there are variables which had known effects on the outcome measures. Older age was found to be an adverse prognostic indicator of functional outcomes in patients with stroke (Jorgensen et al. 1999; Wade et al. 1985), and a negative correlation was found between age and muscle strength in healthy elderly subjects (Winegard et al. 1996). Although some previous studies showed that there was no relationship between gender and stroke outcome (Jongbloed 1986), gender differences was found to exist in muscle strength which was measured in the present study (Lexell et al. 1988). In a prospective study on 536 stroke patients of consecutive rehabilitation admissions using functional improvement on Functional Independence Measure (FIM), patients with right hemisphere lesions (left hemiparesis) were found to have poorer outcomes than those with left hemisphere lesions (right hemiparesis). Finally, Levin and Hui-Chan (1992) reported that TENS could reduce the Composite spasticity Scores in stroke subjects with moderate to severe level of spasticity in ankle plantarflexors. Therefore, subjects in the present study were stratified according to these 4 variables.
2.4 Treatment Protocol

Treatment period lasted for 4 weeks. With initial demonstrations by and instructions from the therapist, all subjects were required to perform the rehabilitation program daily, at 5 days per week. Most treatments were subsequently carried out at home by the subjects. During the first and second week, all subjects were required to attend instruction sessions in the laboratory of The Hong Kong Polytechnic University, 5 and 3 times respectively, in order to learn how to use the TENS machine and perform the exercises prescribed. The main aim of the instruction sessions is to ensure that all subjects would follow the home program properly and for the physiotherapist to progress the exercise level as necessary. One more instruction session during the third week of the intervention period, together with daily log book entered by all subjects, and regular telephone contacts by the therapist 3 times a week, were aimed to increase the treatment compliance of the subjects.

2.4.1 Transeutaneous Electrical Nerve Stimulation (TENS)

2.4.1.1 Stimulation Parameters

The model CEFAR Dumo 2.4 K (Cefar Medical Products AB, Lund, Sweden) TENS stimulators (Fig 2.1) were used in both TENS and placebo TENS groups. The stimulator was calibrated, and delivered a high-frequency constant current of 100 Hz with single square pulses of 0.2 ms duration. Two pairs of
surface electrodes (4.5 cm x 3.5 cm) were placed over the selected acupuncture points of the affected lower extremity. Stimulus amplitude was set at 2 to 3 times that of sensory threshold. The anode was applied to the distal aspect and the cathode to the proximal aspect. Subjects and/or their family members were instructed in the use of the portable TENS stimulator. Subjects were required to have 60 minutes of TENS per session, once a day, 5 days a week for 4 weeks.

2.4.1.2 Location of Electrodes and Its Rationale

The acupuncture points used were ST 36 (Zusanli), LV 3 (Taichong), GB 34 (Yanglingquan), and UB 60 (Kunlun) as shown in Figure 2.2. ST 36 is about 7 to 8 cm below the tibial tuberosity on the lateral aspect of the tibialis anterior muscle. LV 3 is on the dorsum of foot, in between the first and second metatarsal bones. GB 34 is on the anterior-inferior aspect of the capitulum of the tibia. UB 60 is in the depression lateral to the tendon of the calcaneous behind the lateral malleolus.
Selection of these acupoints was based on the recommendation from the literature of traditional Chinese medicine (Chen 1993), and the results of previous studies (Hopwood 1997; Hu et al. 1993; Naeser et al.; Sonde et al. 2000; Wong et al. 1999; Yan and Hui-Chan 2002). In the ancient book of acupuncture, Ling Shu stated that all the organs ascend to the eye, which communicates with many meridians, constituting a system called the "Eye System" which ascends to the vertex, enters the brain, and then surfaces at the nape (Chen 1993). Besides entering the brain, the Eye System interconnects with many meridians around the eyes (UB, ST, SI, GB, SJ, HT, and LV), and with 3 parallel meridians (UB, GB, GV) at the nape. Stimulation of the acupuncture points that interconnect with the Eye System which enters the brain is expected to facilitate recovery in stroke patients (Chen 1993).

The 4 acupoints selected (ST 36, LV 3, GB 34, and UB 60) are the ones most widely and effectively used to treat paresis in stroke subjects (Hopwood 1997; Hu et al. 1993; Naeser et al. 1994; Wensel 1980; Yan and Hui-Chan 2002). In a single-blinded, randomized, placebo-controlled trial with 62 subjects with
acute stroke, Yan and Hui-Chan (2002) found that applying TENS to these 4 acupuncture points, together with conventional rehabilitation training, led to better sensorimotor recovery of lower extremity than conventional training alone. In an uncontrolled clinical trial, Sonde et al. (2000) found that stimulation of acupuncture point ST 36 with high-frequency (100 Hz) TENS for 30 minutes daily, over a period of 3 months, reduced spasticity of knee extensors and ankle plantarflexors in 16 subjects who had a stroke at least 5 months ago. From an anatomical point of view, these acupuncture points are all subcutaneous and close to the nerves and blood vessels (Chen et al. 1996; Wong et al. 1999). Stimulating the acupuncture points covering the paralytic ankle dorsiflexors could be expected to increase ankle movement and improve the foot drop commonly found in hemiplegic subjects.

2.4.2 Placebo (PLBO) TENS

For the placebo stimulation, the TENS device, stimulation parameters, location of electrodes, and treatment protocol were the same as those in the TENS group. The only difference was that the electrical circuit in the device used for placebo stimulation had been manually disconnected inside.

2.4.3 Task-Related Training (TRT) in Walking

2.4.3.1 Rationale of Exercise Program

The task-related locomotor training lasted for 60 minutes in each treatment session: 40 minutes for lower-limb strengthening exercises, 10 minutes for practicing transitional movement, and 10 minutes for gait training with rhythmic
auditory cues generated by a metronome previously set according to the patients’ walking pace.

Having conducted an extensive review of literature on strength training in able-bodied populations, Rutherford (1988) concluded that the effects of strength training are task-related and specific to the particular movement velocity, muscle length or position in which muscles are being trained. He pointed out that task-related strength training therefore needs to be incorporated into the practice of particular functional task, so that the strength and pattern of muscle activation necessary to the task and context can be regained. The exercise protocol in the present study consisted of 5 different weight-bearing exercises (Fig 2.3), using a wooden block 27 cm wide by 23 cm deep by 2.5 cm or 5 cm high. These exercises were derived from an understanding of the biomechanical requirements of the stance phase of walking (Carr and Shepherd 1990, 1998, 2000), which made the subjects generate an overall extensor or support moment through their affected lower limb, as required in walking (Winter 1987). Nugent et al. (1994) and Dean et al. (2000) found that these specially designed lower-limb strengthening and gait re-education exercises could improve the walking outcome in patients with stroke. Sherrington and Lord (1997) also found that this specific type of strengthening exercises is useful in improving gait velocity in frail elderly following hip fracture.

In the present study, rhythmic auditory cues were used for walking practice in the home program. Auditory rhythm had been shown to improve the temporal stride symmetry and the variability of lower limb EMG patterns in normal (Thaut et al. 1993a) and hemiparetic gait (Thaut and McIntosh 1992; Thaut et al. 1993b;
Thaut et al. (1997). Thaut and McIntosh (1992) found that with rhythmic auditory cueing the locomotion in patients with stroke, weight-bearing stance and muscle activation bursts increased on the paretic side, stride rhythm improved, magnitude of muscle activation decreased on the nonparetic side, and EMG activity during the swing phase diminished on the paretic side. In a recent study, Thaut et al. (1997) found that patients with stroke, who received gait training with rhythmic auditory facilitation for 6 weeks improved their gait velocity, stride length and stride symmetry relative to those of the control group who had gait training without rhythmic facilitation.

2.4.3.2 Details of Exercise Protocol

The home program consisted of the following task-related exercises:

1. **Standing on the affected leg with the unaffected leg placed on a wooden block** (Fig 2.3a). This exercise was used to improve weight-bearing through the affected leg.

2. **Standing with the affected leg on a wooden block while stepping up** (Fig 2.3 b & c). This exercise aimed to improve the ability to generate concentric force with the lower limb extensors while keeping the body mass over the foot, and the ability to switch from a concentric to an eccentric mode of contraction to lower the body mass (Shepherd et al. 1996).

3. **Stepping down with the unaffected leg from a wooden block to strengthen the affected leg muscles** (Fig 2.3 d & e). This exercise aimed to improve
the ability to generate eccentric force with the affected lower limb extensors while keeping the body mass over the foot.

4. *Heel lifts in standing to strengthen the affected ankle plantarflexor muscles* (Fig 2.3 f & g). This excises strengthened the calf muscles from their fully extended length to mid-length so as to ensure optimal muscle length, and to train the muscles to generate force in the range from 8-10° of dorsiflexion to 16-19° of plantarflexion necessary for push-off (Winter 1983).

5. *Standing up from a chair, walk a short distance, and return to the chair.* This exercise was used to promote a smooth transition between standing up and walking, and between walking and sitting down.

6. *Walking with rhythmic auditory cues generated by a metronome.* Subjects were provided with a metronome and were required to walk at a speed which synchronized with the rhythm set in the metronome by the physiotherapist. Subjects were required to focus on symmetrical weight bearing and avoid the use of adaptive behavior during walking practice.
Fig 2.3 a  Standing on the affected leg with the unaffected leg placed on a wooden block

Fig 2.3 b & c  Standing with the affected leg on a wooden block, while stepping up
Fig 2.3 d & e  Stepping down with the unaffected leg from a wooden block to strengthen the affected leg muscles

Fig 2.3 f & g  Heel lifts in standing to strengthen the affected ankle plantarflexor muscles
2.4.3.3 Progression of Exercises

Each exercise session lasted one hour, with subjects practicing for 10 minutes for each of the exercise prescribed. Subjects were encouraged to exercise as much as possible and not to use maladaptive (compensatory) movements. Appropriate and customized progression was made by the physiotherapist based on the observed performance of each patient. For the weight-bearing exercises with a wooden block, if subjects were able to perform the exercises with 20 repetitions continuously without any maladaptive movements, they were progressed to the next level by increasing the height of the wooden block. If subjects were able to perform the exercises with 20 repetitions continuously with the higher block, they were progressed to the next level by increasing the number of repetitions completed within 10 minutes of each exercise. Training in walking were progressed by increasing its speed.

2.4.3.4 Safety Considerations

The following strategies were used to ensure safety of the participants:

1. When training began, subjects were encouraged to steady themselves by holding onto immobile furniture or walking aids with their unaffected arm while exercising. In order to avoid the usage of compensatory strategies, subjects were encouraged to decrease the support as soon as their performance allowed.

2. Registered physiotherapists supervised the patients during instruction sessions so as to ensure that the amount and intensity of each exercise was graded according to each subject's level of functioning. Subjects were encouraged to
work as hard as possible. They were given verbal feedback and instructions aimed at improving their performance.

3. Subjects were instructed to terminate the exercise if they experienced any chest pain or discomfort, or any musculoskeletal pain. Emphasis was constantly placed on being aware of the signs of muscle fatigue such as "burn", ache, or loss of co-ordination.

4. Intensity of both strengthening and endurance was monitored using the rate of perceived exertion (RPE) (Borg 1982).

5. Progression of strengthening exercises was slow initially in order to avoid excessive muscle discomfort (especially in the early stages of exercise), to allow time for muscle and soft tissue adaptation, and to avoid demotivation (Kramer and Harman 1998).

6. Technique and the importance of responding to day-to-day fluctuations in health, energy, and mood were constantly emphasized as essential for injury prevention and gaining optimal benefits.

7. When performing exercises, participants were advised not to hold their breath and were encouraged to count out loud to counteract such a tendency, as holding a breath during exercise may lead to a sudden, sharp rise in blood pressure.

2.4.3.5 Plans for Enhancing Retention and Compliance

The following strategies were used to enhance subject retention and compliance:

1. During instruction sessions in the laboratory at The Hong Kong Polytechnic University, registered physiotherapists checked whether the exercises were
done correctly and to progress the exercises as necessary by increasing the
height of wooden block or number of repetitions.

2. Subjects were given an exercise book with photographs and written
description of each exercise. They were also required to fill in an exercise
diary in order to record the number of repetitions done each day. Such a
method was suggested to increase or maintain the motivation of the patients to
found it to be effective in a home exercise program for frail elderly with hip
fracture.

3. Regular telephone contacts by therapist are known to increase exercise
compliance of the subjects. Campbell et al. (1997) used an individualized
approach, with adequate initial instructions on exercise postures. They made
regular telephone contacts to maintain motivation and monitor progress. At 1-
year follow-up, 42% of subjects were still doing at least 3 sessions of exercise
a week.

2.4.4 Control

Subjects in this group did not receive any active training. However, they
were required to attend the assessment sessions at the same 5 time intervals as the
other 3 treatment groups.

2.5 Measurements

2.5.1 Measurement Battery and Intervals

Outcome measures in the main study included measurements of:
1. spasticity of the affected ankle plantarflexors using the Composite Spasticity Scale;

2. muscle function in terms of maximum isometric voluntary contraction of ankle muscles via peak torque measurement and surface electromyography;
   - integrated EMG signals (IEMG) from tibialis anterior and medial gastrocnemius muscles (mV.s)
   - peak dorsiflexor and plantarflexor torques (Nm)
   - EMG co-contraction ratio (%)

3. gait performance in terms of temporal-spatial gait parameters;
   - gait velocity (cm/s)
   - step and stride length (cm)
   - stance time (% of gait cycle)
   - single-leg support and double-leg support duration (% of gait cycle)

4. walking endurance in terms of the 6-minute walk (6 MW) test (cm)

5. functional mobility in terms of the timed “Up & Go” (TUG) test (s)

To detect treatment effects over time, measurement intervals were divided into 2 stages:

1. short-term effects: before treatment ($T_0$), immediately after the first treatment ($T_1$), once bi-weekly for the 4 weeks of treatment ($T_2$ to $T_3$);

2. long-term effects: at 4 weeks after treatment at follow-up ($T_{FU}$).

All measurement protocols were evaluated for data repeatability in the pilot study described in the next chapter (Chapter 3).
2.5.2  Time Schedule of Treatment and Assessment Protocol

The whole program lasted for 4 weeks and subjects were requested to perform the home-based program daily as instructed by the therapist. Details of the schedule are summarized in Fig 2.4.

2.5.3  Evaluation of Spasticity in the Affected Ankle Plantarflexors

2.5.3.1  Rationale of Measurement

As described in Chapter 1 (section 1.2.1), the most widely accepted definition of spasticity to-date is a “motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex, as one component of the upper motor neuron syndrome” (Lance 1980, p.485). More recently, Lance (1990, p.606) reiterated this definition and added that “spasticity does not include impaired voluntary movement and abnormal posture”. Therefore, the primary feature of spasticity is currently considered to be an exaggeration of stretch reflexes, both tonic and phasic components.

It is generally believed that spasticity is the major obstacle to improving function in patients with stroke (Bobath 1970, 1990). Though not without controversy, results of several recent studies showed that reducing spasticity could improve the functional capacities in hemiplegic patients (Hesse et al. 1994, 1996; Hsu et al. 2003; Reiter et al. 1998). According to the definition of spasticity, any spasticity assessment should include tonic stretch reflex (muscle tone) and phasic stretch reflex (tendon jerk reflex) as well as clonus (Chan 1986; Mayer 1997; Rymer and Katz 1994).
Fig. 2.4 Flow chart of subject recruitment and time schedule of treatment and assessment protocol.
2.5.3.2 Composite Spasticity Scale

The Composite Spasticity Scale was proposed by Chan (1986) and further developed by Levin and Hui-Chan (1992). It is an ordinal scale which consists of the clinical assessment of (1) Achilles tendon jerks, (2) resistance to passive ankle dorsiflexion, and (3) the amount and duration of ankle clonus. The evaluation of the scale is done by the same examiner using a 4-point scale for clonus, and a 5-point scale for the other indexes. Because the score for “resistance to passive dorsiflexion” most closely represents tone (Berardelli et al. 1983), it was doubly weighted. These 3 scores will be then summed to generate the “total spasticity score”. The total scores on this scale ranging from 1 to 6 are considered as representing “no spasticity”, 7 to 9 as “mild spasticity”, 10 to 12 as “moderate spasticity”, and 13 to 16 as “severe spasticity” (Levin and Hui-Chan 1992). Detailed guidelines for this scale can be found in Appendix II. The Composite Spasticity Scale has been demonstrated to be both reliable and valid in people with stroke (Levin and Hui-Chan 1992, 1993, 1994; Nadeau et al. 1998). It has also been used in a number of other studies (Goulet et al. 1996; Levin et al. 2000; Yan 2002). Nadeau and colleagues (1998) used this scale to evaluate spasticity of the ankle joint in 19 subjects with chronic stroke. They found that the 3 scale items had good internal consistency, with Cronbach’s X at 0.70, indicating that this scale was suitable for assessing spasticity in stroke subjects.

2.5.4 Maximum Isometric Voluntary Contraction (MIVC) of Ankle Dorsiflexors and Plantarflexors

2.5.4.1 Rationale of Measurement
Muscle weakness and paralysis together with impairments in motor control are prominent consequences of stroke (Adams et al. 1990; Colebatch and Gandevia 1989; Davies et al. 1996; Schneider and Gautier 1994). They are recognized as major causes of disability in patients with upper motor neuron lesions (Fellows et al. 1994; Gowland et al. 1992; Sahrmann and Norton 1977). Weakness of agonist muscles in patients with stroke may be due to inadequate recruitment of agonist motor units and/or inappropriate co-contraction of antagonist muscles leading to active restraint during agonist activation (Bourbonnais and Vanden Noven 1989; Ng and Shepherd 2000). Weakness after stroke is typically measured as maximum isometric torque or force, and this measure has been shown to be a prognostic indicator (Bohannon and Smith 1987; Bohannon and Walsh 1992; Canning et al. 1999; Hagbarth 1994; Sunderland et al. 1989). In this study, 2 elements of muscle weakness in patients with stroke were addressed, namely the peak torque generated and the EMG co-contraction ratio between agonists and antagonists during maximal isometric voluntary contraction of ankle dorsiflexors and plantarflexors.

Muscle co-contraction can be defined as the simultaneous activation of agonist and antagonist muscle groups crossing the same joint to act in the same plane (Olney 1985). Although co-contraction is a common motor control strategy primarily activated when a person needs increased joint stability or improved movement accuracy (Damiano 1993), excessive co-contraction had been shown in patients with stroke (Hammond et al. 1988; Knutsson and Martensson 1980; Levin and Hui-Chan 1994). Increased antagonist restraint through co-contraction could be one of the main causes for the pervasive weakness documented in
patients with stroke. Hammond et al. (1988) suggested that the EMG co-contraction ratio could be an objective assessment before and after therapy in patients with stroke. Recently, Levin and Hui-Chan (1994) used surface EMG electrodes to examine the muscle activities in ankle dorsiflexors and plantarflexors of spastic hemiparetic and healthy subjects. The computation of co-contraction of their study was based on antagonist-to-total (agonist + antagonist) EMG activity. They found a high interclass correlation (0.99) of EMG co-contraction ratios for dorsiflexion in the affected leg and a moderate correlation coefficient for plantarflexion (0.53). Adopting this approach in the present study, 2 EMG co-contraction ratios were calculated to evaluate the differences before and after treatment. One was for the dorsiflexion of the ankle joint, and the other for plantarflexion.

2.5.4.2 Measurement Procedures

Each subject underwent bilateral maximum isometric strength testing of ankle dorsiflexors (tibialis anterior) and plantarflexors (medial gastrocnemius). Muscle strength and electromyographic activity were recorded by means of the torque measurements with a load cell mounted on a custom-built foot frame and surface EMG respectively.

After the skin was shaved and prepared by vigorous rubbing with an alcohol pad (Morris 1999), 2 bar-shaped surface EMG electrodes (B & L Engineering®) were placed over the tibialis anterior (TA) and medial gastrocnemius (MG) muscles. These electrodes were low noise, with a pre-amplifier having a gain of 388. The input impedance was greater than 100
megaohms, the common mode rejection ratio was 95 db, and the bandwidth was 12 Hz-3.4 kHz. The EMG data recorded from both TA and MG muscles were used to compute EMG co-contraction ratio for each leg.

The EMG electrodes were positioned using anatomical references proposed by Knutson et al. (1994) and Zipp (1982). First, the distance between the fibular head and the distal edge of the lateral malleolus was measured. Then 25% and 33% of the distance were calculated as the positions for EMG recording from TA and MG muscles, respectively. The shank circumference was then measured at the point of the 25% and 33% distance. One set of electrodes was then placed parallel to the muscle fibers of the TA, lateral from the tibial crest at a distance of 10% of the circumference. The other was placed over the MG muscle above the soleus muscle, parallel to the Achilles tendon, and medial from the tibial crest at a distance of 33% of the circumference (Delagi et al. 1994; Knutson et al. 1994; Zipp 1982). The electrode positions were outlined on the skin with a permanent ink marker at the end of each session, and then checked every treatment day to ensure that the array was re-applied accurately when reassessing the subject on different days, to minimize the variability due to different electrode locations.

All maximum isometric strength tests were performed with the subject in a supine position and the lower extremity fixed in a specially designed foot frame with velcro straps (Fig 2.5). The knee and the ankle were kept at about 50° of flexion and at neutral position respectively. A load cell (model: RL 2000A-100, Output: 3.0 MV/V at 100 LBS, capacity: 100, linearity 97%, Rice Lake Weighting System) attached to the foot frame was used to measure the dorsiflexing or plantarflexing force generated. The distance from the lateral malleolus to the
centre of the load cell was measured as the moment arm for calculating the torque. The degree of flexion at the knee joint, and the distance between the lateral malleolus and the center of the load cell was kept constant at each trial and across trials to eliminate variations within and across sessions.

Before recording began, subjects were required to relax as confirmed by the absence of visible EMG signals on a computer monitor, set up with LabView software to simulate an oscilloscope. This helped to ensure artifact-free signal recording during data collection. Brief training on how to produce maximal muscle contraction was given to each subject at each session before recording, so that the latter clearly understood how to perform maximal voluntary contractions according to the measurement protocol.

During assessment of MIVC, all subjects were encouraged to contract either their dorsiflexors or plantarflexors maximally or "as hard as possible" for approximately 3 seconds (DeLuca 1997; Soderberg and Knutson 2000) and then relax. A total of 10 seconds were recorded; 2 to 3 seconds before the contraction were taken as baseline. EMG signals were sampled at a frequency of 1,000 Hz per channel. These raw data were stored and then digitized with a 16 bit analog-
to-digital (A/D) converter for signal processing and analysis. All subjects performed 3 maximal contractions of each muscle after 2 practice trials, with at least 1 minute of resting between to minimize fatigue (DeLuca 1997). To maximize reliability, the same examiner who was blinded to the treatment performed all strength assessments.

2.5.4.3 Analysis of EMG data

Using LabView (5.1 version) as a data collection and analysis program and DAQCARD 1200 (National Instruments, Austin, Texas in the United States) as an interface with the computer, the time course of the torque output from the load cell was captured concurrently with EMG signals. The trial in which a subject produced the highest torque was selected for further statistical analyses. The EMG signals were then full-wave rectified and filtered with a second-order Butterworth low-pass filter, having a cut-off frequency at 2.7 Hz for the tibialis anterior and at 2 Hz for the gastrocnemius muscles. The frequency was calculated using a mean muscle twitch time of 58.0 ms for the tibialis anterior muscle and of 79.0 ms for the medial gastrocnemius muscle (Winter 1990, Chapter 8, p.171). Note that the tibialis anterior muscle consists of a large portion of fast-twitch muscle fibers and the medial gastrocnemius muscle consists of a mixture of fast- and slow-twitch muscle fibers. The recommended cut-off frequencies for these two muscles were between 2 Hz to 3 Hz (Winter 1991, Chapter 5, p.54).

The integrated EMG (IEMG) was defined by Bouisset and Maton (1973) as the total amount of electrical activity in which the value is proportional to the area under the EMG envelop, that is, the quantity of electricity. The EMG signals
were full-wave rectified and integrated over a 500 ms window, beginning 250 ms before and ending at 250 ms after the peak value of MIVC after subtraction of baseline activity. The IEMG values were computed via a customized software programme off-line and confirmed by visual inspection.

To estimate the degree of EMG co-contraction ratio at maximal force production during isometric co-contraction, a sliding window of 500 ms duration was selected. This window began at 250 ms before and ended at 250 ms after the peak value of MIVC. The corresponding integrated EMG signals (mV.s) of the tibialis anterior (TA) and medial gastrocnemius muscles (MG) in either dorsiflexion or plantarflexion were extracted to compute the EMG co-contraction ratio. This ratio was computed based on EMG ratios of antagonist-to-total (agonists+antagonist) activity. For example, the antagonist MG EMG activity during maximum ankle dorsiflexion was divided by the total EMG activity of both TA and MG muscles, as was done in our previous study (Levin and Hui-Chan 1994).

\[
\text{Co-contraction Ratio} = \frac{\text{Integrated Antagonist EMG area}}{\text{Integrated (Agonist + Antagonist) EMG area}}
\]

2.5.5 Gait Performance

2.5.5.1 Rationale of Measurement

Gait performance in patients with stroke is characterized by slower gait velocity (Brandstater et al. 1983; Knutsson and Richards 1979; Olney et al. 1994; Wade et al. 1987), and residual spatial (Dettmann et al. 1987) and temporal (Hill
et al. 1994; Wall and Turnbull 1986) asymmetry when compared with healthy elderly. Impairments in somatosensory functions (Carey 1995), visuospatial perception (Friedman 1990), spasticity (Bohannon and Andrews 1990; Hsu et al. 2003), muscle strength (Knutsson and Richards 1979; Richards et al. 1998; Sahrmann and Norton 1977), and balance (Dettmann et al. 1987; Bohannon 1989) have been suggested to be related to the inability of hemiplegic patients to walk normally. As walking faster with normal gait patterns are perceived by many stroke patients to be the ultimate goals of their rehabilitation (Bohannon et al. 1988, 1991), rehabilitation personnel designing gait-training program should target at improving gait velocity and gait patterns of these patients.

Measurement of gait velocity is recommended as an outcome measure following stroke (Wade 1992). The measurement of gait speed has been shown to be valid, reliable, and responsive to changes in locomotor performance in patients with stroke (Richards and Olney 1996; Wade 1992). Moreover, gait velocity was found to be positively related to strength of muscles of the paretic leg (Bohannon 1986; Richards et al 1998), to the second agonist power burst at push-off (Olney et al. 1991; Richards et al. 1998), to clinical measures of recovery of the lower extremity (Brandstater et al. 1983; Richards et al. 1992), and to the quality of gait movements (Olney and Richards 1996; Richards et al. 1995; Wade et al. 1987), and inversely related to the degree of spasticity in the plantarflexor muscles (Lamontagne et al. 1999).

In the present study, gait performance in terms of temporal-spatial gait parameters such as gait velocity, cadence, step and stride length, stance time, single-leg and double-leg support duration were evaluated. Although variability
has been described for temporal-spatial gait parameters (Bohannon 1987; Brandstater et al. 1983), patients with stroke have shown improvements in gait velocity, cadence, stride length, step length, stance time, and single-leg support duration over time (Friedman 1990; Wade et al. 1987).

2.5.5.2 GAITRite Walkway System

Gait performance in terms of temporal-spatial parameters were measured with a 4.6 m long instrumented carpet (GAITRite, CIRSystems Inc., Clifton, NJ). The carpet was composed of 13,824 pressure-sensitive sensors arranged in a 48 wide x 288 long grid pattern sandwiched between 2 layers of vinyl (Fig. 2.6). As the individual walked along the instrumented walkway, data from the triggered pressure-sensitive sensors were collected by processors connected in series and fed to the notebook computer through a serial port (19,200 baud). The GAITRite software (version 2.2) running on the Window 98 operating system processed the data and calculated the mean values of temporal and spatial gait parameters. The sampling rate was 80 Hz. The GAITRite system has been shown to be a valid instrument for determining gait velocity and other related parameters (Cutlip et al. 2000; McDonough et al. 2001).

During testing, subjects walked with their comfortable foot-wear at a normal walking speed. They were required to walk across the carpet, beginning 1 meter in front and finished at 1 meter past the end of the carpet, so as to allow for acceleration and deceleration. Two practice trials were performed, followed by 3 consecutive trials recorded with one minute of rest in between trials. Data obtained from the 3 trials were averaged for further data analysis. Gait velocity,
as well as other temporal and spatial parameters of a gait cycle were calculated by
the afore-mentioned GAITRite software (version 2.2) running on the Window 98
operating system. Detailed definitions of temporal (velocity, stance time, duration
of single- and double-leg support) and spatial (step length, stride length)
parameters of the GAITRite Walkway System can be found in Appendix IV.

Fig. 2.6 GAITRite Walkway System

2.5.6 Assessment of Walking Endurance

2.5.6.1 Rationale of Measurement

Inactivity (Collen and Wade 1991) and low cardiovascular fitness (Mol
and Baker 1991; Ryan et al. 2000) are common in patients with stroke.
Impairments resulting from stroke, such as pain, spasticity, muscle weakness and
poor balance can result in reduced tolerance to activity and can lead to a sedentary
lifestyle and poor cardiovascular fitness. As low exercise endurance may
compound the increased energy cost of movement associated with residual
hemiparesis and contribute to poor rehabilitation outcomes, endurance was
suggested to be included as a training component and as an outcome measure in
patients with stroke (Ducan and Badke 1987).
2.5.6.2 Six-Minute Walk (6 MW) Test

The 6-minute walk test (6 MW) (Guyatt et al. 1985) is a measure that was originally developed to assess endurance in cardiorespiratory (McGavin et al. 1978) and cardiovascular populations (Guyatt et al. 1985). The distance covered during the 6-minute walk test has been found to be significantly associated with peak oxygen uptake (Cahalin et al. 1996) and heart failure-specific quality of life questionnaire scores (O'Keefe et al. 1998). It has also been shown to be a sensitive measure of heart disease severity (Guyatt et al. 1985; Peeters and Mets 1996), and is a useful predictor of mortality in heart disease (Bittner et al. 1993; Cahalin et al. 1996; Peeters and Mets 1996; O'Keefe et al. 1998). More, recently, the 6 MW test has been validated as a general indicator of overall physical performance and mobility in populations of older people (Duncan et al. 1993; Harada et al. 1999). Performance in the 6 MW test has also been shown to improve after exercise interventions in frail elderly (Gunnarson et al. 1997; Gowans et al. 1999; Lord and Menz 2002) and in patients with stroke (Ada et al. 2003; Dean et al. 2000; Duncan et al. 1998; Ducan et al. 2003).

During our study, the 6 MW test was conducted along a 33 m corridor that had 1 cm increments marked discretely on a measuring tape in the middle of the hallway (Fig 2.7). Two colored adhesive markers were taped at each end of the walkway. Subjects were instructed to walk from one end to the other, covering as much ground as they could during the allotted time of 6 minutes. They were given standardized encouragement at 1, 3, and 5 minutes during the walk (Guyatt et al. 1984): "You're doing a good job" (minute 1), "You’re halfway done"
(minute 3), "You have 1 minute to go" (minute 5). The investigator stood by the side of the walkway to ensure patient safety. Subjects walked alone during the 6 MW unless it was felt to be unsafe by the investigator. When accompanying the subject if such was needed, the investigator walked slightly behind and not beside the subject, so as to avoid influencing the subject's self-selected walking pace. The distance covered in 6 minutes was recorded to the nearest centimeters. Subjects were allowed to stop and rest as they deemed necessary.

Fig. 2.7 Six-Minute Walk (6MW) Test

2.5.7 Functional Mobility Assessment

2.5.7.1 Timed "Up & Go" Test
The timed Up & Go test (TUG) is a simple and quick mobility test that is commonly used to examine functional mobility in community-dwelling, frail older adults (Podsiadlo and Richardson 1991). The test requires a subject to stand up, walk 3 meters, turn, walk back, and sit down. Time taken to complete the test has been found to be strongly correlated with the level of functional mobility. More specially, Podsiadlo and Richardson (1991) validated the timed “Up & Go” test using elderly subjects (aged 60-90 years) with stroke, Parkinson’s disease, arthritis, cerebellar disorders, or general deconditioning. They found a very good to excellent reliability in timed scores between raters (ICC=0.99), as well as within the same raters during consecutive clinic visits (ICC=0.99). Moreover, the TUG time correlated moderately well with gait speed (r=-0.55), scores on the Berg Balance Scale (r=-0.72), and the Barthel Activities of Daily Living Index (r=-0.51).

Several studies have shown good test-retest reliability of TUG measurements in specific subject populations including community-dwelling older adults (Hughes et al. 1998; Shumway-Cook et al. 2000; Thompson and Medley 1995), people with Parkinson’s disease (Morris et al. 2001; Thompson and Medley 1998) and those with unilateral lower limb amputation (Schoppen et al. 1999). Several other researches reported test scores for patient populations including elderly with walking aids (Medley and Thompson 1997), frail elderly patients (Di Fabio 1997; Nikolaus et al. 1996). More recently, Dean et al. (2000) used TUG scores to document the changes in functional mobility after 4 weeks of exercise training in 12 people with chronic stroke.
In our study, the test began with each subject sitting, back against the chair, arms resting on the lap, feet just behind the distance-marker on the floor, and a walking aid if needed at hand. A 3-meter distance was marked off on the floor in front of a firm chair with arms and a seat height of 46 cm (Fig 2.8). Subjects wore their regular footwear and used their normal walking aids if such were used. They were instructed as follows, “One, two, three, ‘go’, stand up, walk comfortably and safely to the marker at the other end of the marked walkway, walk across the marked line, come back, and sit all the way back in your chair.” All subjects were informed that the trial would be timed. Timing began on the word “go” and ended when the subject’s back rested against the chair upon returning, and was recorded in seconds. Two practice trials were performed, followed by 3 recorded trials. Data obtained during the 3 recorded trials were averaged for use in data analysis.

![Fig. 2.8 Timed “Up & Go” Test](image)

### 2.6 Statistical Analysis

Statistical methods included descriptive statistics for the subjects’ relevant characteristics. Parametric and non-parametric statistics were applied to analyze continuous data and ordinal data, respectively. Measurement of spasticity, maximum isometric voluntary contraction of ankle muscles, gait parameters,
walking endurance and functional mobility were analyzed with repeated measures of analysis of variance (ANOVA), using SPSS (version 11.5) to compare the main effects pre-, during and post-treatment. The design employed in this study had 2 main factors. The between-subjects factor was the 4 groups: (1) TENS, (2) TENS+TRT, (3) PLBO+TRT, and (4) Control. The within-subjects factors were the 5 assessment intervals: before treatment ($T_0$), immediately after the first treatment ($T_1$), after 2 weeks and 4 weeks of treatment ($T_2$ and $T_3$), and 4 weeks after treatment at follow-up ($T_{FU}$). If there were interactions in the results of repeated measure ANOVA, one-way ANOVA followed by multiple comparisons (post-hoc test) were used to compare treatment effects between groups. Relationships or correlations among relevant measurements were examined using Pearson’s correlation coefficients. The significance level was set at 5%.

As randomization was used in the present study, we assumed that variances of subjects were equally distributed among groups before treatment. The data in the outcome measurements were continuous data. Thus, the main statistical test used was repeated ANOVA. However, if there were statistically significant differences in the subjects’ characteristics, such as age, type of stroke, gender, method of analysis for co-variance (ANCOVA) would be applied.

2.7 Ethical Consideration

This research study involved non-invasive treatment modalities, namely TENS and TRT exercises, which are known to pose negligible risks to the subjects. The project was approved by the Ethics Committee of The Hong Kong Polytechnic University, Hong Kong (SAR), China. Subjects were required to sign
an informed consent (Appendix 1) prior to starting the study. They were informed that they could withdraw from the study at any time without prejudice to them.
Chapter 3

Reproducibility of Outcome Measures:
A Pilot Study
3.1 Summary

This chapter contains the result of a pilot study, conducted to examine: (1) the reproducibility of the 5 outcome measures used in the main study; (2) the ability of these 5 outcome measures to differentiate subjects with chronic stroke from healthy elderly; and (3) the association between the impairments of paretic lower limb muscles and locomotor capacities on the one hand, and the scores of the timed “Up & Go” test on the other in subjects with chronic stroke. The 5 outcome measures used in the main study included measurement of ankle plantarflexor spasticity by the Composite Spasticity Scale, maximum isometric voluntary contraction of ankle dorsi- and plantar-flexors by using a load-cell and EMG measurements, temporal-spatial gait parameters by using the GAITRite walkway system, walking endurance by the 6-minute walk (6 MW) test, and functional performance by the timed “Up & Go” (TUG) test.

Ten community-dwelling healthy elderly (5 men, 5 women; mean age, 63.5 ± 6.1 years) and 11 subjects with chronic stroke (6 men, 5 women; mean age, 61.7 ± 7.2 years) participated in the study. All stroke subjects had moderate to severe spasticity in their affected plantarflexors after a single onset of stroke at least 1 year ago, and were able to walk for 10 m independently with or without walking aids. All testing took place in the morning session in the laboratory of the Department of Rehabilitation Sciences at The Hong Kong Polytechnic University. Each participant underwent assessments of ankle plantarflexor spasticity, muscle strength of ankle dorsi- and plantar-flexors during maximum isometric voluntary contraction, gait performance, walking endurance and functional mobility. All
assessments were performed at the same time on different days within 1 week by the same examiner.

The results showed very good to excellent reliability in the 5 outcome measures in both healthy elderly and subjects with stroke. High test-retest repeatability in Composite Spasticity Scale was found between 2 days, with ICC values ranging from 0.80 in healthy elderly in both left and right legs, to 0.97 and 0.80 respectively in the affected and unaffected legs of stroke subjects. The test-retest correlation coefficients for peak torque, IEMG and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion were 0.85 to 0.99 in healthy elderly and 0.69 to 0.98 in subjects with stroke. The test-retest correlation coefficients for gait velocity, cadence, step and stride length, stance time, single-leg and double-leg support duration ranged from 0.85 to 0.99 and from 0.96 to 0.99 in healthy elderly and subjects with stroke respectively. The ICC values for the distance covered in 6 MW were 0.91 in healthy elderly and 0.98 in subjects with stroke, while the values for TUG scores were 0.97 in healthy elderly and 0.95 in subjects with stroke.

Moreover, our findings demonstrated that subjects with chronic stroke had significantly higher level of spasticity in ankle plantarflexors, weaker plantarflexors, slower walking speed, poorer walking endurance and poorer functional mobility when compared with those of healthy elderly. Correlation analyses with Spearman correlation revealed that, except for plantarflexor spasticity, muscle strength of the affected ankle muscles, gait parameters and walking endurance were moderately to strongly associated with TUG scores in subjects with chronic stroke.
In conclusion, the results of this pilot study revealed that all the outcome measures used in the main study were reproducible when assessing subjects with stroke using the paradigm developed in our laboratory. There were significant differences in the level of spasticity, muscle strength of the affected ankle muscles, gait performance and walking endurance between healthy elderly and subjects with stroke. Of particular interest is that our findings demonstrated that the various parameters of motor performance such as muscle strength of the affected ankle plantarflexors, gait performance and walking endurance had good correlations with TUG scores in adults with chronic stroke. These findings make the TUG test particularly useful for assessing functional mobility in ambulant patients with chronic stroke.
3.2 Introduction

In order to assess the efficacy of an innovative home-based rehabilitation program for subjects with chronic stroke, 5 outcome measures were used to establish their baselines measures, to monitor their changes over time, and to compare their performance with those of the others at a similar stage during the recovery process. As detailed in Chapter 2, the outcome measures used in the main study included the measurements of: (i) spasticity of ankle plantarflexors by the Composite Spasticity Scale; (ii) maximum isometric voluntary contraction of ankle dorsi- and plantar-flexors recorded by a load-cell mounted on a custom-built foot frame and by EMG; (iii) gait performance in terms of temporal-spatial gait parameters by the GAITRite walkway system; (iv) walking endurance by the 6-minute walk (6MW) test; and (v) functional mobility by the timed “Up & Go” (TUG) test.

The objectives of the pilot study were: (1) to quantify the reliability of the 5 outcome measures used in the main study; (2) to examine the differences in spasticity of the ankle plantarflexors, muscle strength of ankle dorsi- and plantar-flexors, temporal-spatial gait parameters, walking endurance and functional mobility between healthy elderly and subjects with chronic stroke; (3) to delineate possible associations between the level of spasticity of ankle plantarflexors, ankle muscle strength, gait performance and 6-minute walk test on the one hand, and TUG scores on the other in subjects with chronic stroke.

3.3 Methods

3.3.1 Subjects
Two groups of subjects participated in the present study. Ten community-dwelling healthy elderly were recruited from several community centers for the elderly. All had no history of neurological disorders and pain of lower extremities during the past 3 months. They were ambulatory, independent in their activities of daily living, and could communicate and follow the testing procedures.

Eleven subjects with hemiplegia resulting from a single onset of stroke who met inclusion and exclusion criteria as detailed in Chapter 2 were recruited from a sample of convenience among the stroke members of the Hong Kong Stroke Association in Hong Kong, one of the largest self-help groups for people with stroke in Hong Kong. Briefly, subjects were included in the study if they had a history and clinical presentation (hemiparesis) of a single stroke at least one year post-stroke; were able to walk at least 10 m unassisted with or without walking aids and to give informed consent; had Abbreviated Mental Test (AMT) (Hodkinson 1972) score of $\geq 7$; and had stable medical condition to allow participation in the testing protocol. Subjects were excluded if they had any comorbidity or disability other than stroke, such as amputation or spinal cord lesion that would hinder proper assessment; any visual impairment or medical, musculoskeletal, neurological, or cardiovascular disorders that affected locomotion; and/or any uncontrolled health condition for which exercise was contra-indicated. The demographic characteristics of subjects with stroke are summarized in Table 3.1.
Table 3.1 Demographic characteristics of subjects with stroke

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>BMI (kg/m²)</th>
<th>Post Onset (yrs)</th>
<th>Side affected</th>
<th>Etiology</th>
<th>Walking Aids</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>67</td>
<td>19.05</td>
<td>3.2</td>
<td>R</td>
<td>Infarction</td>
<td>Quadripod</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>63</td>
<td>26.71</td>
<td>9</td>
<td>L</td>
<td>Infarction</td>
<td>Quadripod</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>64</td>
<td>23.49</td>
<td>2.8</td>
<td>R</td>
<td>Haemorrhage Unaided</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>54</td>
<td>27.17</td>
<td>11.1</td>
<td>R</td>
<td>Haemorrhage Stick</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>62</td>
<td>19.22</td>
<td>6.42</td>
<td>L</td>
<td>Infarction</td>
<td>Stick</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>56</td>
<td>25.49</td>
<td>6.4</td>
<td>R</td>
<td>Haemorrhage Stick + AFO</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M</td>
<td>64</td>
<td>23.86</td>
<td>3.2</td>
<td>R</td>
<td>Haemorrhage Stick + AFO</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>70</td>
<td>20.55</td>
<td>1.4</td>
<td>L</td>
<td>Infarction</td>
<td>Unaided</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>48</td>
<td>23.72</td>
<td>10.9</td>
<td>L</td>
<td>Haemorrhage Stick + AFO</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>68</td>
<td>21.84</td>
<td>4.6</td>
<td>L</td>
<td>Infarction</td>
<td>Stick</td>
</tr>
<tr>
<td>11</td>
<td>F</td>
<td>56</td>
<td>23.72</td>
<td>4.8</td>
<td>L</td>
<td>Haemorrhage Stick</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: M, male; F, female; R, Right; L, Left.

3.3.2 Measurement Procedures

All testing took place in the morning session in the laboratory of the Department of Rehabilitation Sciences at The Hong Kong Polytechnic University.

Each participant underwent the following assessments: spasticity of ankle plantarflexor by the Composite Spasticity Scale, ankle muscle strength by maximum isometric voluntary contraction of the ankle dorsiflexors and plantarflexors, gait performance by the GAITRite walkway system, walking endurance by the 6-minute walk test and functional mobility by the timed “Up & Go” test. The measurement protocols for the 5 outcome measures were exactly as
described in Section 2.5. All assessments were performed by the same investigator (NG-SMS), a physical therapist with more than 10 years of experience in clinical practice. To avoid possible diurnal variations, the 2 assessment sessions were performed at the same time on different days within 1 week.

3.3.3 Statistical Analysis

Descriptive statistics were used to depict subjects’ demographic characteristics and baseline measurements. To determine the test-retest reliability of all the outcome measurements across the 2 testing sessions, ICC(3,1) of Shrout and Fleiss (1979) was used. This model was selected due to the appropriateness of the model for (a) intra-rater reliability, (b) a two-way analysis, and (c) fixed effects of the raters (McGraw and Wong 1996). Intraclass correlation coefficients (ICCs) have been reported to be the best method for reliability analysis in test-retest situations (Baumgartner and Jackson 1987; Huck and Cormier 1996; Portney and Watkins 1993). One advantage cited for use of the ICC over the Pearson product-moment correlation is that ICCs allow comparison of absolute changes in scores between two sets of measures as opposed to change in group position (McGraw and Wong 1996). It has been suggested that an ICC value greater than 0.75 represents excellent reliability, whereas an ICC value between 0.40 and 0.75 represents fair to good reliability (Fleiss 1986). Paired t-tests were used to calculate within-group differences, and one-way analysis of variance (ANOVA) were used to calculate between-group differences of the mean values of all the outcome variables between patient and normal groups. When multiple
testings were performed, the Bonferroni method was applied to adjust for the alpha level (Hochberg and Benjamini 1990). The significance level in all statistical analyses was set at 0.05. When one-way ANOVA was applied in 2 groups comparison, the P-values would be equivalent to those computed by 2 sample independent t-tests by the SPSS (version 11.5) with adjustment due to heterogeneity of variances.

The relationships between spasticity of ankle plantarflexors, ankle muscle strength, gait performance and 6 MW and TUG scores were assessed by using Spearman correlation coefficients. All statistical analyses were performed by using the SPSS (version 11.5) for Windows. A significance level of P less than 0.05 was used for all statistical analyses.

3.4 Results

3.4.1 Comparison of Subjects’ Characteristics Between Groups

Ten healthy elderly (mean age, 63.5 ± 6.1 years, 5 men, 5 women) and 11 patients with chronic stroke (mean age 61.1 ± 6.8 years, 6 men, 5 women) who were similar in age and gender participated in the study. Table 3.2 shows a comparison of age, gender, height, weight and body mass index among these 2 groups of subjects. One-way ANOVA showed no statistically significant differences in the demographic characteristics between groups. All subjects with stroke had a history and clinical presentation (hemiparesis) of a single stroke at least one year post-stroke (mean duration after stroke onset, 5.6 ± 3.3 years; data not shown). Six subjects had left-side hemiparesis, and 5 subjects had right-side
hemiparesis. The etiology for 4 subjects was cerebral infarction, and the rest had cerebral hemorrhage (Table 3.1).

<table>
<thead>
<tr>
<th></th>
<th>Healthy Elderly</th>
<th>Subjects with Stroke</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=10)</td>
<td>(n=11)</td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>63.5 ± 6.1</td>
<td>61.1 ± 6.8</td>
<td>0.400</td>
</tr>
<tr>
<td>Gender (M/F)</td>
<td>5/5</td>
<td>6/5</td>
<td></td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.6 ± 0.1</td>
<td>1.6 ± 0.1</td>
<td>0.906</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.6 ± 9.0</td>
<td>61.3 ± 10.3</td>
<td>0.699</td>
</tr>
<tr>
<td>BMI (kg/m^3)</td>
<td>22.8 ± 2.7</td>
<td>23.2 ± 2.8</td>
<td>0.766</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Abbreviations: F, female; M, male.

### 3.4.2 Differences Between Subject Groups

#### 3.4.2.1 Composite Spasticity Scale (CSS)

High test-retest repeatability in CSS was found between 2 days, with ICC values ranged from 0.80 in healthy elderly in both left and right legs, to 0.97 and 0.80 respectively in the affected and unaffected legs of stroke subjects (Table 3.3). Table 3.3 shows the mean scores to be 5.8 ± 0.4 and 5.8 ± 0.3 respectively in left and right legs of healthy elderly. In subjects with stroke, the mean scores were 11.6 ± 1.4 and 6.2 ± 0.4 respectively for the affected and unaffected legs. The scores were found to be significantly increased (P=.000) in the patients' affected leg when compared with the mean score of both legs in healthy elderly (Table 3.3).
Table 3.3  Mean scores and intraclass correlation coefficients for the composite spasticity scale between days

<table>
<thead>
<tr>
<th></th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Mean Score</td>
<td>5.8 ± 0.4</td>
<td>5.8 ± 0.3</td>
</tr>
<tr>
<td>ICC between days</td>
<td>0.8</td>
<td>0.8</td>
</tr>
<tr>
<td>95% C.I.</td>
<td>0.40 - 0.94</td>
<td>0.40 - 0.94</td>
</tr>
</tbody>
</table>

Values are mean ±SD

* Denotes significant difference at $P < 0.05/13$ or $P < 0.004$ between healthy elderly and subjects with stroke using Bonferroni adjustment.

† Denotes significant difference at $P < 0.05/13$ or $P < 0.004$ between affected and unaffected side in subjects with stroke using Bonferroni adjustment.

3.4.2.2 Maximum Isometric Voluntary Contraction of the Ankle

**Dorsiflexors and Plantarflexors**

The test-retest correlation coefficients for peak force, peak torque, IEMG of agonists during ankle dorsiflexion and plantarflexion were 0.63 to 0.99 and 0.95 to 0.98 in healthy elderly and subjects with stroke respectively (Table 3.4).

Similarly, the EMG co-contraction ratios for dorsiflexion and planarflexion yielded good intraclass correlation coefficients of 0.94 to 0.99 in healthy elderly and 0.90 to 0.99 in subjects with stroke.

Table 3.5 shows mean values of the peak torque, IEMG and EMG co-contraction ratio measurements, in both left and right sides of the participating subjects. Results of paired $t$ test revealed that there were no statistically significant differences between the 2 legs of healthy elderly subject. When the affected side was compared with the unaffected side in subjects with stroke, all
measurements had significant differences (all $P<0.004$ after Bonferroni adjustment; Table 3.5), except for the EMG co-contraction ratio in dorsiflexion. When comparing the affected side of stroke subjects with that of healthy elderly by one-way ANOVA, all the measurements showed significant differences ($P<0.004$ after Bonferroni adjustment; Table 3.5), except for peak force, peak torque and EMG co-contraction ratio during ankle dorsiflexion. Despite the decrease in the peak dorsiflexion force and peak dorsiflexion torque on patients' affected side, it had not reached a significant level when compared with that of healthy elderly. In contrast, patients with stroke were significantly weaker in the mean peak plantarflexion force and torque of their affected leg (mean force and torque, $8.2 \pm 2.6$ and $11.2 \pm 3.5$ Nm Table 3.5), being only half of the mean value from both legs in healthy elderly (mean torque, $24.6 \pm 9.5$ Nm; data not shown in Table 3.5). These findings confirm that muscle strength of the affected plantarflexors was impaired in these stroke patients. Our results also showed that the EMG co-contraction ratio during MIVC of ankle plantarflexors was significantly higher in the affected side of stroke subjects ($P=0.004$), when compared with that of the unaffected side ($P=0.001$) and healthy elderly ($P=0.000$).
Table 3.4: Intraclass correlation coefficients between days for force, peak torque, IEMG and EMG co-contraction ratio measurements

<table>
<thead>
<tr>
<th></th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td><strong>Peak Force (kg)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>(0.95-1.00)</td>
<td>(0.96-1.00)</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>0.99</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(0.95-1.00)</td>
<td>(0.92-0.99)</td>
</tr>
<tr>
<td><strong>Peak Torque (Nm)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td></td>
<td>(0.95-0.99)</td>
<td>(0.96-0.99)</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>0.99</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(0.97-0.99)</td>
<td>(0.94-0.99)</td>
</tr>
<tr>
<td><strong>Integrated EMG(mV.s)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA in dorsiflexion</td>
<td>0.95</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>(0.83-0.99)</td>
<td>(0.78-0.98)</td>
</tr>
<tr>
<td>MG in plantarflexion</td>
<td>0.97</td>
<td>0.63</td>
</tr>
<tr>
<td></td>
<td>(0.89-0.99)</td>
<td>(0.47-0.89)</td>
</tr>
<tr>
<td><strong>Co-contraction Ratio(%)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>(0.91-0.99)</td>
<td>(0.78-0.98)</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>0.95</td>
<td>0.98</td>
</tr>
<tr>
<td></td>
<td>(0.82-0.99)</td>
<td>(0.91-0.99)</td>
</tr>
</tbody>
</table>

Values are ICCs with 95% coefficient interval in brackets. TA denotes the tibialis anterior muscle and MG denotes the medial gastrocnemius muscles.
Table 3.5 Comparison of force, torque, IEMG and EMG co-contraction ratio during ankle dorsiflexion and plantar-flexion between left and right sides of elderly subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Peak Force (kg)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>12.7 ± 6.0</td>
<td>13.8 ± 8.9</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>17.1 ± 7.2</td>
<td>17.3 ± 4.7</td>
</tr>
<tr>
<td>Peak Torque (Nm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>18.4 ± 9.3</td>
<td>20.1 ± 13.9</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>25.1 ±12.1</td>
<td>25.2 ± 8.2</td>
</tr>
<tr>
<td>Integrated EMG (mV.s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TA in dorsiflexion</td>
<td>0.13 ± 0.06</td>
<td>0.14 ± 0.06</td>
</tr>
<tr>
<td>MG in plantarflexion</td>
<td>0.09 ± 0.05</td>
<td>0.08 ± 0.03</td>
</tr>
<tr>
<td>Co-contraction Ratio(%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>9.7 ± 7.0</td>
<td>8.4 ± 3.6</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>25.3 ± 13.4</td>
<td>27.1 ± 13.4</td>
</tr>
</tbody>
</table>

Values are mean ± SD. TA denotes tibialis anterior muscle and MG denotes medial gastrocnemius muscles.

∗ Denotes significant difference at P <0.05/13 or P < 0.004 between healthy elderly and subjects with stroke using Bonferroni adjustment.

† Denotes significant difference at P <0.05/13 or P < 0.004 between affected and unaffected legs in subjects with stroke using Bonferroni adjustment.

3.4.2.3 Gait Performance

The test-retest correlation coefficients for gait velocity, cadence, step and stride length, stance time, single-leg and double-leg support duration ranged from 0.66 to 0.99 and from 0.94 to 0.99 in healthy elderly and subjects with stroke respectively (Table 3.6).
Table 3.6  Intra-class correlation coefficients of gait parameters in healthy elderly and subjects with stroke.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Gait Parameters</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Velocity (cm/s)</td>
<td>0.98 (0.94-1.0)</td>
<td>0.99 (0.96-1.0)</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>0.95 (0.81-0.99)</td>
<td>0.98 (0.94-0.99)</td>
</tr>
<tr>
<td>Step Length (cm)</td>
<td>0.93 (0.77-0.98)</td>
<td>0.97 (0.73-0.99)</td>
</tr>
<tr>
<td>Stride Length (cm)</td>
<td>0.99 (0.87-1.00)</td>
<td>0.99 (0.96-1.00)</td>
</tr>
<tr>
<td>Stance Time (% of gait cycle)</td>
<td>0.83 (0.46-0.96)</td>
<td>0.85 (0.51-0.96)</td>
</tr>
<tr>
<td>Duration of (% of gait cycle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-Leg Support</td>
<td>0.66 (0.41-0.90)</td>
<td>0.83 (0.36-0.96)</td>
</tr>
<tr>
<td>Double-Leg Support</td>
<td>0.91 (0.70-0.98)</td>
<td>0.94 (0.76-0.98)</td>
</tr>
</tbody>
</table>

Values are ICCs with 95% coefficient interval in brackets

Table 3.7 presents the mean values of gait velocity and other temporal-spatial gait parameters in both sides of the participating subjects. Results of paired t test revealed no statistically significant differences between the two legs of the healthy elderly group. When comparing the affected side with that of the unaffected side in subjects with stroke by paired t test, there were significant differences in stance time and single-leg support duration (% of gait cycle) (P<0.004 after Bonferroni adjustment; Table 3.7), which suggest the existence of temporal asymmetry in patients' gait pattern.
Table 3.7 Mean values for gait parameters in healthy elderly and subjects with stroke.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gait Parameters</strong></td>
<td>Left</td>
<td>Right</td>
</tr>
<tr>
<td>Velocity (cm/s)</td>
<td>125.6 ± 23.8</td>
<td>48.7 ± 22.1*</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>114.9 ± 9.7</td>
<td>84.3 ± 20.7*</td>
</tr>
<tr>
<td>Step Length (cm)</td>
<td>65.2 ± 7.6</td>
<td>64.7 ± 7.5</td>
</tr>
<tr>
<td>Stride Length (cm)</td>
<td>130.5±14.9</td>
<td>131.5 ± 15.3</td>
</tr>
<tr>
<td>Stance Time (% of gait cycle)</td>
<td>61.1 ± 1.8</td>
<td>61.7 ± 1.5</td>
</tr>
<tr>
<td>Duration of (% of gait cycle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single-Leg Support</td>
<td>38.8 ± 1.9</td>
<td>38.4 ± 1.5</td>
</tr>
<tr>
<td>Double-Leg Support</td>
<td>23.7 ± 3.0</td>
<td>23.6 ± 3.1</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

* Denotes significant difference at P<0.05/13 or P<0.004 between healthy elderly and subjects with stroke using Bonferroni adjustment.
† Denotes significant difference at P<0.05/13 or P<0.004 between affected and unaffected legs in subjects with stroke using Bonferroni adjustment.

Results of one-way ANOVA showed that there were statistically significant differences (P<0.001) in gait velocity, cadence between healthy elderly and subjects with stroke (Table 3.7). Patients with stroke walked significantly slower (mean gait velocity, 48.7 ± 22.1 cm/s) and with significantly reduced cadence (84.3 ± 20.7 steps/min) when compared with those of healthy elderly (respectively 125.6 ± 23.8 cm/s and 114.9 ± 9.7 steps/min). When the affected side of stroke subjects was compared with mean values of both sides from healthy elderly by means of one-way ANOVA, all measurements showed significant differences (P<0.004 after Bonferroni adjustment; Table 3.7), except for stance time and
double-leg support duration (% of gait cycle) of the affected leg and single-leg support duration of the unaffected leg. Subjects with stroke had significantly shorter step and stride length ($P=0.000$) on both affected and unaffected sides when compared with those of their healthy counterparts.

3.4.2.4 Six-Minute Walk (6 MW) Test

The test-retest correlation coefficients for the distance covered in 6 MW were 0.91 in healthy elderly and 0.98 in subjects with stroke (Table 3.8). Table 3.8 shows the mean distance covered in 6 MW in both groups. There were statistically significant differences in the distance covered between groups ($P=0.000$). The healthy elderly walked $416.5 \pm 95.2$ m in 6 minutes, while subjects with stroke walked only $202.3 \pm 88.0$ m, showing a reduction of slightly more than twofold.

| Table 3.8 Mean scores and intraclass correlation coefficients for distance covered in 6 MW between days |
|---------------------------------------------------------------|---------------------------------------------------------------|
| Healthy Elderly (n=10) | Subjects with Stroke (n=11) |
| Mean distance covered in 6 MW (m) | $416.5 \pm 95.2$ | $202.3 \pm 88.0^*$ |
| ICC between Days | 0.91 | 0.98 |
| (95% C.I.) | (0.60-0.98) | (0.94-0.99) |

Note: Values are mean ± SD. ICC denotes intraclass correlation coefficient. C.I. denotes coefficient interval.
* Denotes significant difference at $P<0.05/13$ or $P<0.004$ between healthy elderly and subjects with stroke using Bonferroni adjustment.
3.4.2.5 Timed “Up & Go” (TUG) Test

The test-retest correlation coefficients for TUG scores were 0.97 in healthy elderly and 0.95 in subjects with stroke (Table 3.9). Statistically significant differences were found in the time scores between groups ($P=0.000$; Table 3.9). The healthy elderly performed the test in $9.1 \pm 1.6$ seconds, while subjects with stroke took $22.6 \pm 8.6$ seconds, showing an increase of more than twofold.

Table 3.9 Mean scores and intraclass correlation coefficients for time scores in TUG between days

<table>
<thead>
<tr>
<th></th>
<th>Healthy Elderly (n=10)</th>
<th>Subjects with Stroke (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean score of TUG (s)</td>
<td>$9.1 \pm 1.6$</td>
<td>$22.6 \pm 8.6^*$</td>
</tr>
<tr>
<td>ICC between Days</td>
<td>0.97</td>
<td>0.95</td>
</tr>
<tr>
<td>(95% C.I.)</td>
<td>(0.87-0.99)</td>
<td>(0.84-0.99)</td>
</tr>
</tbody>
</table>

Values are mean ± SD. ICC denotes intraclass correlation coefficient. C.I. denotes coefficient interval.
* Denotes significant difference at $P<0.05/13$ or $P<0.004$ between healthy elderly and subjects with stroke using Bonferroni adjustment.

3.4.3 Correlations Between TUG scores and Other Variables

Relationships between the level of spasticity, muscle strength, gait performance, distance covered in 6MW test and TUG scores are presented in Table 3.10. Spearman correlation analyses revealed that there were no significant associations between the spasticity of ankle plantarflexors of both affected and unaffected legs and TUG scores (Table 3.10). The peak plantarflexion torque generated by MIVC of the affected and unaffected plantarflexors were moderately to strongly correlated with TUG scores in a negative manner ($r=-0.91$ and $r=-0.57$
respectively; \( P<0.01 \) (Fig 3.1A), while the IEMG of tibialis anterior muscle was moderately correlated with the TUG scores \( (r = -0.50, \ P<0.05) \). Significant negative relationships were found between the gait velocity \( (r = -0.86, \ P<0.01) \); Table 3.10) (Fig 3.1B) and cadence \( (r = -0.61, \ P<0.01) \) on the one hand, and TUG scores on the other. For the gait parameters, the step length and stride length of both affected and unaffected leg were significantly associated with TUG scores in

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Spearman correlation coefficients ( ( r ) )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Affected</td>
</tr>
<tr>
<td><strong>Composite Spasticity Scale</strong></td>
<td>-0.32</td>
</tr>
<tr>
<td><strong>MVIC</strong></td>
<td></td>
</tr>
<tr>
<td>Peak Torque (Nm)</td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>-0.42</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>-0.91*</td>
</tr>
<tr>
<td><strong>Integrated EMG (mV.s)</strong></td>
<td></td>
</tr>
<tr>
<td>TA in dorsiflexion</td>
<td>-0.50†</td>
</tr>
<tr>
<td>MG in plantarflexion</td>
<td>-0.42</td>
</tr>
<tr>
<td><strong>Co-contraction Ratio (%)</strong></td>
<td></td>
</tr>
<tr>
<td>Dorsiflexion</td>
<td>0.24</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td>0.10</td>
</tr>
<tr>
<td><strong>Gait Parameters</strong></td>
<td></td>
</tr>
<tr>
<td>Velocity (cm/s)</td>
<td>-0.86*</td>
</tr>
<tr>
<td>Cadence (steps/min)</td>
<td>-0.61*</td>
</tr>
<tr>
<td>Step Length (cm)</td>
<td>-0.60*</td>
</tr>
<tr>
<td>Stride Length (cm)</td>
<td>-0.73†</td>
</tr>
<tr>
<td>Stance Time (s)</td>
<td>-0.19</td>
</tr>
<tr>
<td>Duration of (s)</td>
<td></td>
</tr>
<tr>
<td>Single-Leg Support</td>
<td>-0.60*</td>
</tr>
<tr>
<td>Double-Leg Support</td>
<td>0.45†</td>
</tr>
<tr>
<td><strong>Six-Minute Walk Test (m)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td>-0.93*</td>
</tr>
</tbody>
</table>

*\( P<0.01 \), †\( P<0.05 \), Spearman correlation coefficients.
Fig 3.1 Relationships between:
(A) peak plantarflexor torque generated by affected leg ($r=-0.91$, $P<0.01$);
(B) gait velocity ($r=-0.86$, $P<0.01$);
(C) step length of unaffected leg ($r=-0.77$, $P<0.01$);
(D) stance time of unaffected leg ($r=-0.57$, $P<0.05$);
(E) single-leg support duration of affected leg ($r=-0.60$, $P<0.01$);
(F) distance covered in 6 MW ($r=-0.93$, $P<0.01$), and timed "Up & Go" scores.
a negative manner ($r=-0.60 \text{ to } -0.77; P<0.05; \text{ Table 3.10}$) (Fig 3.1C). The stance time ($\%$ of gait cycle) of the unaffected leg (Fig 3.1D) and double-leg support duration ($\%$ of gait cycle) of both affected and unaffected legs were moderately associated with the TUG scores in a positive manner ($r=0.45 \text{ to } 0.57; \text{ Table 3.10}$), while single-leg support duration ($\%$ of gait cycle) of the affected leg was associated with the TUG scores in a negative manner ($r=-0.60; P<0.01$) (Fig 3.1E). Finally, a significant negative relationship was found between the distance covered during the 6 MW test and TUG scores ($r=-0.93, P<0.01; \text{ Table 3.10}$) (Fig 3.1F).

3.5 Discussion

3.5.1 Composite Spasticity Scale

The results of the pilot study demonstrated that data from the Composite Spasticity Scale were reproducible when being used to evaluate stroke subjects with moderate to severe level of spasticity on different days. Results of our study in chronic stroke subjects with spastic plantarflexors are consistent with similar findings in stroke patients with variable spasticity in their lower extremities (Levin and Hui-Chan 1992, 1993, 1994; Goulet et al. 1996; Nadeau et al. 1999).

Spastic hypertonia or spasticity is a motor disorder characterized by a velocity-dependent increase in muscle tone resulting from hyperactivity of the stretch reflexes. The stretch reflexes comprise both phasic and tonic components. Many methods have been proposed to measure spasticity, and controversies arise whether these clinical tests only measure the stretch reflex itself (Bohannon and Smith 1987; Fowler et al. 1998). Chan (1986) had developed a new subjective
index of spasticity. The index is a composite score consisting of the Achilles tendon reflex, resistance to passive stretching as evaluated by the modified Ashworth scale, and clonus. This scale evaluates both tonic and phasic stretch reflexes. Nadeau and colleagues (1998) used this scale to evaluate spasticity of the ankle joint in 19 subjects with chronic stroke. They found that the 3 scale items had good internal consistency, indicating that this scale was suitable for assessing spasticity in stroke subjects. According to the scoring criteria of Composite Spasticity Scale (Levin and Hui-Chan 1992), 1-6 represent no spasticity, whereas 7-9, 10-12 and 13-16 denote mild, moderate and severe spasticity respectively. The subjects with stroke who participated in the present study had moderate to severe spasticity in the affected ankle plantarflexors.

3.5.2 Maximum Isometric Voluntary Contraction of Ankle Dorsiflexors and Plantarflexors

Our results of high test-retest repeatability in MIVC measurements support the recent contention that muscle strength of the affected extremities of stroke patients is quantifiable, and that its measurements are reliable even in the presence of moderate to severe spasticity. Several reasons may account for the high test-retest reliability found in the present study. First, the test and retest sessions of muscle strength were scheduled for 2 days within a week, which may have prevented both learning and fatigue effects on the reproducibility of muscle strength measures. Previous studies (Anderson 1996; Holmback et al. 1999; Woodson C et al. 1995) have shown that the test-retest reliability of isokinetic muscle testing is generally higher when the intersession interval ranges between
24 hours and 7 days. Second, the 1-minute resting interval adopted between trials in this study may have prevented muscle fatigue (DeLuca 1997). Third, brief training on how to produce maximal muscle contraction before data recording may have effectively familiarized the subjects with the testing equipment and protocol which, in turn, may have enhanced the reproducibility for muscle strength measures. Finally, the use of consistent testing protocol, positioning, stabilization, environment, and instructions during the 2 testing sessions may have also contributed to the test-retest reliability of isometric strength measures.

The ICC for the plantarflexor IEMG in healthy subjects was relatively low and the confidence interval was wide when compared with the other MIVC parameters. Two reasons may account for such wide confidence interval in the present study. The first reason may be due to the small sample size in our study (i.e. 11 healthy elderly). The second reason may be due to difficulties in isolating ankle plantarflexion during assessment of MIVC despite fixation of the lower leg because gastrocnemius is a two-joint muscle.

Our results also showed that peak MIVC torque and IEMG of the affected ankle plantarflexors were significantly weaker than those of healthy elderly ($P<0.004$; Table 4). In a study delineating muscle strength in patients with chronic stroke, Levin and Hui-Chan (1994) reported that the peak force generated during MIVC of ankle dorsiflexors ($3.4 \pm 2.9$ kg) and plantarflexors ($15.1 \pm 6.9$ kg) of affected legs in patients with chronic stroke were significantly decreased when compared with age-matched controls. Our finding of the peak force generated by the ankle plantarflexors ($8.2 \pm 2.6$ kg) was lower when compared with that of Levin and Hui-Chan (1994). This difference could be due to
differences in the positioning of the patient during assessment of MIVC in the 2 studies. In our study, ankle dorsi- and plantar-flexor strength was assessed in the lying position with the knee in 50° of flexion, whereas Levin and Hui-Chan assessed MIVC of ankle muscles in standing with the knee straight. In other words, the gastrocnemius was in a more shortened position in our study, thereby decreasing their torque generating capability from a biomechanical perspective (Herbert 1988).

Muscle weakness and paralysis of upper and lower limbs contralateral to the brain lesion are prominent consequences of stroke (Adams et al. 1990; Andrews 2000; Colebatch and Gandevia 1989; Davies et al. 1996; Schneider and Gautier 1994). Such weakness was found to be particularly pronounced in the distal lower leg muscles of stroke individuals (Adams et al. 1990; Sjostrom et al. 1980). There may be several causes for the loss of muscle strength including decreased capacity to activate the motor units, reduced number of functioning motor units, reduced motor unit firing rates, and co-contraction of antagonists during movement (Bourbonnais and Vanden Noven 1989; Ng and Shepherd 2000). Although strength deficits on the unaffected side have also been identified in other studies (Colebatch and Gandevia 1989; Bohannon and Andrews 1995), we cannot find any significant differences when comparing the unaffected leg of patients with stroke with the normal leg of the healthy elderly (Table 3.5). In our study, all subjects were community-dwelling stroke survivors who were active members of self-help groups after being discharged from hospital. Their functional status may have been relatively higher than that of the general population of stroke survivors in Hong Kong.
Aside from the overall decrease in peak torque generated by the affected ankle dorsi- and plantarflexors, our finding revealed a significant increase in EMG co-contraction ratio during ankle plantarflexion (Table 3.5). Muscle co-contraction has been defined as the simultaneous activation of agonist and antagonist muscle groups crossing the same joint and acting in the same plane (Olney 1985). Although co-contraction is commonly associated with spasticity, it is also observed in persons with normal muscle tone when muscle weakness is present or during the learning of novel motor skills and the performance of precision motor task (Damiano 1993). Increased co-contraction has been shown quantitatively in patients with stroke (Chen et al. 2000; Levin and Hui-Chan 1994). Such impaired antagonist inhibition could have resulted from the disordered descending motor command (Kasai and Komiyama 1988; Lundberg et al. 1987). Lesion of the pre-central cortex, often occurring after cerebrovascular accidents, may result in disturbances of the co-ordination between reciprocal and co-activation command systems (Humphrey and Reed 1983). The disrupted agonist recruitment and increased EMG co-contraction ratios during voluntary ankle plantarflexion in the lower limb of our subjects is consistent with similar findings in the lower limbs of hemiparetic patients studied by our research group and other investigators (Chen et al. 2000; Knutsson and Martensson 1980; Levin and Hui-Chan 1994).

3.5.3 Gait Performance

In agreement with previous findings in healthy young and elderly subjects (Bilney et al. 2003; Menz et al. 2003), the present study showed that the
GAITRite walkway system provided reliable measurement of temporal-spatial gait parameters in healthy elderly and subjects with chronic stroke. The system, therefore, can be used with confidence to measure the effects of interventions over a course of treatment in stroke populations.

The ICC for the stance time and duration of single-support in healthy subjects was relatively low and the confidence interval was wide when compared with other gait parameters. Two reasons may account for such wide confidence interval in the present study. The first reason may be due to the small sample size in our study (i.e. 11 healthy elderly). The second reason may be due to the known wide variability of stance time and duration of single-leg support duration in healthy elderly (Olney and Richards 1996).

All stroke subjects showed significantly decreased gait velocity, cadence, step and stride length, shorten single-leg support duration (% of gait cycle) on affected legs, and lengthen stance time and double-leg support duration (% of gait cycle) than did healthy elderly (Table 3.7). These results were in agreement with the observations of other investigators (Bohannon 1987; Dettman et al. 1987; von Schroeder et al. 1995). Variations in the magnitude of these parameters were due to the wide variability of gait after stroke, as reflected by the high standard deviations of the gait parameters. Comfortable walking speeds of our healthy elderly and stroke subjects ranged from 0.99 to 1.8 m/s and 0.13 to 0.91 m/s respectively, which were consistent with the previous findings. Empirical data have shown that the gait velocity of healthy adults averaged about 1.4 m/s (Murray et al. 1969), whereas patients with stroke of varying severity of similar ages ranged from approximately 0.18 to 1.03 m/s (Brandstater et al. 1983;
Knutsson and Richards 1979; Olney et al. 1994; Wade et al. 1987). Consistent with the decrease in gait velocity, both cadence and stride length were lower than those of healthy elderly (Table 3.7), which is considered to be a result of poorer motor control (Bohannon 1987).

The hemiplegic gait in stroke subjects was found to be characterized by decreased walking speed, decreased stance time on the affected side and increased stance time on the sound side (Brandstater et al. 1983). The stance time (% of gait cycle) on the unaffected leg (76.0 ± 6.2 %; Table 3.7) was longer than that of the affected leg (60.1 ± 7.8 %; \( P \leq 0.004 \)). It is possible that reduced single-leg support duration (% of gait cycle) of the affected leg (24.3 ± 6.0 %) when compared with that of the unaffected leg (39.3 ± 7.7 %) could increase the stance time (% of gait cycle) on the unaffected limb. Another possibility could be due to balance deficiencies and difficulty in moving the body over an unstable affected limb. Moreover, patients with stroke tended to spend more time in double-leg support (% of gait cycle) than healthy elderly (Table 3.7), presumably because this was a more stable arrangement to compensate for their poorer balance.

In most of our patients, the step length of the unaffected leg was shorter than that of the affected leg (Table 3.7). It is possible that decreased stability of single-leg support duration of the affected leg would decrease the time for the contralateral unaffected limb to swing, resulting in decreased step and stride length when compared with those of the affected leg. Another possibility would be the presence of spasticity or contracture of the affected plantarflexors in stroke subjects, which may limit the forward rotation of tibia over the foot in midstance.
of gait cycle. This would obstruct the centre of gravity of the whole body moving forward and cause a smaller step length of the unaffected leg.

3.5.4 Six-Minute Walk (6 MW) Test

The result showed that intra-rater reliability for the measurement of 6 MW was good to excellent in healthy elderly and patients with stroke, with ICC values of 0.91 and 0.98 respectively (Table 3.8). As far as we are aware, this is the first study to demonstrate the reliability of 6 MW in patients with stroke. This finding suggests that the distance covered in the 6 MW can be used to measure the effects of interventions over a period of treatment in stroke populations.

Our results showed that the distance covered in 6 WM were significantly shorter in subjects with stroke when compared with that of healthy elderly (Table 3.8). Several reasons may account for these differences. Subjects with hemiparetic gait deficits had been found to consume 1.5 to 2 times the energy costs for ambulation, when compared with controls who walked overground at the same velocity (Corcoran et al. 1970; Gerston and Orr 1971). Physical deconditioning along with age-associated declines in fitness and muscle mass can further contribute to activity intolerance, compromising patients’ capacity to meet the high-energy demands of hemiparetic gait (Hagberg 1987; Schwartz and Buchner 1994). The mean walking distance of our stroke subjects (202.3 ± 88.0 m; Table 3.8) were comparable with the range of 150 to 207 m reported in previous studies (Dean et al. 2000; Duncan et al. 1998). Since measure of endurance in terms of walking distance requires some lower limb strength and
balance control from stroke patients, any baseline differences in these variables among the different studies may account for such variability.

3.5.5 Timed "Up & Go" (TUG) Test

This is the first systematic study to investigate the test-retest reliability obtained with the TUG in people with chronic stroke. Our results are encouraging because excellent between-days test-retest reliability (=0.95; Table 3.9) was found, indicating that performance-based measures such as the timed "Up & Go" test can be incorporated into the evaluation process to assess the mobility of the patients with stroke. The high test-retest reliability of TUG scores found in the present study, with ICC values (=0.95-0.97) in both healthy elderly and patients with stroke, were similar to those reported in the majority of studies on the elderly population (N=10-30) (ICC=0.81-0.99) (Hughes et al. 1998; Podsiadlo and Richardson 1991; Shumway-Cook et al. 2000). Our well-defined clinical protocol, which standardized the chair type, movement sequencing, and instructions, may have resulted in the high reliability of the data recorded in individuals who had a stroke.

Our mean data for TUG scores (22.6 ± 8.6; Table 3.9) obtained in subjects with chronic stroke were similar to those reported by Dean et al. (2000), but slower than those of our healthy elderly (9.1 ± 1.6; Table 3.9) and of older adults who functioned independently (Hughes et al. 1998; Podsiadlo and Richardson 1991; Newton 1997). Dean et al. (2000) showed that TUG scores ranged from 27.4 (SD 23.2) to 29.1 (SD 29.4) seconds in 12 subjects with chronic stroke before a 4-week training program. In the study by Hughes et al. (1998), 20
independent community-dwelling elderly people, aged 65 to 86 years (mean 81 ± 4.7 years), had a mean TUG score of 13.05 seconds. In another study by Newton (1997), 251 older adults including 31 people who used an ambulatory device, aged 60 to 95 years (mean 74 ± 7.7 years), were found to have a mean TUG score of 15 seconds. The increase in TUG time score found by our study is consistent with the symptomatology of stroke including muscle weakness and spasticity. Muscle weakness is characterized by difficulty in generating appropriately timed and sufficient muscle force to accomplish a given functional task. When spasticity is severe enough, it may lead to “stiffness” of the affected limb that is characterized by a lack of movement or movement with abnormal posture. Either of or both symptoms could explain the lengthened time score of TUG in subjects with stroke.

Podsiadlo and Richardson (1991) found that older adults who were able to complete the TUG task in less than 20 seconds were independent in the transfer tasks involved in activities of daily living, while those requiring 30 seconds or longer to complete the task tended to be more dependent in their activities of daily living and required assistive devices for ambulation. Results of our study are largely consistent with these findings. The mean TUG scores for our subjects with stroke were 22.6 seconds, which fell in the inconclusive range cited by Podsiadlo and Richardson (1991). Note that although our entire stroke subject group was made up of community dwelling individuals who were independent in the basic motor skills like chair transfers and going outside alone, none of them lived alone. Nearly all of them required some help with activities involving more
complex mobility skills such as shopping, housework, laundry and meal preparation.

3.5.6 Correlations with TUG scores

In this study, the relationship between direct impairment (spasticity of affected ankle plantarflexors, and muscle strength), gait performance (gait velocity, temporal and spatial asymmetry), functional measures (6 MW) and TUG scores in patients with chronic stroke were examined.

Although the presence of moderate to severe hypertonus is believed to contribute to the inability of persons with hemiparesis to walk faster, the results of correlation analyses revealed that TUG scores did not correlate with ankle spasticity. No previous studies have addressed the relations between lower limb spasticity and TUG scores. However, research has shown controversial results regarding the relationship between ankle plantarflexor spasticity and walking speed in patients with hemiplegia. Similar results, i.e. low correlations between the level of spasticity and locomotor function in the lower limb of ambulant chronic stroke individuals have also been found in many other studies (Bohannon et al. 1987; De Bujanda et al. 2003; Nadeau et al. 1999; Norton et al. 1975). By using Composite Spasticity Scale, Nadeau et al. (1999) did not find a significant correlation ($r=-0.009, P>0.05$) between the spasticity of the affected ankle plantarflexors and comfortable walking speed of patients with mild to moderate stroke. In contrast, several studies (Hesse et al. 1994c, 1996; Reiter et al. 1998) reported that injection of botulinum toxin type A into spastic plantarflexors reduced the muscle tone and premature activity of these muscles during the
terminal swing and early stance of the gait cycle, thus improving the gait velocity of patients with hemiparesis. In a study on 26 subjects with mild to moderate spastic hemiparesis after onset of a single stroke, Hsu et al. (2003) found that spasticity of the affected plantarflexors was the most important independent determinant of temporal and spatial gait asymmetry during walking at comfortable \((R^2=0.76\) for temporal asymmetry; \(R^2=0.46\) for spatial asymmetry) and fast speeds \((R^2=0.75\) and \(R^2=0.45\)). Eng et al. (2002a, 2002b) also showed that self-selected gait speed and 6 MW distance were related to spasticity, muscle strength and balance in persons with stroke.

Our finding of a low correlation between the level of spasticity and TUG scores in the lower limb may have 2 explanations. First, the small sample size in the present study may not be sufficient to detect the correlations between plantarflexor spasticity and TUG scores. Secondly, our stroke subjects suffered from moderate to severe level of spasticity in their affected ankle plantarflexors. In order to compensate for the increased plantarflexion caused by their spastic plantarflexors, they may use a compensatory strategy such as increased hip and knee flexion to clear the affected foot during the swing phase. This would lengthen the swing trajectory and swing-phase duration of the affected leg. Longer swing-phase duration of the affected leg is equivalent to longer single-leg support duration (% of gait cycle) on the unaffected side. In our study, we found that single-leg support (% of gait cycle) on the affected leg was significantly shorter than that on the unaffected leg (Table 3.7), and the stance time (% of gait cycle) of the unaffected leg was moderately correlated with the TUG scores \((r=0.57, P<0.01; \text{Table 3.10})\). This finding thus supported our presupposition.
A strong negative association was identified between the peak torque generated by medial gastrocnemius during maximum isometric plantarflexion and the TUG scores \( r=-0.91 \) in the affected leg and \( r=-0.57 \) in the unaffected leg; \( P < 0.01 \); Table 3.10) (Fig 3.1A). Although no previous study has investigated the relations between lower limb muscle strength and TUG scores, many researchers have shown that the strength of the affected ankle plantarflexors correlated with comfortable and/or fast gait velocities in patients with stroke of varying severity (Bohannon 1989; Olney et al. 1991, 1994; Winter 1983, 1991). Nadeau et al. (1999) found that muscle strength of the affected ankle plantarflexors significantly predicted the fastest walking speed in stroke patients. Plantarflexor muscles are an important muscle group in gait speed regulation in healthy subjects, because they generate a large part of the energy required to move the legs forward during the push-off phase (Winter 1983). The shortening or concentric contraction of the plantarflexor muscles during the push-off phase results in an energy generation which allows the lower limb to be moved forward (Winter 1991). Consequently, if the plantarflexors were weakened, they could lengthen the time required to perform TUG. Such findings support the idea that treatment techniques improving the motor function of the paretic lower limb, particularly those aiming to strengthen the ankle plantarflexors, would improve gait performance and functional abilities in adults with chronic stroke.

The lack of a relationship between EMG co-contraction ratio and TUG scores during either dorsiflexion or plantarflexion is somewhat surprising. One might suspect that because excessive co-contraction is considered abnormal, subjects with a greater co-contraction ratio in their ankle muscles would have
poorer performance of functional tasks requiring ankle movements. This was not the case in the present study. Such a negative finding could be related to our small sample size and limited spectrum of the functional status tested. Moreover, the degree of EMG co-contraction required during isometric maximal exertions and walking are known to be different, because of the inherently different nature of each task. In fact, similar negative findings have been reported in patients with stroke (Bohannon and Andrews 1996).

A strong negative association was identified between the gait velocity and TUG scores recorded at a comfortable walking speed ($r=-0.86; P<0.01$; Table 3.10) (Fig 3.1B). Similar results in ambulant chronic stroke individuals have also been found in a number of other studies (Bohannon et al. 1987; De Bujanda et al. 2003; Nadeau et al. 1999; Norton et al. 1975; Richards et al. 1999). For example, Richards et al. (1999) reported a Pearson correlation coefficient of $r=-0.80$ between gait velocity and TUG score in a group of 35 patients with acute or subacute stroke. The relationship was even stronger for the group without a walking aid ($r=-0.85$) than the group needing an aid ($r=-0.57$). The TUG is not a "simple" walking task. It includes a series of motor tasks that also challenge balance control in addition to muscle strength and co-ordination, e.g. when rising up from a chair to take the first step and then turning. Nevertheless, it is not surprising that the relationship between gait speed and TUG score was stronger when compared with some other clinical measures, because the TUG test includes walking per se. Results of previous studies (Brandstater et al. 1983; Knutsson and Richards 1979; Olney et al. 1994; Wade et al. 1987) had shown that, consistent with decreased gait velocity decreased, step length, stance time and double-leg
support duration of both affected and unaffected legs were shortened when compared with those of the healthy elderly. This may explain why step length (Fig 3.1C) and double-leg support duration (% of gait cycle) of the affected and unaffected legs (Table 3.10) were correlated with TUG scores.

A strong negative association was also identified between the distance covered in the 6 MW test and TUG scores ($r=-0.93; P<0.01; \text{Table 3.10}$) (Fig 3.1F). The 6 MW test was originally developed to assess exercise endurance in cardiorespiratory and cardiovascular populations (Guyatt et al. 1985; McGavin et al. 1978). More recently, the test has been recognized as a general indicator of overall physical performance and mobility in older populations (Duncan et al. 1993; Harada et al. 1999). It has also been used to document the improvement of walking endurance after exercise interventions in subjects with stroke (Dean et al. 2000; Duncan et al. 1998). In a recent study, Eng et al. (2002a) found that self-selected gait speed was strongly correlated ($r=0.92; P<0.01$) with the distance covered in 6 MW in 25 subjects with chronic stroke. The investigators (2002a) suggested that besides cardiovascular performance, factors such as spasticity, muscle weakness and balance impairment could potentially influence the gait speed and the distance walked. As gait speed were strongly correlated with TUG scores in a negative manner, it is reasonable to expect that the distance covered in 6 MW would have a negative correlation with TUG scores.

Generalization of the results of this study should be limited to stroke patients with moderate to severe level of spasticity in the ankle plantarflexors. It would be interesting for future studies to examine the effects of treatment on TUG scores
and related measures and their relationships in ambulant hemiparetic subjects with chronic stroke.

3.6 Conclusions

The results of this pilot study revealed that the measurement protocols for spasticity of ankle plantarflexors, maximum isometric voluntary contraction of ankle dorsi- and plantar-flexors, temporal-spatial gait parameters, walking endurance in terms of 6-minute walk test and functional mobility in terms of timed "Up & Go" test were reproducible, when assessing subjects with stroke using the experimental paradigm developed in our laboratory. They would be valid tests for evaluating the effectiveness of a given rehabilitation regime in subjects with chronic stroke fulfilling the inclusion criteria of our study.

Results of the present study also demonstrated that there were significant differences in the level of spasticity, muscle strength of the ankle plantarflexors, gait performance and walking endurance between the healthy elderly and subjects with stroke. These between-group differences remained statistically significant when a non-parametric test (Mann-Whitney U test) was used. Specifically, our findings showed that subjects with chronic stroke had a significantly higher level of spasticity in their affected ankle plantarflexors, weaker plantarflexors, slower walking speed, more asymmetrical gait pattern and poorer walking endurance and functional mobility when compared with those of healthy elderly. Of special interest is that, this study also demonstrated the existence of strong relationships between the TUG scores on the one hand, and strength of ankle plantarflexors, spatio-temporal gait parameters and walking endurance as assessed by the 6 MW
test on the other. These findings make the TUG test particularly useful for assessing functional mobility in ambulant patients with chronic stroke.
Chapter 4

A Comparison of the Relative Effectiveness of Four Treatment Protocols on Spasticity and Muscle Function in Subjects with Chronic Stroke
4.1 Summary

The objectives of the present study were to compare the relative treatment effectiveness of (i) TENS, (ii) TENS+task-related training (TRT); (iii) placebo TENS (PLBO)+TRT, and (iv) control without active treatment on spasticity and muscle functions in patients with chronic stroke. Improvements of muscle functions were measured in terms of the peak torque generated, integrated EMG of the agonist muscle and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion.

The present study is a single-blinded randomized controlled trial. The sample size was calculated a priori. Eighty-eight subjects with single onset of stroke at least one year ago were recruited. The subjects were 57.3 ± 8.1 years old, 67 males and 13 females, 46 with ischemic stroke and 34 with hemorrhagic stroke, 47 with left hemiparesis and 33 with right hemiparesis. The average duration since onset of stroke was 5.3 ± 3.5 years.

Subjects were randomly assigned to 1 of 4 groups: TENS, TENS+task-related training (TRT), PLBO+TRT and control groups. All subjects received daily treatment according to the group being assigned, once a day, 5 days a week for 4 weeks. Eighty subjects completed the study: 19 in the TENS group, 21 in the TENS+TRT group, 20 in each of PLBO+TRT and control groups. Outcome measurements included spasticity of the affected ankle plantarflexors assessed by the Composite Spasticity Scale, and muscle functions in terms of maximum isometric voluntary contraction (MIVC) of ankle dorsi- and plantar-flexor muscles, recorded by peak torque and surface electromyography (EMG) of the tibialis anterior (TA) and medial gastrocnemius (MG) muscles from which IEMG and
EMG co-contraction ratios were computed. These were measured before treatment on day 1 ($T_0$), immediately after treatment on day 1 ($T_1$); after 2 weeks ($T_2$) and 4 weeks of treatment ($T_3$); and at 4-weeks follow-up after treatment ended ($T_{FU}$). All data were analyzed with SPSS (version 11.5) software package.

When compared with baseline values within each group, our results showed that both TENS+TRT and PLBO+TRT groups produced significant % decrease in spasticity at $T_3$ and $T_{FU}$. Interestingly, significant increases in most muscle functions of the affected ankle dorsiflexors and plantarflexors occurred even earlier, from $T_2$ to $T_{FU}$ for most measures. The TENS group demonstrated significant within-group % decrease in spasticity at $T_3$ and $T_{FU}$, with improved muscle functions found mostly in the affected ankle dorsiflexors but seldom in the affected ankle plantarflexors. In contrast to the 3 intervention groups, there were negligible changes in either spasticity or muscle functions of the affected leg in the control group over the entire 8-week period.

When comparing among groups, all 3 intervention groups demonstrated significant % decreases in Composite Spasticity Scores (CSS) after 4 weeks of treatment when compared with that of control. Among the 3 intervention groups, both TENS and TENS+TRT groups demonstrated greater decreases earlier (from $T_2$ on) when compared with those of the PLBO+TRT group (from $T_3$ on). Of special interest is that all 3 intervention groups were able to maintain the decreases in CSS scores even 4 weeks after treatment ended at $T_{FU}$.

Subjects in all 3 intervention groups showed significant increases in the peak torque and integrated EMG of the affected tibialis anterior muscles during dorsiflexion after 4 weeks of treatment ($T_3$) when compared with those of control.
Furthermore, the 2 TENS and TENS+TRT groups showed earlier % increases in peak dorsiflexion torques (respectively from T1 to T3 and from T1 on) than those of the PLBO+TRT group (from T3 to TFU), when compared with those of the control group showing negligible change over the 8-week period. However, only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the significant increases at TFU. For the EMG co-contraction ratio during dorsiflexion, the same 2 TENS groups showed significant % reduction when compared with that of the control group after 4 weeks of treatment, but not the PLBO+TRT group.

With regard to the affected ankle plantarflexors, the 2 exercise (TENS+TRT and PLBO+TRT) groups but not the TENS group had significant % increases in peak torque, IEMG of the MG muscle and EMG co-contraction ratio after 4 weeks of treatment (T3) when compared with those of the control group. Moreover, the combined TENS+TRT group showed earlier % increases in peak plantarflexion torques (from T1 on) and in IEMG of the MG muscle (T2 and T3) than those of the PLBO+TRT group (respectively from T2 on and at T3 only), when compared with control group values. For the co-contraction ratio during plantarflexion, the same combined (TENS+TRT) group also showed significantly greater % reductions than those of both TENS and control groups, respectively from T2 and T3 on.

The conclusion from this study is that a home-based rehabilitation program involving TENS and/or task-related training is feasible. More importantly, TENS and TRT applied separately or in combination daily, 5 days a week for 4 weeks, were effective in reducing spasticity and improving aspects of ankle muscle functions even in patients who had stroke at least one year ago.
Moreover, the results demonstrated that 20 sessions of combined TENS+TRT treatment was superior to either TENS alone or PLBO+TRT in enhancing recovery of muscle strength in chronic stroke survivors.
4.2 Introduction

Although TENS has been used in stroke rehabilitation over the last decades, there were only 2 single-blinded randomized clinical trials conducted with placebo groups on the influence of high frequency TENS in stroke patients between 1966 and 2003 (Levin and Hui-Chan 1992; Yan and Hui-Chan 2002). Levin and Hui-Chan (1992) studied the effects of 3 weeks of high-frequency (99 Hz) TENS, applied over the peroneal nerve in 13 subjects with chronic stroke. They found that, in contrast to placebo stimulation which produced no significant effects in the control group, repeated applications of TENS over 3 weeks decreased clinical spasticity, stretch reflexes in the spastic ankle plantarflexors and EMG co-contracting ratios. The treatment also increased vibratory inhibition of the soleus H reflex and voluntary ankle dorsiflexing force up to 820%. As a pioneering study in this area, there are some limitations in this study such as small sample size, and lack of follow-up data beyond the completion of treatment.

In addressing the problems of previous studies, Yan and Hui-Chan (2002) examined the efficacy of 3 weeks of high frequency TENS with standardized physiotherapy and occupational therapy training in 56 subjects with acute stroke. TENS was applied over 4 acupuncture points of the affected lower extremity: ST 36 (Zusanli), LR 3 (Taichong), GB 34 (Yanglingquan), and UB 60 (Kulun). In contrast to placebo stimulation, they showed that repeated TENS significantly slowed the development of spasticity in the affected ankle planatreflexors, and improved motor recovery in the affected lower leg, as denoted by increased ankle dorsiflexion torque and decreased EMG co-contracting ratio during ankle dorsiflexion in patients with acute stroke.
Although muscle weakness is recognized as a major cause of disability in patients with stroke (Fellows et al. 1994; Gowland et al. 1992; Sahrmann and Norton 1977), strengthening exercises are often not included in the physiotherapy programs designed for them. This is due to a traditional presumption that strengthening exercises could increase spasticity, and hence movement control in stroke patients (Bobath 1990; Cornall 1991). Such views are presented even in the recent textbooks on stroke management (Edwards 1996; Ryerson and Levit 1997). Preliminary findings of some recent research studies actually do not support the belief that strength training leads to an increase in spasticity (hyperreflexia), hypertonia (resistance to passive movement) or abnormal muscle activities (Brown and Kautz 1998; Hsiao and Newham 1998; Miller and Light 1997; Teixeira-Salmela et al. 1999). Regretfully, there were some limitations in these studies, such as the absence of a control group and small sample size. More robust studies such as randomized controlled trials are desirable to determine the effects of strengthening exercises on spasticity in stroke patients.

When designing effective physical rehabilitation for neurological patients, “task specificity” is another important consideration. Carr and Shepherd (1998) pointed out that task specificity is central to skill acquisition, muscle strengthening, and postural control. Although task-related training is gaining theoretical and experimental support as a means of improving motor functions after stroke (see 1.4.3 for details), few properly designed studies had been conducted to validate such a treatment approach. There were only 4 single-blinded randomized clinical trials reported between 1966 and 2004 (Ada et al. 2003; Dean et al. 2000; Dean and Shepherd 1997; Richards et al. 1993). Most of
these studies involved the use of expensive and sophisticated training equipment which may limit the applicability of their findings. Moreover, there is still little consensus on the optimal exercise protocol for stroke patients.

There has been no study examining the combined use of TENS and contemporary task-related training (TRT) in a home-based rehabilitation program for subjects with chronic stroke. As TENS and task-related training appear to be capable of separately inducing plastic changes in the nervous system with beneficial consequences (see 1.4.2. and 1.4.3 for details), we hypothesize that their combined applications would augment motor recovery more so than either TENS or TRT alone, even in subjects who had stroke at least one year ago.

Therefore, the objectives of the present study were to compare relative treatment effectiveness of (i) TENS, (ii) TENS+TRT; (iii) placebo TENS (PLBO)+TRT and (iv) control without active treatment on spasticity and muscle functions in patients with chronic stroke. Improvements of muscle functions were measured in terms of the peak torque generated, integrated EMG of the agonist muscle and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion.

4.3 Methods

4.3.1 Subjects

Subjects were recruited via advertisements on notice boards of local community centres or in newsletters of the Hong Kong Stroke Association in Hong Kong. They were screened for entry into the study from March 1, 2003 to April 30, 2004. All subjects received examination by a registered physiotherapist to determine whether all inclusion criteria were met. The inclusion and exclusion
criteria for the present study were described in section 2.3 (see 2.3.1 and 2.3.2 for details).

4.3.2 Study Design

This study applied a single-blinded stratified randomized controlled design. The sample size is calculated using PASS (version 6.0) statistical software package, with the minimal effect size on the recovery of muscle force set at 0.38, as calculated from our previous study on the recovery of ankle dorsiflexion force (Levin and Hui-Chan 1992). This effect size was found to be the lowest, according to a meta-analysis performed by Glanz et al. (1996) on 4 randomized controlled trials in post-stroke rehabilitation using electrical stimulation, by employing muscle force recovery as a common end point in all 4 studies including that of Levin and Hui-Chan (1992). Presuming a dropout rate of 10% during treatment, the sample size was estimated to be 88 (=80+8), with 22 for each of the 4 groups. The statistical significance was set at 5% (alpha level = 0.05) and the power at 80%.

Informed consent (see Appendix I) was obtained from all eligible patients. Randomization procedures were done by a computer program of stratified randomization, called “Minimize” (Jensen 1991) (see 2.3.4 for details). Subjects were randomly allocated into 1 of 4 groups: TENS, TENS+TRT, PLBO+TRT and control without active treatment.
4.3.3 Treatment Protocol

The whole treatment program was administered for 4 weeks. With initial
demonstrations by and instructions from a physiotherapist, all subjects were
required to perform the home-based rehabilitation program daily, at 5 days per
week. Most treatments were carried out at home by the subjects themselves. All
subjects were required to attend instruction sessions in the laboratory of The Hong
Kong Polytechnic University, 5 and 3 times respectively during the first and
second week of the intervention period, in order to learn how to use TENS and to
perform the exercises. The main aim of the instruction sessions was to ensure that
all subjects could follow the home program properly and for the physiotherapist to
progress the exercise level as necessary. One more instruction session during the
third week of the intervention period, together with daily log books being entered
by all subjects and regular telephone contacts by the therapist 3 times a week,
were designed to increase subjects’ treatment compliance.

4.3.3.1 Transcutaneous Electrical Nerve Stimulation (TENS) Group

Subjects received daily conventional TENS to the affected lower extremity
for 60 minutes per session, once a day, 5 days a week for 4 weeks. The model
CEFAR Dumbo 2.4 K (Cefar Medical Products AB, Lund, Sweden) TENS
stimulator (Fig 2.1) was used in this study. The stimulator was calibrated and
delivered a high-frequency constant current of 100 Hz with single 0.2 ms square
pulses. Two pairs of surface electrodes (4.5 cm x 3.5 cm) were placed over 4
selected acupuncture points of the affected lower extremities, namely ST 36
(Zusanli), LV 3 (Taichong), GB 34 (Yanglingquan), and UB 60 (Kunlun) (Fig. 2.2).
Stimulation amplitude was set at 2 to 3 times of sensory threshold. Each subject was advised to administer the treatment around the same time of day throughout the treatment period.

4.3.3.2 TENS and Task-Related Training (TENS+TRT) Group

Subjects in this group received 60 minutes of TENS first, followed by 60 minutes of task-related training. The latter consisted of 40 minutes of lower-limb strengthening exercises, 10 minutes of transitional movement practice, and 10 minutes of gait training with rhythmic auditory cues generated by a metronome previously set to accommodate the patient’s walking pace. The exercise protocol consisted of 5 different weight-bearing exercises using a wooden block (27cm wide by 23cm deep by 5 cm or 2.5 cm high). These exercises were derived from an understanding of the biomechanical requirements of the stance phase of walking (Carr and Shepherd 1998). They were aimed to make the subjects generate an overall extensor or support moment through their affected lower limb as required in walking (Winter 1987). Details of the exercise protocol were already described in section 2.3.4 and will only be highlighted here. They were: (1) standing on the affected leg with the unaffected leg placed on the wooden block to improve weight-bearing through the affected leg (Figure 2.3a); (2) standing with the affected leg on the wooden block, while stepping up (Figure 2.3b and 2.3 c); (3) stepping down with the unaffected leg from the wooden block to strengthen the affected leg muscles (Figure 2.3 d and 2.3 e); (4) heel lifts in standing to strengthen the affected ankle plantarflexor muscles (Figure 2.3 f and 2.3 g); (5) standing up from a chair, walking a short distance, and returning to the
chair to promote a smooth transition between sit-to-stand and walking tasks; (6) walking with rhythmic auditory cues.

Subjects were encouraged to exercise as much as possible and not to use compensatory movements. Appropriate and customized progression was made by the physiotherapist based on the observed performance of each patient. For the weight-bearing exercises with wooden blocks, if subjects could perform the exercise with 20 repetitions continuously without any compensatory movements, subjects would be progressed by increasing the height of the wooden block (i.e. use a higher one). If subjects could perform the exercise with 20 repetitions continuously with the higher block, they would be progressed by increasing the number of repetitions completed within 10 minutes for each exercise. For walking, the exercise would be progressed by increasing its speed.

4.3.3.3 Placebo TENS and Task-Related Training (PLBO+TRT) Group

For the placebo stimulation, the TENS device, stimulation parameters, location of electrodes, and treatment protocol were the same as those employed in the TENS group. The only difference was that the electrical circuit in the device used for placebo stimulation was disconnected manually inside the device. In order to “blind” the subjects from the placebo effect, all subjects were told that they might or might not feel the stimulation.

Subjects received placebo TENS and task-related training on each treatment session. Subjects first received 60 minutes of placebo TENS, followed by 60 minutes task-related training. The exercise protocol in Group 3 was the same as that in Group 2.
4.3.3.4 Control Group

Subjects in this group did not receive any active training. However, they were required to attend the assessment on the same 5 time intervals as the other 3 treatment groups.

4.3.4 Outcome Measurements

Outcome measurements were the same as those described in section 2.5, including measurements of:

(i) spasticity of the affected ankle plantarflexors by the Composite Spasticity Scale

(ii) muscle functions in terms of maximum isometric voluntary contraction of ankle muscles recorded by peak torque and surface electromyography

These were measured before treatment on Day 1 ($T_0$), immediately after treatment on Day 1 ($T_1$); after 2 weeks ($T_2$) and 4 weeks of treatment ($T_3$); and 4 weeks after treatment ended at follow-up ($T_{FU}$). Details of these measurement protocols were described in sections 2.5.3 and 2.5.4.

4.3.5 Data Analysis

Statistical methods included descriptive statistics for the subjects' relevant characteristics. Parametric and non-parametric statistics were applied for continuous data and ordinal data, respectively.

Measurements of spasticity of ankle plantarflexors and muscle function were analyzed with repeated measure of analysis of variance (ANOVA), using SPSS (version 11.5) to compare the main effects before, during and after
treatment and at follow-up. The design employed in this study had 2 main factors. The between-subjects factors were the 4 groups: (1) TENS, (2) TENS + task related training, (3) placebo TENS + task-related training, and (4) Control. The within-subjects factors were the 5 assessment intervals: before treatment, immediately after first treatment, at 2 and 4 weeks during treatment, and 4 weeks post-treatment. If there were some interactions in the results of repeated measure ANOVA, one-way ANOVA followed by multiple comparisons (post-hoc tests) were used to compare treatment effects between groups. Relationships or correlations among relevant measurements were analysed using Pearson’s correlation coefficient. The significance level was set at 5%. To maintain an overall type I error at 5%, all P-values are subjected to the adjustment suggested by Benjamini and Hochberg (1995).

4.4 Results

4.4.1 Demographic Data

Eighty-eight patients with chronic stroke agreed to participate in the study and gave the informed consent. There were 5 dropouts, 2 from the TENS group, 1 each from TENS+TRT and PLBO+TRT and control groups. These subjects withdrew due to some medical and orthopedic problems unrelated to the training. There were 2 subjects having acute exacerbation of chronic obstructive airway disease, 1 subject having eye surgery for cataract, 1 subject having acute exacerbation of gouty arthritis and 1 subject having fracture of the metatarsal bone after being hit by a falling object. Besides, data from 3 subjects (1 each from the TENS, PLBO+TRT and control groups) were excluded from the analysis because
of subjects' inability to follow instructions thoroughly. Table 4.1 displays the demographic data of the patients with stroke who participated in the 4-week treatment programs. There were no significant differences ($P > 0.05$) among the 4 groups in terms of baseline measurements such as age, gender, type of stroke, side of hemiparesis, years since onset of stroke, weight and height, body mass index, Abbreviated Mental Test (AMT) scores and CSS.

### 4.4.2 Influence of the 4 Treatment Protocols on Spasticity

The influence of the 4 treatment protocols on the Composite Spasticity Scores (CSS) immediately after treatment on Day 1 ($T_1$) is shown in Table 4.2. No statistically significant differences in the raw CSS scores were found before treatment among groups. Immediately after the first treatment ($T_1$), the CSS score tended to be slightly reduced within each of the 4 groups, though none had reached statistical significance.

When comparing the improvement within group, % decreases in CSS scores from $T_1$ to $T_3$ and $T_{FU}$ were compared with those of $T_0$ within each group using one-way ANOVA. Subjects within each of the 3 intervention groups demonstrated significant % decreases after 4 weeks of treatment ($T_3$). Of interest is that these significant within-group decreases were maintained even 4 weeks after treatment ended at $T_{FU}$. In contrast, negligible change of the CSS score was found in the control group over the entire 8-week period.
Table 4.1 Comparison of subject characteristics among the 4 treatment groups

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>TENS</th>
<th>TENS + TRT</th>
<th>PLBO + TRT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of Subjects</td>
<td>20</td>
<td>19</td>
<td>21</td>
<td>20</td>
<td>80</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>57.3 ± 8.6</td>
<td>56.4 ± 9.1</td>
<td>58.4 ± 7.1</td>
<td>57.1 ± 7.8</td>
<td>57.3 ± 8.1</td>
</tr>
<tr>
<td>Gender:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (%)</td>
<td>17 (85.0)</td>
<td>17 (89.5)</td>
<td>16 (76.2)</td>
<td>17 (85.0)</td>
<td>67 (83.8)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>3 (15.0)</td>
<td>2 (10.5)</td>
<td>5 (23.8)</td>
<td>3 (15.0)</td>
<td>13 (16.2)</td>
</tr>
<tr>
<td>Type of stroke:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischaemia (%)</td>
<td>13 (65.0)</td>
<td>10 (52.6)</td>
<td>11 (52.4)</td>
<td>12 (60.0)</td>
<td>46 (57.5)</td>
</tr>
<tr>
<td>Hemorrhage (%)</td>
<td>7 (35.0)</td>
<td>9 (47.4)</td>
<td>10 (47.6)</td>
<td>8 (40.0)</td>
<td>34 (42.5)</td>
</tr>
<tr>
<td>Paretic side</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left (%)</td>
<td>13 (65.0)</td>
<td>10 (52.6)</td>
<td>14 (66.7)</td>
<td>10 (50.0)</td>
<td>47 (58.8)</td>
</tr>
<tr>
<td>Right (%)</td>
<td>7 (35.0)</td>
<td>9 (47.4)</td>
<td>7 (33.3)</td>
<td>10 (50.0)</td>
<td>33 (41.2)</td>
</tr>
<tr>
<td>Years since onset of stroke (yrs)</td>
<td>5.2 ± 2.9</td>
<td>6.2 ± 4.1</td>
<td>5.0 ± 3.0</td>
<td>4.7 ± 4.1</td>
<td>5.3 ± 3.5</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>67.9 ± 11.6</td>
<td>71.7 ± 9.2</td>
<td>68.4 ± 10.8</td>
<td>68.2 ± 12.6</td>
<td>69.0 ± 11.0</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
<td>1.7 ± 0.1</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.6 ± 6.0</td>
<td>25.8 ± 2.6</td>
<td>24.9 ± 3.0</td>
<td>24.4 ± 3.8</td>
<td>24.6 ± 4.1</td>
</tr>
<tr>
<td>AMT (score)</td>
<td>9.4 ± 0.8</td>
<td>9.0 ± 1.3</td>
<td>9.4 ± 0.9</td>
<td>9.1 ± 0.9</td>
<td>9.2 ± 1.0</td>
</tr>
<tr>
<td>CSS (score)</td>
<td>11.7 ± 1.6</td>
<td>12.2 ± 1.7</td>
<td>12.2 ± 1.7</td>
<td>12.1 ± 1.6</td>
<td>12.0 ± 1.6</td>
</tr>
</tbody>
</table>

For this and subsequent tables, values are mean ± SD. TENS, TENS+TRT, PLBO+TRT and control denote the groups receiving TENS, TENS and task-related training, placebo TENS and task-related training, and control without active treatment. T₁ denotes before treatment. T₂ denotes immediately after first treatment. T₃ and T₄ denote after 2 weeks and 4 weeks of treatment respectively. T₄ denotes 4 weeks after treatment ended.
Table 4.2  Mean scores and the percentage changes of CSS scores before treatment (T₀), immediately after first treatment (T₁), once bi-weekly during the 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (TᵢFU).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₀ (score)</td>
<td>11.8 ± 1.7</td>
<td>12.2 ± 1.7</td>
<td>12.1 ± 1.7</td>
<td>12.2 ± 1.5</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>-0.9</td>
<td>-3.3</td>
<td>-1.7</td>
<td>-1.6</td>
</tr>
<tr>
<td>T₂ (score)</td>
<td>11.7 ± 1.7</td>
<td>11.8 ± 1.7</td>
<td>11.9 ± 1.5</td>
<td>12.0 ± 1.8</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>-0.9</td>
<td>-6.6 ** ###</td>
<td>-6.6 ** ###</td>
<td>11.9 ± 1.5</td>
</tr>
<tr>
<td>T₃ (score)</td>
<td>11.6 ± 1.6</td>
<td>11.0 ± 1.7</td>
<td>11.0 ± 1.4</td>
<td>11.2 ± 1.7</td>
</tr>
<tr>
<td>TᵢFU (score)</td>
<td>11.7 ± 1.6</td>
<td>11.5 ± 1.7</td>
<td>11.2 ± 1.5</td>
<td>11.4 ± 1.5</td>
</tr>
<tr>
<td>(TᵢFU-T₀)/T₀ (%)</td>
<td>-0.8</td>
<td>-5.7 * **</td>
<td>-7.4 * **</td>
<td>-6.6 * **</td>
</tr>
</tbody>
</table>

Within group: *P<0.01 when T₃ and TᵢFU were compared with T₀. Among groups: ** P<0.01 when compared with control group; # P<0.01 when compared with PLBO+TRT group.

When comparing the improvements among groups, Fig. 4.2 shows that the CSS scores had decreased by a mean of -6.6% in the 2 TENS and TENS+TRT groups after only 2 weeks of treatment (T₂). These percentage decreases were significantly greater than those of PLBO+TRT (-2.5%) and control groups (-0.9%; Table 4.2). At the end of the 4-week treatment (T₃) and follow-up (TᵢFU), all 3 intervention groups had significantly greater % decreases in CSS scores when compared with that of the control group (P<0.01).
Fig. 4.1 Mean % changes of the CSS scores of the affected ankle plantar-flexors over time and among groups. For this and subsequent figures, T₀ denotes before treatment. T₁ denotes immediately after first treatment. T₂ and T₃ denote after 2 weeks and 4 weeks of treatment respectively. T₁₀ denotes 4 weeks post-treatment. Vertical dotted line denotes the time when treatment ended for this and subsequent figures. ** P<0.01 when compared with control group; *** P<0.01 when compared with PLBO+TRT group.

4.4.3 Influence of the 4 Treatment Protocols on Maximum Isometric Voluntary Contraction (MIVC) of Ankle Dorsiflexors and Plantarflexors

Table 4.3 to 4.8 and Fig. 4.1 to 4.7 present the results of maximum isometric voluntary contraction of dorsi- and plantar-flexors of both affected and unaffected ankles of subjects from all 4 groups (Table 4.7 to 4.8 are in Appendix IV). Note the lack of statistically significant differences in peak torque generated, integrated EMG of agonists and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion before treatment.
4.4.3.1 Peak Torque Generated by Ankle Dorsiflexion

When comparing with the baseline values, subjects in the TENS+TRT group showed significant % increases in the torque generated by both the affected (Table 4.3) and unaffected (Table 4.4) dorsiflexors from T1 to TFU, while those in the PLBO+TRT group showed significant increases in the affected leg from T2 to T3 only, and from T1 to TFU in the unaffected leg. After 4 weeks of treatment at T3, there was a 49.9 % cumulative increase in the peak dorsiflexion torque generated by the affected leg in the TENS+TRT group, which was comparable with that of 50.3% in the TENS and of 42% in the PLBO+TRT group (Table 4.3). Subjects in the TENS group showed significant increases from T1 to T3 in the affected leg, and at T1 and T3 only in the unaffected leg. However, only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the improvement in the affected leg at TFU, but not the TENS group. Moreover, only the combined treatment (TENS+TRT) group managed to maintain the gain in peak dorsiflexion torque in the unaffected leg at follow-up (TFU; Table 4.4). In contrast to the 3 intervention groups, the control group showed negligible change in both affected and unaffected ankles over the 8-week period.

When comparing the improvements among groups (Figure 4.3), subjects in the 2 TENS (TENS and TENS+TRT) groups showed significant increases in peak dorsiflexion torque in the affected leg earlier (from T1 on) than those in the PLBO+TRT group (from T3 on), when compared with that of the control. Of interest, only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the significant increases at follow-up (TFU). The increase in the TENS group was not maintained at TFU and was significantly lower than that of the 2 exercise groups.
Our results showed that the peak torque generated during ankle dorsiflexion in the TENS+TRT group at T₄ (16.9 ± 4.8 Nm) was close to that of the healthy elderly in our pilot study (18.4 ± 9.3 Nm) (see 3.4.2.2, Table 3.5).

Table 4.3  Peak torques generated by maximum isometric voluntary contraction of the affected ankle muscles before treatment (T₀), immediately after first treatment (T₁), once bi-weekly during the 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (Tᵢᵣu)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dorsiflexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (Nm)</td>
<td>13.9 ± 8.9</td>
<td>13.2 ± 8.0</td>
<td>11.3 ± 4.8</td>
<td>10.3 ± 5.8</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>2.2</td>
<td>21.0 **##</td>
<td>12.8 * *⁺</td>
<td>6.0</td>
</tr>
<tr>
<td>T₂ (Nm)</td>
<td>15.1 ± 9.6</td>
<td>16.9 ± 7.8</td>
<td>14.8 ± 5.3</td>
<td>12.0 ± 6.3</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>8.6</td>
<td>28.3 **##</td>
<td>31.0 ***##</td>
<td>15.7 b</td>
</tr>
<tr>
<td>T₃ (Nm)</td>
<td>15.2 ± 9.0</td>
<td>19.8 ± 8.1</td>
<td>16.9 ± 4.8</td>
<td>14.7 ± 6.2</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>9.7</td>
<td>50.3 ***</td>
<td>49.9 * **</td>
<td>42.0 * b**</td>
</tr>
<tr>
<td>Tᵢᵣu (Nm)</td>
<td>15.0 ± 9.2</td>
<td>14.7 ± 7.4</td>
<td>16.5 ± 5.1</td>
<td>14.7 ± 6.5</td>
</tr>
<tr>
<td>(Tᵢᵣu-T₀)/T₀ (%)</td>
<td>8.1</td>
<td>11.8 *##</td>
<td>46.3 ***++</td>
<td>42.3 **</td>
</tr>
<tr>
<td>Plantarflexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (Nm)</td>
<td>17.8 ± 11.5</td>
<td>16.4 ± 10.8</td>
<td>17.5 ± 7.0</td>
<td>12.8 ± 6.7</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>-1.2</td>
<td>7.7 b**</td>
<td>5.8 *</td>
<td>7.1</td>
</tr>
<tr>
<td>T₂ (Nm)</td>
<td>17.5 ± 11.3</td>
<td>17.6 ± 11.6</td>
<td>20.7 ± 7.5</td>
<td>14.4 ± 8.0</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>-1.2</td>
<td>7.1</td>
<td>7.9 ***+++</td>
<td>13.1 b *</td>
</tr>
<tr>
<td>T₃ (Nm)</td>
<td>18.3 ± 10.5</td>
<td>19.5 ± 11.5</td>
<td>23.8 ± 8.5</td>
<td>20.3 ± 16.0</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>2.9</td>
<td>18.8</td>
<td>35.7 * **</td>
<td>59.2 * **</td>
</tr>
<tr>
<td>Tᵢᵣu (Nm)</td>
<td>19.0 ± 11.8</td>
<td>18.1 ± 10.8</td>
<td>22.7 ± 8.4</td>
<td>16.1 ± 8.0</td>
</tr>
<tr>
<td>(Tᵢᵣu-T₀)/T₀ (%)</td>
<td>7.1</td>
<td>10.2</td>
<td>29.4 ***+++</td>
<td>26.3 * **</td>
</tr>
</tbody>
</table>

Within group: bP<0.05, aP<0.01 when T₁, T₂, T₃ and Tᵢᵣu were compared with T₀
Among groups: * P<0.05, ** P<0.01 when compared with control group; #b# P<0.01 when compared with PLBO+TRT group; *⁺P<0.05, ++P<0.01 when compared with TENS group
Table 4.4 Peak torques generated by MIVC of unaffected ankle muscles before treatment ($T_0$), immediately after first treatment ($T_1$), once bi-weekly during the 4 weeks of treatment ($T_2$ and $T_3$), and at 4 weeks post-treatment ($T_{FU}$)

<table>
<thead>
<tr>
<th></th>
<th>Control ($n=20$)</th>
<th>TENS ($n=19$)</th>
<th>TENS+TRT ($n=21$)</th>
<th>PLBO+TRT ($n=20$)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_0$ (Nm)</td>
<td>26.0 ± 10.4</td>
<td>26.3 ± 9.5</td>
<td>25.9 ± 8.4</td>
<td>25.6 ± 7.1</td>
</tr>
<tr>
<td>($T_1-T_0)/T_0$ (%)</td>
<td>3.2</td>
<td>5.21 $^b$</td>
<td>5.0 $^b$</td>
<td>4.8 $^b$</td>
</tr>
<tr>
<td>$T_2$ (Nm)</td>
<td>26.5 ± 10.0</td>
<td>27.6 ± 9.1</td>
<td>27.2 ± 8.8</td>
<td>26.8 ± 7.4</td>
</tr>
<tr>
<td>($T_2-T_0)/T_0$ (%)</td>
<td>1.9</td>
<td>5.1</td>
<td>10.0 $^a$</td>
<td>6.2 $^b$</td>
</tr>
<tr>
<td>$T_3$ (Nm)</td>
<td>27.3 ± 10.3</td>
<td>30.0 ± 10.2</td>
<td>29.6 ± 8.5</td>
<td>29.1 ± 7.6</td>
</tr>
<tr>
<td>($T_3-T_0)/T_0$ (%)</td>
<td>5.2</td>
<td>14.1 $^a$</td>
<td>14.3 $^e$</td>
<td>13.8 $^a$</td>
</tr>
<tr>
<td>$T_{FU}$ (Nm)</td>
<td>26.8 ± 9.9</td>
<td>28.2 ± 8.9</td>
<td>29.5 ± 7.9</td>
<td>28.3 ± 7.1</td>
</tr>
<tr>
<td>($T_{FU}-T_0)/T_0$ (%)</td>
<td>3.4</td>
<td>7.3</td>
<td>14.1 $^{***}$</td>
<td>10.7 $^a$</td>
</tr>
<tr>
<td><strong>Plantarflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_0$ (Nm)</td>
<td>32.8 ± 12.1</td>
<td>34.5 ± 13.2</td>
<td>32.0 ± 8.0</td>
<td>29.8 ± 9.0</td>
</tr>
<tr>
<td>($T_1-T_0)/T_0$ (%)</td>
<td>1.8</td>
<td>0.8</td>
<td>4.3 $^b$</td>
<td>3.4</td>
</tr>
<tr>
<td>$T_2$ (Nm)</td>
<td>33.4 ± 12.1</td>
<td>34.8 ± 13.0</td>
<td>33.4 ± 9.2</td>
<td>30.8 ± 8.3</td>
</tr>
<tr>
<td>($T_2-T_0)/T_0$ (%)</td>
<td>1.1</td>
<td>2.4</td>
<td>9.7 $^{*}^{**}$</td>
<td>7.2 $^b$</td>
</tr>
<tr>
<td>$T_3$ (Nm)</td>
<td>33.2 ± 12.5</td>
<td>35.3 ± 13.6</td>
<td>35.1 ± 9.5</td>
<td>31.9 ± 10.0</td>
</tr>
<tr>
<td>($T_3-T_0)/T_0$ (%)</td>
<td>1.1</td>
<td>2.4</td>
<td>9.7 $^{*}^{**}$</td>
<td>7.2 $^b$</td>
</tr>
<tr>
<td>$T_{FU}$ (Nm)</td>
<td>32.9 ± 12.1</td>
<td>37.3 ± 14.3</td>
<td>38.0 ± 9.1</td>
<td>35.4 ± 11.1</td>
</tr>
<tr>
<td>($T_{FU}-T_0)/T_0$ (%)</td>
<td>0.4</td>
<td>8.0 $^b$</td>
<td>18.6 $^{<em>}^{</em>**}$</td>
<td>18.8 $^{*}^{**}$</td>
</tr>
</tbody>
</table>

Within group: $^bP<0.05$, $^*P<0.01$ when $T_1$, $T_2$, $T_3$ and $T_{FU}$ when compared with $T_0$

Among groups: ** $P<0.01$ when compared with control group; $^{**}P<0.01$ when compared with PLBO+TRT group; $^P<0.05$, $^{**}P<0.01$ when compared with TENS group
Fig. 4.2 Mean % changes of the peak torques generated in dorsiflexion of the affected ankle over time and among groups. * $P<0.05$, ** $P<0.01$ when compared with control group; † $P<0.05$, ‡ $P<0.01$ when compared with PLBO+TRT group; ‡‡ $P<0.05$, ‡‡‡ $P<0.01$ when compared with TENS group.

4.4.3.2 Peak Torque Generated by Ankle Plantarflexion

When comparing the improvements within group, subjects in the 2 exercise (TENS+TRT and PLBO+TRT) groups showed significant increases in peak torques generated by the affected leg from $T_1$ and/or $T_2$ to $T_{FU}$ (Table 4.3). There were significant increases in the peak dorsiflexion and plantarflexion torques generated by the unaffected leg at $T_1$ and/or $T_3$ to $T_{FU}$ in the TENS group and from $T_1$ and/or $T_2$ to $T_{FU}$ in the PLBO+TRT group (Table 4.4). After 4 weeks of treatment, there were cumulative gains of 35.7% and 59.2% in peak plantarflexion torques generated by the affected ankle in these 2 exercise (TENS+TRT and PLBO+TRT) groups respectively, and significant differences were maintained at follow-up ($T_{FU}$). In contrast, the TENS group only showed
significant increases at $T_1$ in the affected ($P<0.05$) and at $T_3$ in the unaffected leg ($P<0.05$), while the control group showed negligible changes over the 8 weeks.

When comparing the improvements among groups (Fig. 4.3), the TENS+TRT group demonstrated significant % increases in peak plantarflexion torques earlier than those in the PLBO+TRT group, when the 2 groups were compared with those of the control group in both affected (from $T_1$ on in the TENS+TRT group vs from $T_2$ on in the PLBO+TRT group; Table 4.3) and unaffected legs (respectively from $T_2$ on and from $T_3$ on; Table 4.4). Moreover, the TENS+TRT group showed significantly greater % increases in peak plantarflexion torques when compared with those of the TENS group at $T_2$ and $T_{FU}$ ($P<0.01$) in the affected leg (Table 4.3), and at $T_3$ and $T_{FU}$ in the unaffected leg (Table 4.4).

![Graph showing mean % changes of the peak torque generated in plantarflexion of the affected ankle over time and among groups. * $P<0.05$, ** $P<0.01$ when compared with control group; *$P<0.05$, **$P<0.01$ when compared with TENS group.](image-url)
4.4.3.3 Integrated EMG (IEMG) of Agonist During Ankle Dorsiflexion and Plantarflexion

When comparing with the baseline values during ankle dorsiflexion (Table 4.5), all 3 intervention groups demonstrated significant increases in IEMG of tibialis anterior muscle during ankle dorsiflexion at T_2, but only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the increases at T_FU. Fig. 4.5 also indicates that the 3 intervention (TENS, TENS+TRT and PLBO+TRT) groups showed significantly greater increases in IEMG of tibialis anterior muscle at T_3 when compared with that of our control group (P<0.01).

During plantarflexion, the TENS+TRT group showed significant within-group % increases in IEMG of medial gastrocnemius muscle from T_2 to T_FU (P<0.01) while the PLBO+TRT group showed significant % increases later from T_3 to T_FU (P<0.01), when compared with baseline values (Table 4.5). In contrast, negligible changes were found in both TENS and control groups over the 8-week period. Fig. 4.5 also demonstrated that the TENS+TRT group showed significantly greater increases when compared with TENS group at T_2 (P<0.01) and T_3 (P<0.05), when compared with PLBO+TRT group at T_2 (P<0.01), and when compared with those of the control group at T_2 and T_3 (P<0.01).
Table 4.5  Integrated EMG of agonists developed in maximum isometric voluntary contraction of the affected ankle muscles before treatment (T₀), immediately after first treatment (T₁), once bi-weekly during the 4 weeks of treatment protocol (T₂ and T₃), and 4 weeks post-treatment (TᵢFU).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IEMG of TA in Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (mVs)</td>
<td>0.052 ± 0.038</td>
<td>0.052 ± 0.042</td>
<td>0.047 ± 0.029</td>
<td>0.042 ± 0.023</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>1.2</td>
<td>11.5</td>
<td>13.4</td>
<td>4.8</td>
</tr>
<tr>
<td>T₂ (mVs)</td>
<td>0.056 ± 0.041</td>
<td>0.066 ± 0.043</td>
<td>0.057 ± 0.030</td>
<td>0.053 ± 0.031</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>7.3</td>
<td>26.9 *</td>
<td>23.9 *</td>
<td>26.2 *</td>
</tr>
<tr>
<td>T₃ (mVs)</td>
<td>0.054 ± 0.038</td>
<td>0.075 ± 0.041</td>
<td>0.064 ± 0.031</td>
<td>0.062 ± 0.030</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>3.3</td>
<td>42.3 **</td>
<td>39.1 **</td>
<td>47.6 * **</td>
</tr>
<tr>
<td>TᵢFU (mVs)</td>
<td>0.057 ± 0.041</td>
<td>0.057 ± 0.033</td>
<td>0.061 ± 0.033</td>
<td>0.057 ± 0.024</td>
</tr>
<tr>
<td>(TᵢFU-T₀)/T₀ (%)</td>
<td>9.6</td>
<td>7.7</td>
<td>32.6 *</td>
<td>35.7 *</td>
</tr>
</tbody>
</table>

| **IEMG of MG in Plantarflexion** |                |             |                 |                 |
| T₀ (mVs)    | 0.024 ± 0.026  | 0.017 ± 0.014 | 0.023 ± 0.024  | 0.008 ± 0.007  |
| (T₁-T₀)/T₀ (%) | 2.3           | 5.2       | 12.1          | 6.4             |
| T₂ (mVs)    | 0.025 ± 0.026  | 0.018 ± 0.015 | 0.026 ± 0.024  | 0.008 ± 0.007  |
| (T₂-T₀)/T₀ (%) | 2.5           | 2.1       | 36.4 *** #**   | 10.2            |
| T₃ (mVs)    | 0.024 ± 0.028  | 0.020 ± 0.015 | 0.036 ± 0.035  | 0.014 ± 0.013  |
| (T₃-T₀)/T₀ (%) | 1.7           | 16.2      | 57.6 * **      | 77.7 * **      |
| TᵢFU (mVs) | 0.026 ± 0.030  | 0.018 ± 0.014 | 0.031 ± 0.028  | 0.014 ± 0.013  |
| (TᵢFU-T₀)/T₀ (%) | 9.2          | 3.4       | 37.3 *       | 77.1 *         |

Values are mean ± SD in mV.s. TA denotes tibialis anterior muscle and MG denotes medial gastrocnemius muscle.

Within group: *P<0.05, **P<0.01 when T₁, T₂, T₃ and TᵢFU were compared with T₀

Among groups: ** P<0.01 when compared with control group; *** P<0.01 when compared with PLBO+TRT group; *P<0.05, **P<0.01 when compared with TENS group.
Fig. 4.4 Mean % changes in integrated EMG of tibialis anterior during dorsiflexion of the affected ankle over time and among groups. ** $P<0.01$ when compared with control group.

Fig. 4.5 Mean % changes in integrated EMG of medial gastrocnemius during plantarflexion of the affected ankle over time and among groups. ** $P<0.01$ when compared with control group; * $P<0.05$ when compared with PLBO+TRT group; $^+$ $P<0.05$, $^{**} P<0.01$ when compared with TENS group.
4.4.3.4 EMG Co-Contraction Ratio During Ankle Dorsiflexion and Plantarflexion

Table 4.6 shows that the EMG co-contraction ratio in dorsiflexion was significantly decreased in the TENS+TRT group from T₃ to T₃FU (\(P<0.05\)), and in the TENS group from T₂ to T₃FU (\(P<0.05\)) when compared with the baseline values. In contrast, there were negligible changes in PLBO+TRT and control groups over the 8-week period. Moreover, the 2 TENS and TENS+TRT groups showed significant decreases in the EMG co-contraction ratios during dorsiflexion at T₂ and T₃ (\(P<0.01\)) and at T₃ (\(P<0.01\)) respectively, when compared with those of the control group (Fig. 4.6). Our results showed that the EMG co-contraction ratio during ankle dorsiflexion in the TENS+TRT group at T₃ (10.9 ± 8.3 %) was comparable with that of the healthy elderly in our pilot study (9.7 ± 7.0 %) (see 3.4.2.2, Table 3.5).

During plantarflexion (Table 4.6), significant reductions of EMG co-contraction ratios was found in the TENS+TRT group from T₂ to T₃FU (\(P<0.01\)), and in the PLBO+TRT group from T₃ to T₃FU (\(P<0.01\)). In addition, the TENS+TRT group demonstrated significantly greater reductions of EMG co-contraction ratios when compared with those of the TENS group from T₂ to T₃FU (\(P<0.05\)), and with those of the control group at T₃ and T₃FU (\(P<0.01\)) (Fig. 4.7). The PLBO+TRT group also showed significantly greater reductions of EMG co-contraction ratios when compared with those of the TENS and control groups at T₃ and T₃FU (\(P<0.01\)). Our results showed that the EMG co-contraction ratio during ankle plantarflexion in the TENS+TRT group at T₃ (32.5 ± 15.8 %) was significantly reduced when compared with that of T₀ (43.5 ± 21.3 %), but was still
higher when compared with that of the healthy elderly in our pilot study (25.3 ± 13.4 %) (see 3.4.2.2, Table 3.5).

Table 4.6 Mean values and the percentage changes of the EMG co-contraction ratios in the affected ankle muscles before treatment (T₀), immediately after first treatment (T₁), once bi-weekly during the 4 weeks of treatment protocol (T₂ and T₃), and at 4 weeks post-treatment (Tᵢₙ₅).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (%)</td>
<td>20.4 ± 20.8</td>
<td>24.5 ± 23.7</td>
<td>20.4 ± 16.1</td>
<td>19.6 ± 16.6</td>
</tr>
<tr>
<td>T₁ (%) (T₁-T₀)/T₀ (%)</td>
<td>21.7 ± 24.1</td>
<td>17.4 ± 18.1</td>
<td>17.5 ± 17.1</td>
<td>19.4 ± 16.7</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>21.8 ± 24.8</td>
<td>14.0 ± 15.9</td>
<td>15.2 ± 13.0</td>
<td>16.1 ± 12.5</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>20.1 ± 23.3</td>
<td>12.9 ± 15.1</td>
<td>10.9 ± 8.3</td>
<td>13.5 ± 10.7</td>
</tr>
<tr>
<td>Tᵢₙ₅ (%) (Tᵢₙ₅-T₀)/T₀ (%)</td>
<td>21.5 ± 25.0</td>
<td>16.0 ± 16.4</td>
<td>13.3 ± 12.3</td>
<td>13.3 ± 10.2</td>
</tr>
<tr>
<td><strong>Plantarflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (%)</td>
<td>37.3 ± 19.8</td>
<td>45.5 ± 20.1</td>
<td>43.5 ± 21.3</td>
<td>58.6 ± 17.7</td>
</tr>
<tr>
<td>T₁ (%) (T₁-T₀)/T₀ (%)</td>
<td>35.5 ± 18.1</td>
<td>46.9 ± 17.6</td>
<td>39.5 ± 20.6</td>
<td>56.5 ± 18.9</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>39.2 ± 22.2</td>
<td>46.9 ± 21.0</td>
<td>35.5 ± 20.7</td>
<td>53.6 ± 18.4</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>35.9 ± 19.3</td>
<td>42.6 ± 17.7</td>
<td>32.5 ± 15.8</td>
<td>44.2 ± 18.6</td>
</tr>
<tr>
<td>Tᵢₙ₅ (%) (Tᵢₙ₅-T₀)/T₀ (%)</td>
<td>36.0 ± 19.7</td>
<td>47.4 ± 16.4</td>
<td>34.4 ± 13.5</td>
<td>45.4 ± 18.6</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Within group: b P<0.05, * P<0.01 when T₁, T₂, T₃ and Tᵢₙ₅ when compared with T₀.
Among groups: ** P<0.01 when compared with control group; # P<0.01 when compared with PLBO+TRT group; * P<0.05, ** P<0.01 when compared with TENS group.
Fig. 4.6 Mean % changes in the EMG co-contraction ratios during dorsiflexion of affected ankle over time and among groups. ** $P<0.01$ when compared with control group.

Fig. 4.7 Mean % changes in the EMG co-contraction ratios during plantarflexion of affected ankle over time and among groups. ** $P<0.01$ when compared with control group; " $P<0.01$ when compared with PLBO+TRT group; * $P<0.05$, ** $P<0.01$ when compared with TENS group.
4.4.3.5 Correlations Among Torques, IEMG and EMG Co-contraction Ratios

In order to determine if any correlation existed among peak torques, IEMG of agonists and the EMG co-contraction ratios during ankle dorsi- and plantar-flexion, Pearson correlation coefficients were calculated for both the affected and the unaffected sides (Table 4.7). Significant positive correlations were found between the IEMG of agonists and peak torques in the affected leg ($r=0.50$ and $0.61$ respectively for dorsi- and plantar-flexion). Significant negative associations were also found between and IEMG of agonists and the EMG co-contraction ratios, and between the EMG co-contraction ratios and peak torques in the affected leg ($r=-0.62$, -0.49 for dorsiflexion, and $r=-0.61$, -0.60 for plantarflexion).

<table>
<thead>
<tr>
<th></th>
<th>Affected side</th>
<th>Unaffected side</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dorsiflexion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IEMG of TA and Peak Torque</td>
<td>0.50 (0.00)</td>
<td>0.33 (0.00)</td>
</tr>
<tr>
<td>Co-contraction ratio and Peak Torque</td>
<td>-0.49 (0.00)</td>
<td>-0.40 (0.00)</td>
</tr>
<tr>
<td>Co-contraction ratio and IEMG of TA</td>
<td>-0.62 (0.00)</td>
<td>-0.48 (0.00)</td>
</tr>
<tr>
<td><strong>Plantarflexion</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IEMG of MG and Peak Torque</td>
<td>0.61 (0.00)</td>
<td>0.30 (0.00)</td>
</tr>
<tr>
<td>Co-contraction ratio and Peak Torque</td>
<td>-0.55 (0.00)</td>
<td>-0.11 (0.03)</td>
</tr>
<tr>
<td>Co-contraction ratio and IEMG of MG</td>
<td>-0.61 (0.00)</td>
<td>-0.36 (0.00)</td>
</tr>
</tbody>
</table>

Values are Pearson correlation coefficients and (P value). IEMG denotes integrated EMG. TA denotes the tibialis anterior muscle, and MG denotes gastrocnemius muscle.
4.5 Discussions

4.5.1 Effects of 4 Treatment Protocols on Spasticity

Contrary to the findings of Joodaki (2001) and Alfieri (1982), our results showed no statistically significant differences in the spasticity of affected ankle plantarflexors among the 4 groups immediately after the first session of treatment. More specially, Joodaki et al. (2001) reported that there was a significant reduction of spasticity, in terms of amplitudes of H-reflexes and F-waves, H/M and F/M ratios, immediately, 5 minutes and 10 minutes after applying high-frequency TENS on the common peroneal nerve for 30 minutes in 3 spastic patients with multiple sclerosis.

Alfieri (1982) found that applying electrical stimulation at about 50 Hz directly over the paretic muscles of the lower extremity for 5 to 16 minutes resulted in decrease of the spasticity in antagonist muscles, lasting from 10-15 minutes to 2-3 hours in hemiparetic patients. Note that these 2 studies had no control group. Furthermore, differences in patient types, electrode positions, stimulation parameters of TENS and outcome measures from these studies may account for our finding of a lack of immediate antispastic effect. Besides, in subjects of the TENS+TRT group, measurement of spasticity took place after 1 hour of TENS plus 1 hour of task-related training. By then, any positive effects of TENS could have been reduced or disappeared.

The present study did find that the 2 TENS and TENS+TRT groups demonstrated more significant reductions of CSS scores earlier (from T2 on) than the PLBO+TRT (from T3 on; Table 4.2), when compared with those of the control group. This finding is in accord with that of Levin and Hui-Chan (1992), who
reported that a decrease in spasticity was evident after 2 weeks of TENS but not placebo stimulation. Furthermore, the results of this study show that the antispastic effects of TENS were maintained even 4 weeks after its cessation either with or without task-related training.

In the present study, we found that composite spasticity scores were significantly decreased in both exercise (TENS+TRT and PLBO+TRT) groups respectively from T2 and from T3 on, rather than being increased. These results are consistent with those of previous studies showing that spasticity (hypereflexia), hypertonia (resistance to passive movement) or abnormal muscle activities (muscle tone or abnormal muscle activities) did not increase after a single bout of activities (Brown and Kautz 1998; Davies et al. 1996; Hsiao and Newham 1998; Miller and Light 1997) or a short-term exercise program (Butefisch et al. 1995; Engardt et al. 1995; Sharp and Brouwer 1997; Teixeira-Salmela et al. 1999). Hence, the traditional belief by clinicians that exercise could aggregate spasticity is not substantiated.

4.5.2 Effects of 4 Treatment Protocols on Muscle Functions

In general, the 2 TENS and TENS+TRT groups demonstrated significant within-group increases in peak dorsiflexion torque of the affected ankle earlier (from T1 on; Table 4.3) than the PLBO+TRT group (from T2 on; Fig 4.3) when compared with baseline values. Moreover, these 2 groups showed significant within-group reductions in the EMG co-contraction ratio during dorsiflexion at T2 and T3 respectively when compared with the baseline values, while the PLBO+TRT and control groups had negligible changes over the 8-week period.
Interestingly, the improvements of peak torque generated during dorsiflexion in the TENS+TRT (46.3%) was still significantly larger than those of the TENS (11.8%) and control groups (8.1%), and comparable with that of PLBO+TRT group (42.3%) at 4 weeks after cessation of treatment (T_FU).

The result is in accord with that of Levin and Hui-Chan (1992). In their study on chronic hemiplegic subjects (29.0 ± 21.2 months post-stroke) with 11.5 ± 2.7 scores in the Composite Spasticity Scale, these researchers found that, in contrast to placebo stimulation which produced no significant effects, repeated applications of TENS over 3 weeks decreased clinical spasticity, stretch reflexes in the spastic ankle plantarflexors and the EMG co-contraction ratio during ankle dorsiflexion. The treatment also increased vibratory inhibition of the soleus H reflex and voluntary ankle dorsiflexing force up to 820%, but not plantarflexing force. The magnitude of improvement in their study was much larger than that of our study. The different positioning of the subjects during assessment of MIVC may account for such differences, as muscle activation pattern may change according to different starting position. In the study of Levin and Hui-Chan (1992), the subjects were examined in the standing position with the knee straight. Hence, the gastrocnemius was placed in a more stretched position than that in the present study with the knee bent at 50° of flexion when lying.

Our findings indicate that the 2 exercise (TENS+TRT and PLBO+TRT) groups appeared to be effective in improving peak torque generated by ankle dorsiflexors and plantarflexors, though the improvement in peak torque was delayed if TENS was absent. Evidence from several randomized controlled trials with stroke subjects (Inaba et al. 1973; Lindsley et al. 1994; Richards et al. 1993)
showed that intensive, short-term strength training could improve both muscle strength of lower extremity and aspects of functional performance after stroke. The addition of TENS to task-related training produced an earlier increases in the peak torques during ankle dorsiflexion and plantarflexion in our study. This might be explained by the antispastic effect produced by TENS, which enabled patients to exert extra efforts during the early phase of exercise training, thus achieving earlier improvement of the peak torques during ankle dorsiflexion and plantarflexion.

For the TENS group, there was a decrease of peak torque generated by ankle dorsiflexion 4 weeks after cessation of treatment at $T_{FU} (14.7 \pm 7.4 \text{ Nm})$ when compared with $T_3 (19.8 \pm 8.1 \text{ Nm})$. The change of muscle functions after TENS stopped had not been addressed by previous studies. Interestingly, we found that the detraining effect became smaller if task-related training was added to TENS. It is generally believed that continued physical training is needed to maintain gains in physical performance. This belief is now supported by the fact that the performance of the PLBO+TRT group at $T_3$ was more or less maintained up to 4 weeks after treatment ended.

It is interestingly to note that subjects in the combined TENS+TRT group demonstrated significantly greater improvements in the peak plantarflexor torques generated by the affected leg from $T_1$ to $T_{FU}$, which were found in the PLBO+TRT group from $T_2$ to $T_{FU}$ and in the TENS group at $T_1$ only when compared with those of the control group (Fig. 4.3). Moreover, the integrated EMG of medial gastrocnemius muscle was significantly increased in the TENS+TRT group at $T_2$ and $T_3$, and in the PLBO+TRT group at $T_3$ when compared with those of the
control group, but not the TENS and control groups. The EMG co-contraction during plantarflexion was significantly decreased in the 2 exercise (TENS+TRT and PLBO+TRT) groups at T3 and T_FU, though the reduction in the EMG co-contraction ratio was delayed if TENS was absent. There were negligible changes in the EMG contraction during plantarflexion in the TENS and control groups.

The exercise program in the present study involved concentric and eccentric training of the ankle plantarflexors in closed-chained position. Besides, repetitive stretching exercises of tight plantarflexors with body weight were also included in our training protocol. Therefore, it is not surprising to note that subjects in the 2 exercise groups achieved better improvements of peak torque, integrated EMG of medial gastrocnemius and EMG co-contraction ratio during plantarflexion when compared with those in the TENS and control groups. The addition of TENS to task-related training produced an earlier reduction of EMG co-contraction ratio during ankle plantarflexion in our study. This might be explained by the antispastic effect produced in the ankle by TENS, which enabled the patients to achieve earlier reduction of the EMG co-contraction ratio during ankle plantarflexion.

Significant reductions of the CSS scores and improvements in ankle muscle functions in the PLBO+TRT group were only found at the end of 4 weeks of treatment (T3) when compared with those of the control group. Previous studies of individuals with stroke have shown significant increases in strength after 4 weeks (Inaba et al. 1973; Dean et al. 2000) to 6 weeks of strength training (Engardt et al. 1995; Sharp and Brouwer 1997). Thus, it seems that the intensity of our task-related training program was sufficient to induce improvements in a
relatively short period. It was interestingly to note that although our program was
designed to improve muscle strength of the lower extremity in walking, the
exercise effect was also generalized to ankle muscle strength when subjects were
tested in a lying position, despite the fact that muscles were not trained in that
position.

Pearson’s correlation analysis revealed a significant positive correlation
between IEMG of agonists and peak torques, while negative correlations was
found between the IEMG of agonists and the EMG co-contraction ratio, and
between the EMG co-contraction ratio and peak torques. These findings indicated
that the increase in peak torques following 4 weeks of the home-based
rehabilitation program can be attributed to both increases in agonist EMG
activities and decreases in antagonist co-contractions.

4.5.3 Possible Mechanism of Repeated TENS on Spasticity and Muscle
Functions

Spasticity is abnormal muscle tone, recognized clinically as resistance to
passive muscle stretches that increases with the velocity of stretch. It is the result
of hyperexcitability of the stretch reflex, as one component of the upper motor
neuron syndrome (Lance 1980). Following stroke, loss of descending inputs from
the higher centers is thought to contribute to impaired modulation of
monosynaptic and polysynaptic input from muscle spindle afferent (Ia) fibers
(stretch reflexes), and polysynaptic afferent inputs from cutaneous receptors and
Golgi tendon organs, resulting in alpha motor neuron hyperexcitability (Brown
1996). Spinal interneurons also play a crucial part in this altered modulation, in
particular through defective presynaptic and reciprocal Ia inhibition. In fact, inappropriate muscle co-contraction may arise through reduced reciprocal Ia inhibition (Bhakta 2000).

Our present findings showed that repetitive stimulation of large diameter afferents via TENS over a prolonged period of time (weeks) could lead to a reduction in spasticity, simultaneously with an improvement in muscle function. Several possible mechanisms may explain the beneficial effects of such a TENS protocol. One possible mechanism may due to an enhancement of presynaptic inhibition of the spastic muscles by TENS. The TENS parameters used in the present study (low intensity, high frequency) have been shown to activate mainly large diameter afferent A-beta fibers (Levin and Hui-Chan 1993). Levin and Hui-Chan (1992) showed that repeated high frequency TENS enhanced vibratory inhibition of the H reflex. Since vibratory inhibition of the H-reflex has been attributed in part to presynaptic inhibition of group Ia terminals (Burke et al. 1976; Gillics et al. 1969), it is possible that repeated TENS applications increased vibratory inhibition of the H-reflex via an enhancement of presynaptic inhibition, which has been thought to be suppressed in hemiplegic spasticity (Ashby and Verrier 1976).

Another possible mechanism could be the disinhibition of descending voluntary commands to the motor neurons of the paretic muscles, as suggested by Levin and Hui-Chan (1992). Hyperactive segmental activity from the spastic muscle (e.g. ankle plantarflexors) could effectively "mask" or override any descending motorneuronal excitation of the paretic agonist muscle, by producing excessive reciprocal Ia inhibition. Repetitive TENS stimulation might be able to
improve the paretic muscle function, by increasing presynaptic inhibition of the hyperactive stretch reflex in the spastic muscle concomitant with reducing the EMG co-contraction ratio, thus improving the muscle strength of the paretic muscles.

The beneficial effects of TENS in enhancing the motor recovery in subjects with chronic stroke may also be explained by plastic changes in the central nervous system. Intracellular recordings of cortical neurons in primates as well as neuroimaging and neurophysiological studies in humans have demonstrated that cortical sensorimotor representation areas ("cortical maps") can be modified by sensory stimulation (Johansson 2000). The latter could be triggered by TENS, as evidenced by the vibratory sensation it produces. Besides enhancing the plastic changes in the sensory maps of cerebral cortices, sensory stimulation might also enhance the functional plasticity of the brain (Hopwood 1996; Johansson et al. 1993; Magnusson et al. 1994). Indeed, cutaneous signals are reported to have an excitatory influence on motor neurons, and a stronger motor command by increasing the sensory stimulation via TENS application, could compensate for the reduced corticomotoneural activities a result of damaged cortical neurons (Lundy-Ekman 1998).

4.5.4 Placebo Effect

A placebo is defined as any therapeutic procedure (or component of a therapy) which is given deliberately to have an effect, or unknowingly has an effect on a patient, symptom, syndrome, or disease, but which is objectively without specific activity for the condition being treated (Shapiro 1961). Placebo
effects are explained psychologically as well as physiologically as expectations of improvement, learned response from previous experience under a particular treatment, decreased stress and anxiety by release of endorphins (Shapiro and Shapiro 1997). McQuay et al. (1995) found that the relationship between the mean scores of placebo treatment and the mean scores of active treatment varies. Age and diagnosis of subject groups, study design, therapist and patient relationship, cultural differences may all contribute to the extent of the placebo response. Bourne (1971) suggested that patients with chronic conditions respond better to placebo treatment than those with acute conditions.

In the present study, the placebo stimulation was exactly the same as active TENS in its appearance, with the same electrodes and electrode location, except that the placebo stimulation did not deliver any actual electrical current. In addition, subjects in the placebo group received the same treatment procedure as those in the active TENS group, including the same stimulation parameters (except for the circuit being disconnected internally), for the same treatment duration and period. With such a study design, the treatment effect of the TENS group relative to that of the placebo group must be “real”.

4.5.5 Possible Mechanism of Task-Related Training on Spasticity and Muscle Functions

In the present study, task-related training consisted of repetitive practice of weight-bearing (close-kinetic-chain) exercises. Resistance was provided by the body weight. These exercises take into account the specificity of training principles, ensuring that the force generated by the muscles is directly related to
the function being trained. Practising such exercise is likely to result in increased muscle strength (increased force-generating capacity), increased skill (increased coordination of muscle activations), and increased extensibility and decreased stiffness of soft tissues (Carr and Shepherd 1998).

Studies on the physiological responses of strength training in patients with stroke are lacking. Based on the studies of able-bodied individuals, improvement of muscle strength after resistance training may be due to neural adaptation and muscle hypertrophy. Neural adaptation consists of increasing the number of motor units activated, increasing the rate of motor unit activation, and increasing the synchronization of activation. Moritani and deVries (1979) monitored the contribution of neural and hypertrophy factors to the strength gains achieved during 8 weeks of progressive resistance training in able-bodied. They concluded that for young men, neural factors are primarily responsible for the gains during the first 3 to 4 weeks, and hypertrophy thereafter. However, for men 60 and older, the improvement in strength while training is highly dependent on neural factors. Since most stroke patients are older, neural factors may be primarily responsible for improvements in muscle strength. Increased skill which involves improved synchronization of motor units and improved agonist-antagonist and synergic coordination may partly account for strength gains in stroke subjects. In addition, reconditioning of the neuromuscular system by reversing disuse atrophy may also contribute to the gain of muscle strength.

Taub et al. (1999) suggested that changes that occur quickly after intensive practice more likely represent an “unmasking” of dormant neuromuscular pathways. However, our findings showed that treatment effect of the task-related
training program appeared to be sustained up to 4 weeks after completion of treatment which is consistent with the time frame for possible neuroplasticity to occur. For example, a recent study in primates suggests that after local damage to the motor cortex, active repetitive training of the hemiparetic limb in task-specific activities for 2 weeks shaped subsequent functional reorganization in the adjacent intact cortex and that the undamaged motor cortex played an important role in motor recovery (Nudo and Milliken 1996; Nudo et al. 1996a). In a clinical study with fMRI, Jang et al. (2003) found that 4 weeks of task-oriented training aiming to improve hemiparetic upper extremity function induced cortical reorganization in the affected primary sensorimotor cortex, together with functional recovery of upper extremity functions in 4 patients with chronic stroke. In another recent fMRI study, Dobkin et al. (2004) found that 10 weeks of partial-weight support treadmill gait training evoked practice-induced representational plasticity (i.e. more focused activation of the foot representation) which was associated with gains in speed, endurance, motor control and kinematics of walking in 4 subjects with chronic stroke. By measuring cortical activities with an optical imaging system in 8 patients with acute stroke, Miyai et al. (2003) found that 8 weeks of inpatient treadmill gait training reduced the asymmetry of activities in the medial primary sensorimotor cortex (SMC), and enhanced the premotor cortex activation especially in the affected hemisphere. The improvement in SMC activation was significantly correlated with the improvement in gait performance (i.e. swing phase laterality index). In a recent fMRI analysis of ankle movement tracking training in a single subject who was 20 months post-stroke, Carey et al. (2004) reported that 16 sessions of tracking waveforms on the computer screen with
ankle movement produced training effects in both ankle function (in terms of self-rating of failure of the toes to clear floor during the swing phase) and brain reorganization (in terms of increased activations in the frontal and parietal lobes).

### 4.6 Conclusions

To conclude, all 3 interventions in the present study produced significant improvements in spasticity and muscle functions in patients with chronic stroke, when compared with those of the control group without any active treatment. However, the TENS+TRT group demonstrated the best overall improvements among the 3 intervention groups.

Although the improvements in ankle spasticity and muscle functions were similar to those in the PLBO+TRT group after 4 weeks of treatment, the TENS+TRT group - like the TENS group, demonstrated earlier within-group and/or between-group improvements in spasticity of ankle plantarflexors, and in muscle functions during ankle dorsiflexion such as peak torque, integrated EMG of tibialis anterior and EMG co-contraction ratio when compared with those of the PLBO+TRT group. The combined TENS+TRT group was superior to the TENS group, as it also demonstrated significant improvements in muscle functions during plantarflexion, when such improvements were absent in the TENS group. More importantly, the improvements in ankle spasticity and muscle functions of the affected ankle muscles (except integrated EMG of tibialis anterior during dorsiflexion) were maintained 4 weeks after cessation of training. Hence, there is now solid scientific evidence for combining TENS with task-related training into
a comprehensive therapeutic regimen, to enable patients with chronic stroke to obtain more optimal recovery of their muscle function.
Chapter 5

A Comparison of the Relative Effectiveness of Four Treatment Protocols on Locomotor Capacities in Subjects with Chronic Stroke
5.1 Summary

The objectives of the present study were to compare relative treatment effectiveness of (i) TENS, (ii) TENS + task-related training (TRT); (iii) placebo TENS (PLBO) + TRT and (iv) control without active treatment on locomotor capacities in patients with chronic stroke. Locomotor capacities were measured in terms of temporal-spatial gait parameters, walking endurance by six-minute walk (6MW) test and functional mobility by timed “Up & Go” (TUG) test.

The present study is a single-blinded randomized controlled trial. The sample size was calculated a priori. Eighty-eight subjects with single onset of stroke at least one year ago were recruited. Subjects were 57.3 ± 8.1 years old, 67 males and 13 females, 46 with ischemic stroke and 34 with hemorrhagic stroke, 47 with left hemiparesis and 33 with right hemiparesis. The average duration since onset of stroke was 5.3 ± 3.5 years.

Subjects were randomly assigned to 1 of 4 groups: TENS, TENS+TRT, PLBO+TRT and control groups. All subjects received daily treatment according to the group being assigned, once a day, 5 days a week for 4 weeks. Eighty subjects completed the study: 19 in the TENS group, 21 in the TENS+TRT group, 20 in each of PLBO+TRT and control groups. Outcome measurements included temporal-spatial gait parameters, walking endurance by 6MW and functional mobility by TUG. These were measured before treatment on Day 1 (T₀), immediately after treatment on Day 1 (T₁); after 2 weeks (T₂) and 4 weeks of treatment (T₃); and at 4-weeks follow-up after treatment ended (T₄₀). All data were analyzed with SPSS (version 11.5) software package.
When comparing among groups, the TENS+TRT group demonstrated significantly greater % increases in gait velocity after 4 weeks of treatment, when compared with those of the other 3 (control, TENS and PLBO+TRT) groups (all $P<0.01$). Such improvement was maintained even 4 weeks after treatment ended at $T_{FU}$. Accompanying the increase in gait velocity, significant among-group increases in cadence, step and stride length, stance time and single support duration (% of gait cycle) and decreases in double support duration (% of gait cycle) were found at $T_{FU}$ or earlier. No significant differences were found between the TENS and control groups in all the gait parameters over the 8-week period, except single support duration (% of gait cycle) of the affected leg at $T_3$ and double support duration (% of gait cycle) of the unaffected leg at $T_3$.

Significant differences between the PLBO+TRT and control groups were found in step length of affected and unaffected legs at $T_{FU}$ and $T_3$ respectively, stride length of both affected and unaffected leg at $T_3$ to $T_{FU}$, stance time (% of gait cycle) on the unaffected leg and single support duration (% of gait cycle) of the affected leg at $T_2$ and $T_3$.

For the distance covered in 6MW, the combined TENS+TRT group demonstrated earlier within-group improvement (from $T_1$ on) than the PLBO+TRT group (from $T_3$ on) when compared with baseline values. Among the groups, significantly greater % increases of the distance covered in 6MW were found in the combined TENS+TRT group when compared with those of the TENS and control groups from $T_2$ to $T_{FU}$ ($P<0.01$). The PLBO+TRT group showed significantly greater % increase than that of the control group only at $T_3$. 

(P<0.01), while the TENS group achieved negligible differences from that of the control groups over the whole 8-week period.

For the TUG scores, the combined TENS+TRT group demonstrated earlier within-group improvement (from T₁ on) than the PLBO+TRT group (from T₃ on) when compared with baseline values. Significantly greater % decreases of TUG scores were found in the TENS+TRT group when compared with those of the TENS group at T₄ (P<0.01), and of the control group from T₂ to T₅ (P<0.01). In contrast, the PLBO+TRT group showed significantly greater % decrease than that of the control group only at T₅ (P<0.01), while the TENS and control groups showed negligible among-group and within-group changes over the 8 weeks.

In conclusion, this study demonstrated that a home-based rehabilitation program involving TENS and/or task-related training is feasible, and effective in improving locomotor capacities in patients who had stroke at least one year ago. Moreover, the results demonstrated that 20 sessions of combined TENS+TRT treatment was superior to either TENS alone or PLBO+TRT in enhancing recovery of locomotor functions in chronic stroke survivors. This is the first randomized controlled clinical trial which shows that combining passive (TENS) and active (TRT) treatment was more effective than either treatment strategy in improving gait performance, walking endurance and functional mobility of patients with a mean of 5.3 years after stroke.
5.2 Introduction

Decreased locomotor capacities including poor gait performance, reduced walking endurance and decreased functional mobility in patients with stroke has been shown in our pilot study (see 3.4.2.3 for details). Gait performance in patients with stroke is characterized by slower gait speed (Brandstater et al. 1983; Knutsson and Richards 1979; Olney et al. 1994; Wade et al. 1987) and residual spatial (Dettmann et al. 1987) and temporal (Wall and Turnbull 1986) asymmetry when compared with healthy elderly. Walking faster with more normal gait patterns is perceived by many stroke patients to be their ultimate goals of rehabilitation (Bohannon et al. 1988, 1991). Thus, rehabilitation personnel designing gait-training program for these patients should target at improving gait velocity and other gait parameters of these patients. In our pilot study, temporal-spatial gait parameters including gait velocity, cadence, stride and step length, stance time, duration of single-support and double-support were found to be reproducible from day to day in subjects with chronic stroke (see 3.4.2.3 for details).

Muscle weakness is recognized as a major cause of disability in patients with stroke (Fellows et al. 1994; Gowland et al. 1992; Sahrmann and Norton 1977), and has been implicated as a factor underlying deficits in gait performance in subjects with stroke (Bohannon and Andrews 1990). Several preliminary clinical trials using pre- and post-test designs have revealed the positive effects of strength training on gait performance in subjects with stroke (Sharp and Brouwer 1997; Teixeira-Salmela 2001).
Common exercise training protocols consist of isometric, isotonic and isokinetic exercises. Having conducted an extensive review of literature on strength training in able-bodied populations, Rutherford (1988) concluded that strength training responses are task-related and specific to the particular movement velocity, muscle length or position in which muscles are being trained. Therefore, strength training needs to be incorporated into the practice of specific functional task, so that the muscle strength and pattern of muscle activation necessary to the task and context can be regained. Successful achievement of the task will probably then strengthens existing and potential neural connections.

Training for a given period of time at an appropriate intensity is believed to produce the greatest increase in muscle strength relevant to the task being performed. However, studies on the effects of optimal intensity, frequency and duration of task-related training in patients with stroke are still lacking.

Several studies have provided evidences for the efficacy of task-related training in walking (Ada et al. 2003; Dean et al. 2000; Malouin et al. 1992; Monger et al. 2002; Richards et al. 1993). However, findings from these studies must be interpreted critically in light of methodological considerations. For example, some studies were not randomized controlled trails (Malouin et al. 1992; Monger et al. 2002) and the sample size were small (Ada et al. 2003; Dean et al. 2000; Malouin et al. 1992; Monger et al. 2002; Richards et al. 1993). Most of these studies (Ada et al. 2003; Dean et al. 2000; Malouin et al. 1992; Richards et al. 1993) involved the use of expensive specialized training equipment including Kinetron or treadmill, which may also limit the applicability of their findings to community or home settings.
In addition to muscle weakness, gait performance, walking endurance and functional mobility of patients with stroke can be hindered by the presence of spasticity. The effectiveness of TENS in reducing excessive spasticity (hyperreflexia) (Aiferi 1984; Levin and Hui-Chan 1992; Tekeoolu et al. 1995), decreasing passive resistive torque during passive mobilization (Potisk et al. 1995), and increasing the strength of paralyzed muscle (Levin and Hui-Chan 1992) has been reported by various studies. However, outcome measures in most of these studies (Aiferi 1984; Levin and Hui-Chan 1992; Potisk et al. 1995) were limited to motor impairment measures only, and the impact of the intervention on the physical activity domain remains unknown. Moreover, follow-up data beyond the completion of treatment were not pursued in these studies so that the long-term effects of the intervention remained unclear.

In fact, there has been no study examining the combined use of TENS and contemporary task-related training (TRT) in a home-based rehabilitation program for subjects with chronic stroke. As TENS and task-related training appear to be capable of separately inducing plastic changes in the nervous system with beneficial consequences (see 1.4.2. and 1.4.3 for details), we hypothesize that their combined applications would augment motor recovery more so than either TENS or TRT alone, even in subjects who had stroke at least one year ago.

Therefore, the objectives of this study were to compare the relative treatment effectiveness of (i) TENS, (ii) TENS+TRT, (iii) placebo TENS+TRT and (iv) control without active treatment on the locomotor capacities of patients with chronic stroke. Improvements in locomotor capacities were measured by gait performance in terms of temporal-spatial gait parameters, walking endurance
in terms of the 6-minute walk test, and functional mobility in terms of the timed "Up & Go" test.

5.3 Methods

The methodology of the present study including subjects, study design and treatment protocol were the same as those described in Chapter 4.

5.3.1 Subjects

See 4.3.1 for details.

5.3.2 Study Design

See 4.3.2 for details.

5.3.3 Treatment Protocol

See 4.3.3 for details.

5.3.4 Outcome Measurements

The outcome measurements were already detailed in section 2.5 and they include:

(i) gait performance in terms of temporal-spatial gait parameters as recorded by GAITRite Walkway System

(ii) walking endurance in terms of distance covered in the Six-Minute Walk test

(iii) functional mobility in terms of time scores obtained in the timed "Up & Go" test
These were measured before treatment on Day 1 ($T_0$), immediately after treatment on Day 1 ($T_1$); after 2 weeks ($T_2$) and 4 weeks of treatment ($T_3$); and 4 weeks after treatment ended ($T_{FU}$). Details of these measurement protocols were described in Section 2.5.5, 2.5.6 and 2.5.7.

5.3.5 Data Analysis

Statistical methods included descriptive statistics for the subjects’ relevant characteristics. Parametric and non-parametric statistics were applied for continuous data and ordinal data, respectively.

Measurements of temporal-spatial gait parameters, distance covered in the 6MW and the TUG scores were analyzed with repeated measure of analysis of variance (ANOVA), using SPSS (version 11.5) to compare the main effects before, during and after treatment and at follow-up. The design employed in this study had 2 main factors. The between-subjects factors were the 4 groups and the within-subjects factors were the 5 assessment intervals. If there were some interactions in the results of repeated measure ANOVA, one-way ANOVA followed by multiple comparisons (post-hoc tests) were used to compare treatment effects between groups. Relationships or correlations among relevant measurements were examined using Pearson’s correlation coefficient. The significance level was set at 5%. To maintain an overall type I error at 5%, all $P$-value are subjected to the adjustment suggested by Benjamini and Hochberg (1995).
5.4 Results

5.4.1 Demographic Data

The demographic data had been reported in Chapter 4 (see 4.4.1 for details).

5.4.2 Influence of the 4 Treatment Protocols on Walking Performance

5.4.2.1 Gait Velocity

The influence of the 4 treatment protocols on gait velocity is shown in Table 5.1. There was no statistically difference in gait velocity before treatment. When comparing with baseline values (Table 5.1), there was a cumulative within-group increase in gait velocity of 34.9% in the TENS+TRT group, 14.8% in the TENS group and 18.5% in the PLBO+TENS group by the end of the 4-week treatment period (T3). Subjects in the combined TENS+TRT group demonstrated earlier within-group improvement (from T1 on) than those in TENS (in T3 only) and PLBO+TRT groups (in T3 and TRU). Of special interest is that only subjects in the 2 exercise (TEN+TRT and PLBO+TRT) groups maintained such improvements at follow-up (TRU). Our results showed that the gait velocity in the TENS+TRT group at TRU (72.2 ± 34.0 cm/s) was significantly improved when compared with that of T0 (50.6 ± 28.3 cm/s), but was still lower when compared with that of the healthy elderly in our pilot study (125.6 ± 23.8 cm/s) (see 3.4.2.3, Table 3.7).
Table 5.1 Gait velocity and percentage changes from baseline before treatment ($T_0$), immediately after first treatment ($T_1$), after 2 weeks and 4 weeks of treatment ($T_2$ and $T_3$), and at 4 weeks post-treatment ($T_{FU}$)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$T_0$ (cm/s)</td>
<td>62.6 ± 24.6</td>
<td>54.8 ± 25.6</td>
<td>50.6 ± 28.3</td>
<td>48.7 ± 25.0</td>
</tr>
<tr>
<td>($T_1-T_0$)/$T_0$ (%)</td>
<td>63.8 ± 25.3</td>
<td>57.1 ± 25.4</td>
<td>57.1 ± 32.2</td>
<td>49.6 ± 26.3</td>
</tr>
<tr>
<td>$T_2$ (cm/s)</td>
<td>63.2 ± 25.8</td>
<td>58.1 ± 27.1</td>
<td>64.9 ± 34.0</td>
<td>53.9 ± 27.8</td>
</tr>
<tr>
<td>($T_2-T_0$)/$T_0$ (%)</td>
<td>0.8</td>
<td>6.0</td>
<td>28.3 **## ++</td>
<td>10.8</td>
</tr>
<tr>
<td>$T_3$ (cm/s)</td>
<td>63.9 ± 24.1</td>
<td>62.9 ± 28.4</td>
<td>68.2 ± 34.5</td>
<td>57.7 ± 29.8</td>
</tr>
<tr>
<td>($T_3-T_0$)/$T_0$ (%)</td>
<td>2.0</td>
<td>14.8 b</td>
<td>34.9 **## ++</td>
<td>18.5 *</td>
</tr>
<tr>
<td>$T_{FU}$ (cm/s)</td>
<td>64.5 ± 23.8</td>
<td>58.8 ± 26.5</td>
<td>72.2 ± 34.0</td>
<td>58.3 ± 28.8</td>
</tr>
<tr>
<td>($T_{FU}-T_0$)/$T_0$ (%)</td>
<td>3.0</td>
<td>7.2</td>
<td>42.8 **## ++</td>
<td>19.6 *</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: $^b$P<0.05; $^a$P<0.01 when $T_1$, $T_2$, $T_3$ and $T_{FU}$ were compared with $T_0$.

Among groups: ** P<0.01 when compared with control group; ## P<0.01 when compared with PLBO+TRT group; ++P<0.01 when compared with TENS group.

When comparing among groups (Fig. 5.1), only the combined TENS+TRT group showed significantly greater % increase in gait velocity, when compared with those of the other 3 groups. Significant differences from those of PLBO+TRT and control groups were noted as early as $T_1$ after the first treatment, and from all the other 3 groups from $T_2$ on till 4 weeks after treatment ended ($T_{FU}$). In contrast, the other 2 treatment (TENS and PLBO+TRT) groups did not achieve significant among-group differences over the entire 8-week period.
Fig. 5.1 Mean % changes of gait velocity over time and among groups. For this and subsequent figures, T₀ denotes before treatment, T₁ denotes immediately after first treatment. T₂ and T₃ denote after 2 weeks and 4 weeks of treatment respectively. T_FU denotes 4 weeks post-treatment. Vertical dotted line denotes time when treatment ended for this and subsequent figures. ** P<0.01 when compared with control group; ## P<0.01 when compared with PLBO+TRT group; ***P<0.01 when compared with TENS group.

5.4.2.2 Cadence

The influence of the 4 treatment protocols on cadence is shown in Table 5.2. There was no statistically difference in cadence before treatment. When comparing with baseline values (Table 5.2), significant cumulative within-group increases in cadences were found only in the combined TENS+TRT group, starting as early as T₁ (P<0.05) and lasting until T_FU (P<0.01). Such improvements in the TENS+TRT group were significantly greater when compared with the control group at T₃ (P<0.01), and with all the 3 groups at T_FU.
\((P<0.01)\) (Fig. 5.2). In fact, there were negligible within- or among-group changes in the other 3 groups over the 8 weeks.

Table 5.2 Cadence and percentage changes from baseline before treatment (\(T_0\)), immediately after first treatment (\(T_1\)), after 2 weeks and 4 weeks of treatment (\(T_2\) and \(T_3\)), and at 4 weeks post-treatment (\(T_{FU}\)).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(T_0) (step/min)</td>
<td>90.1 ± 23.2</td>
<td>84.8 ± 22.9</td>
<td>81.8 ± 25.2</td>
<td>77.5 ± 19.0</td>
</tr>
<tr>
<td>((T_1-T_0)/T_0)</td>
<td>1.0</td>
<td>0.2</td>
<td>3.9</td>
<td>3.9</td>
</tr>
<tr>
<td>(T_2) (step/min)</td>
<td>90.6 ± 24.2</td>
<td>85.1 ± 22.3</td>
<td>88.0 ± 27.1</td>
<td>78.8 ± 19.8</td>
</tr>
<tr>
<td>((T_2-T_0)/T_0)</td>
<td>0.6</td>
<td>0.3</td>
<td>7.5</td>
<td>1.7</td>
</tr>
<tr>
<td>(T_3) (step/min)</td>
<td>90.1 ± 21.7</td>
<td>88.6 ± 21.4</td>
<td>90.5 ± 27.5</td>
<td>81.0 ± 20.5</td>
</tr>
<tr>
<td>((T_3-T_0)/T_0)</td>
<td>0.1</td>
<td>4.4</td>
<td>10.5</td>
<td>4.4</td>
</tr>
<tr>
<td>(T_{FU}) (step/min)</td>
<td>90.7 ± 21.7</td>
<td>84.7 ± 22.1</td>
<td>93.9 ± 29.0</td>
<td>81.2 ± 19.0</td>
</tr>
<tr>
<td>((T_{FU}-T_0)/T_0)</td>
<td>0.7</td>
<td>-0.1</td>
<td>14.8</td>
<td>4.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: \(^bP<0.05, ^*P<0.01\) when \(T_1, T_2, T_3\) and \(T_{FU}\) were compared with \(T_0\).

Among groups: \(**P<0.01\) when compared with control group; \(##P<0.01\) when compared with PLBO+TRT group; \(***P<0.01\) when compared with TENS group.
Fig. 5.2. Mean % changes of cadence over time and among groups. ** $P<0.01$ when compared with control group; *** $P<0.01$ when compared with PLBO+TRT group; +++ $P<0.01$ when compared with TENS group.

5.4.2.3 Step Length

The influence of the 4 treatment protocols on step length is shown in Table 5.3. There was no statistically difference in step length before treatment. When comparing with baseline values (Table 5.3), subjects in the combined TENS+TRT group showed earlier within-group improvements in both affected and unaffected legs (from T1 and from T2 on respectively) than those of TENS (at T3 only) and PLBO+TRT groups (from T3 on). In contrast, the control group had negligible changes over the 8 weeks.
Table 5.3  Step length and percentage changes from baseline in affected and unaffected sides before treatment (T₀), immediately after first treatment (T₁), after 2 weeks and 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (T₄).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (cm)</td>
<td>43.7 ± 7.5</td>
<td>42.0 ± 9.8</td>
<td>35.5 ± 13.1</td>
<td>40.4 ± 12.3</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>0.9</td>
<td>3.5</td>
<td>9.8 ***#</td>
<td>2.2</td>
</tr>
<tr>
<td>T₁ (cm)</td>
<td>44.1 ± 8.1</td>
<td>43.5 ± 9.5</td>
<td>39.0 ± 12.6</td>
<td>41.3 ± 12.8</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>0.9</td>
<td>3.1</td>
<td>21.3 *<strong>#</strong></td>
<td>7.0</td>
</tr>
<tr>
<td>T₂ (cm)</td>
<td>44.1 ± 7.8</td>
<td>43.3 ± 10.7</td>
<td>43.1 ± 13.9</td>
<td>93.2 ± 12.7</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>0.9</td>
<td>3.1</td>
<td>21.3 *<strong>#</strong></td>
<td>7.0</td>
</tr>
<tr>
<td>T₃ (cm)</td>
<td>44.7 ± 7.5</td>
<td>45.2 ± 10.9</td>
<td>44.5 ± 13.5</td>
<td>44.3 ± 13.5</td>
</tr>
<tr>
<td>(T₄-T₀)/T₀ (%)</td>
<td>2.5</td>
<td>7.5</td>
<td>25.4 *<strong>#</strong></td>
<td>9.8 b</td>
</tr>
<tr>
<td>T₄ (cm)</td>
<td>44.6 ± 7.9</td>
<td>44.4 ± 10.1</td>
<td>45.3 ± 12.9</td>
<td>45.3 ± 12.9</td>
</tr>
<tr>
<td>(T₄-T₀)/T₀ (%)</td>
<td>2.2</td>
<td>5.6</td>
<td>27.6 *<strong>#</strong></td>
<td>12.1 * a</td>
</tr>
<tr>
<td><strong>Unaffected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (cm)</td>
<td>38.4 ± 12.1</td>
<td>34.1 ± 16.8</td>
<td>34.9 ± 13.0</td>
<td>32.2 ± 17.1</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>-0.2</td>
<td>5.0</td>
<td>5.5</td>
<td>-0.5</td>
</tr>
<tr>
<td>T₁ (cm)</td>
<td>38.3 ± 12.6</td>
<td>35.8 ± 17.2</td>
<td>36.9 ± 12.9</td>
<td>32.0 ± 17.4</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>-1.2</td>
<td>9.1</td>
<td>17.2 ***</td>
<td>7.4</td>
</tr>
<tr>
<td>T₂ (cm)</td>
<td>37.9 ± 12.6</td>
<td>37.2 ± 17.2</td>
<td>40.9 ± 14.4</td>
<td>34.5 ± 17.2</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>1.8</td>
<td>12.4 *</td>
<td>20.9 ***</td>
<td>15.5 ** a</td>
</tr>
<tr>
<td>T₃ (cm)</td>
<td>39.1 ± 12.5</td>
<td>38.3 ± 17.8</td>
<td>42.2 ± 14.0</td>
<td>37.1 ± 17.6</td>
</tr>
<tr>
<td>(T₄-T₀)/T₀ (%)</td>
<td>1.8</td>
<td>12.4 *</td>
<td>20.9 ***</td>
<td>15.5 ** a</td>
</tr>
<tr>
<td>T₄ (cm)</td>
<td>39.1 ± 12.2</td>
<td>37.0 ± 17.0</td>
<td>44.3 ± 14.3</td>
<td>36.7 ± 18.2</td>
</tr>
<tr>
<td>(T₄-T₀)/T₀ (%)</td>
<td>1.8</td>
<td>8.7</td>
<td>26.7 *<strong>#</strong>++</td>
<td>14.3 a</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Within group: bP<0.05, *P<0.01 when T₁, T₂, T₃ and T₄ were compared with T₀.
Among groups: ** P<0.01 when compared with control group; *** P<0.01 when compared with PLBO+TRT group; ++P<0.01 when compared with TENS group.
Fig. 5.3 Mean % changes of step length in affected leg over time and among groups.

** $P < 0.01$ when compared with control group;  
  ** $P < 0.01$ when compared with 
  PLBO+TRT group;  
  * $P < 0.01$ when compared with TENS group.

When comparing the affected leg among groups (Fig. 5.3), only the combined TENS+TRT group demonstrated significantly greater % increase in step length from $T_2$ to $T_{FU}$ when compared with those of the TENS group, and from $T_1$ to $T_{FU}$ when compared with those of PLBO+TRT and control groups.

For the unaffected leg (Fig. 5.4), the combined TENS+TRT group also showed significantly greater % increase in step length at $T_{FU}$ when compared with those of the TENS and PLBO+TRT groups ($P < 0.01$), and from $T_2$ to $T_{FU}$ when compared with those of the control group ($P < 0.01$). The PLBO+TRT group showed significantly greater % increase in step length only at $T_{FU}$ in the affected leg ($P < 0.05$), and only at $T_3$ in the unaffected leg ($P < 0.01$) when compared with those of the control group. In contrast, the TENS group achieved negligible among-group differences over the entire 8 week period.
Fig. 5.4 Mean % changes of step length in unaffected leg over time and among groups.

** P<0.01 when compared with control group; †† P<0.01 when compared with PLBO+TRT group; ‡‡ P<0.01 when compared with TENS group.

5.4.2.4 Stride Length

The influence of the 4 treatment protocols on stride length is shown in Table 5.4. There was no statistically difference in stride length before treatment. When comparing with baseline values (Table 5.4), subjects in the combined TENS+TRT group showed earlier improvement in both affected and unaffected legs (from T₁ on ) than those of the TENS group (at T₃ only) and the PLBO+TRT group (from T₃ on).
Table 5.4 Stride length and percentage changes from baseline in affected and unaffected sides before treatment (T₀), immediately after first treatment (T₁), after 2 weeks and 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (T₄U)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (cm)</td>
<td>82.1 ± 19.2</td>
<td>75.8 ± 21.7</td>
<td>71.6 ± 24.0</td>
<td>72.3 ± 27.3</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>0.1</td>
<td>4.8</td>
<td>7.0 ***#</td>
<td>1.3</td>
</tr>
<tr>
<td>T₁ (cm)</td>
<td>82.1 ± 20.3</td>
<td>79.4 ± 22.8</td>
<td>76.6 ± 24.5</td>
<td>73.3 ± 27.9</td>
</tr>
<tr>
<td>(T₂-T₁)/T₀ (%)</td>
<td>-0.3</td>
<td>6.4</td>
<td>18.8 ***##+++</td>
<td>7.6</td>
</tr>
<tr>
<td>T₂ (cm)</td>
<td>81.8 ± 20.1</td>
<td>80.7 ± 24.2</td>
<td>85.2 ± 26.6</td>
<td>77.8 ± 27.6</td>
</tr>
<tr>
<td>(T₃-T₂)/T₀ (%)</td>
<td>1.5</td>
<td>10.2 a</td>
<td>22.4 ***##+++</td>
<td>13.3 **a</td>
</tr>
<tr>
<td>T₃ (cm)</td>
<td>83.3 ± 20.6</td>
<td>83.5 ± 24.5</td>
<td>87.7 ± 26.0</td>
<td>81.9 ± 29.6</td>
</tr>
<tr>
<td>(T₄U-T₀)/T₀ (%)</td>
<td>2.0</td>
<td>7.2</td>
<td>27.0 ***##+++</td>
<td>13.7 **a</td>
</tr>
<tr>
<td><strong>Unaffected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (cm)</td>
<td>81.9 ± 19.3</td>
<td>75.7 ± 21.6</td>
<td>71.3 ± 24.2</td>
<td>72.4 ± 27.4</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>0.6</td>
<td>4.2</td>
<td>7.9 ***##+++</td>
<td>1.3</td>
</tr>
<tr>
<td>T₁ (cm)</td>
<td>82.4 ± 20.4</td>
<td>78.9 ± 22.6</td>
<td>76.9 ± 24.7</td>
<td>73.3 ± 27.9</td>
</tr>
<tr>
<td>(T₂-T₁)/T₀ (%)</td>
<td>-0.5</td>
<td>6.5</td>
<td>19.1 ***##+++</td>
<td>8.0</td>
</tr>
<tr>
<td>T₂ (cm)</td>
<td>81.5 ± 20.2</td>
<td>80.7 ± 24.4</td>
<td>85.0 ± 26.7</td>
<td>78.1 ± 28.0</td>
</tr>
<tr>
<td>(T₃-T₂)/T₀ (%)</td>
<td>2.0</td>
<td>10.1 a</td>
<td>23.1 ***##+++</td>
<td>12.7 *a</td>
</tr>
<tr>
<td>T₃ (cm)</td>
<td>83.5 ± 19.7</td>
<td>83.4 ± 24.2</td>
<td>87.8 ± 26.2</td>
<td>81.6 ± 29.2</td>
</tr>
<tr>
<td>(T₄U-T₀)/T₀ (%)</td>
<td>2.1</td>
<td>7.1</td>
<td>27.5 ***##+++</td>
<td>12.7 *a</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: *P<0.01 when T₁, T₂, T₃ and T₄U were compared with T₀
Among groups: *P<0.05, **P<0.01 when compared with control group; *P<0.05, ##P<0.01 when compared with PLBO+TRT group; ##P<0.01 when compared with TENS group
Fig. 5.5 Mean % changes of stride length in affected leg over time and among groups. 
** $P<0.01$ when compared with control group; $^\# P<0.05$, $^{##} P<0.01$ when compared with PLBO+TRT group; $^{+++} P<0.01$ when compared with TENS group.

Fig. 5.6 Mean % changes of stride length in unaffected leg over time and among groups. 
** $P<0.01$ when compared with control group; $^{##} P<0.01$ when compared with PLBO+TRT group; $^{+++} P<0.01$ when compared with TENS group.
When comparing the affected leg among groups (Fig. 5.5), only the combined TENS+TRT group demonstrated significantly greater % increases in stride length from \( T_2 \) to \( T_{FU} \) when compared with those of the TENS group \((P<0.01)\), at \( T_1 \), \( T_2 \) and \( T_{FU} \) when compared with those of the PLBO+TRT group, and from \( T_1 \) to \( T_{FU} \) when compared with those of control group \((P<0.01)\). For the unaffected leg (Fig. 5.6), the combined TENS+TRT group again showed significantly greater % increases in stride length from \( T_2 \) to \( T_{FU} \) when compared with those of the TENS group \((P<0.01)\), and from \( T_1 \) to \( T_{FU} \) when compared with those of the PLBO+TRT and control groups \((P<0.01)\). Again, the TENS group did not achieve significant among-group differences over the 8 weeks.

5.4.2.5 Stance Time (% of Gait Cycle)

The influence of the 4 treatment protocols on stance time in terms of percentage of gait cycle is shown in Table 5.5. There was no statistically difference in stance time (% of gait cycle) before treatment. When comparing with baseline values (Table 5.5), only subjects in the combined TENS+TRT group showed within-group decreases in stance time (% of gait cycle) at \( T_2 \) to \( T_{FU} \) \((P<0.01)\) in the affected leg, and from \( T_1 \) \((P<0.05)\) to \( T_{FU} \) \((P<0.01)\) in the unaffected leg.

When comparing among groups (Table 5.5), no significant differences in stance time on the affected leg were found among the 4 groups (Fig. 5.7). However, the combined TENS+TRT group demonstrated significantly greater % decrease in stance time (% of gait cycle) on the unaffected leg from \( T_2 \) to \( T_{FU} \) when compared with those of the TENS group \((P<0.01)\), at \( T_3 \) and \( T_{FU} \) when compared with those in the PLBO+TRT group \((P<0.01)\), and from after the
Table 5.5  Stance time (% of gait cycle) on affected and unaffected legs and percentage changes from baseline before treatment (T₀), immediately after first treatment (T₁), after 2 weeks and 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (T₄U)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS + TRT (n=21)</th>
<th>PLBO + TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀</td>
<td>61.7 ± 4.4</td>
<td>60.7 ± 6.6</td>
<td>62.0 ± 5.9</td>
<td>61.4 ± 8.6</td>
</tr>
<tr>
<td>(T₁ - T₀)/T₀ (%)</td>
<td>0.1</td>
<td>-2.1</td>
<td>-1.7</td>
<td>0.2</td>
</tr>
<tr>
<td>T₂</td>
<td>61.5 ± 5.3</td>
<td>60.2 ± 5.9</td>
<td>59.6 ± 6.1</td>
<td>61.2 ± 8.1</td>
</tr>
<tr>
<td>(T₂ - T₀)/T₀ (%)</td>
<td>-0.4</td>
<td>-0.8</td>
<td>-3.7</td>
<td>-0.3</td>
</tr>
<tr>
<td>T₃</td>
<td>61.7 ± 5.1</td>
<td>58.7 ± 5.3</td>
<td>59.2 ± 5.8</td>
<td>60.9 ± 7.4</td>
</tr>
<tr>
<td>(T₃ - T₀)/T₀ (%)</td>
<td>-0.1</td>
<td>-3.3</td>
<td>-4.5</td>
<td>-0.8</td>
</tr>
<tr>
<td>T₄U</td>
<td>61.4 ± 4.7</td>
<td>58.6 ± 5.2</td>
<td>59.0 ± 5.4</td>
<td>60.3 ± 7.3</td>
</tr>
<tr>
<td>(T₄U - T₀)/T₀ (%)</td>
<td>-0.6</td>
<td>-3.4</td>
<td>-4.8</td>
<td>-1.8</td>
</tr>
<tr>
<td><strong>Unaffected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀</td>
<td>72.5 ± 7.2</td>
<td>74.9 ± 7.9</td>
<td>74.0 ± 7.3</td>
<td>75.4 ± 7.6</td>
</tr>
<tr>
<td>(T₁ - T₀)/T₀ (%)</td>
<td>0.5</td>
<td>-0.4</td>
<td>-1.4</td>
<td>-0.1</td>
</tr>
<tr>
<td>T₂</td>
<td>73.5 ± 7.9</td>
<td>74.5 ± 7.2</td>
<td>71.8 ± 7.4</td>
<td>74.5 ± 7.4</td>
</tr>
<tr>
<td>(T₂ - T₀)/T₀ (%)</td>
<td>1.4</td>
<td>-0.5</td>
<td>-3.0</td>
<td>-1.3 **</td>
</tr>
<tr>
<td>T₃</td>
<td>72.9 ± 7.3</td>
<td>74.0 ± 7.1</td>
<td>71.2 ± 7.3</td>
<td>74.3 ± 7.8</td>
</tr>
<tr>
<td>(T₃ - T₀)/T₀ (%)</td>
<td>0.6</td>
<td>-1.1</td>
<td>-3.8</td>
<td>-4.1 *</td>
</tr>
<tr>
<td>T₄U</td>
<td>72.4 ± 6.5</td>
<td>74.6 ± 7.1</td>
<td>70.3 ± 7.1</td>
<td>74.1 ± 7.9</td>
</tr>
<tr>
<td>(T₄U - T₀)/T₀ (%)</td>
<td>-0.1</td>
<td>-0.4</td>
<td>-5.0</td>
<td>-1.8</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: bP<0.05, *P<0.01 when T₁, T₂, T₃ and T₄U were compared with T₀
Among groups: * P<0.05, ** P<0.01 when compared with control group; ## P<0.01 when compared with PLBO+TRT group; † † P<0.01 when compared with TENS group
first treatment at $T_1$ when compared with those of the control group ($P<0.01$) (Fig. 5.7). The PLBO+TRT group also showed significantly greater % decreases of stance time (% of gait cycle) on their unaffected leg at $T_2$ and $T_3$ when compared with those of the control group. Again, the TENS group showed negligible among-group differences over the 8 weeks.

![Graph showing % changes of stance time over time and among groups](image)

Fig. 5.7 Mean % changes of stance time (% of gait cycle) in unaffected leg over time and among groups. * $P<0.05$, ** $P<0.01$ when compared with control group; *** $P<0.01$ when compared with PLBO+TRT group; +++ $P<0.01$ when compared with TENS group.

5.4.2.6 Single Support Duration (% of Gait Cycle)

The influence of the 4 treatment protocols on single support duration in terms of percentage of gait cycle is shown in Table 5.6. There was no statistically difference in single support duration (% of gait cycle) before treatment. When
Table 5.6  Single support duration (% of gait cycle) and percentage changes from baseline in affected and unaffected legs before treatment (T₀), immediately after first treatment (T₁), after 2 weeks and 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (TᵟFU)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS + TRT (n=21)</th>
<th>PLBO + TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀</td>
<td>27.6 ± 7.2</td>
<td>24.9 ± 7.5</td>
<td>25.9 ± 7.2</td>
<td>24.6 ± 7.6</td>
</tr>
<tr>
<td>(T₁ - T₀)/T₀ (%)</td>
<td>27.4 ± 7.7</td>
<td>25.5 ± 7.1</td>
<td>27.2 ± 7.5</td>
<td>5.0 *** a</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.4</td>
<td></td>
<td>24.8 ± 7.7</td>
</tr>
<tr>
<td>T₂</td>
<td>26.9 ± 7.3</td>
<td>25.5 ± 7.3</td>
<td>28.3 ± 7.2</td>
<td>25.6 ± 7.4</td>
</tr>
<tr>
<td>(T₂ - T₀)/T₀ (%)</td>
<td>-2.5</td>
<td>2.4</td>
<td></td>
<td>9.1 *** ### ++</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.2 **</td>
</tr>
<tr>
<td>T₃</td>
<td>27.1 ± 7.3</td>
<td>26.1 ± 6.9</td>
<td>28.9 ± 7.2</td>
<td>25.7 ± 7.7</td>
</tr>
<tr>
<td>(T₃ - T₀)/T₀ (%)</td>
<td>-1.8</td>
<td>5.0 **</td>
<td></td>
<td>11.5 ### ### +</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.5 *</td>
</tr>
<tr>
<td>TᵟFU</td>
<td>27.5 ± 6.5</td>
<td>26.7 ± 8.1</td>
<td>29.9 ± 7.0</td>
<td>25.8 ± 7.9</td>
</tr>
<tr>
<td>(TᵟFU - T₀)/T₀ (%)</td>
<td>-0.1</td>
<td>7.2</td>
<td></td>
<td>15.5 *** #</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5.0</td>
</tr>
<tr>
<td><strong>Unaffected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀</td>
<td>37.3 ± 5.4</td>
<td>39.7 ± 6.6</td>
<td>38.1 ± 5.8</td>
<td>38.1 ± 8.6</td>
</tr>
<tr>
<td>(T₁ - T₀)/T₀ (%)</td>
<td>38.2 ± 4.5</td>
<td>40.4 ± 6.1</td>
<td>38.9 ± 6.2</td>
<td>38.4 ± 7.6</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2.2</td>
<td></td>
<td>0.7</td>
</tr>
<tr>
<td>T₂</td>
<td>38.8 ± 5.6</td>
<td>40.0 ± 6.1</td>
<td>40.3 ± 6.2</td>
<td>38.7 ± 8.1</td>
</tr>
<tr>
<td>(T₂ - T₀)/T₀ (%)</td>
<td>3.8</td>
<td>0.7</td>
<td></td>
<td>5.7 b</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.8</td>
</tr>
<tr>
<td>T₃</td>
<td>38.3 ± 5.1</td>
<td>41.1 ± 5.3</td>
<td>40.8 ± 6.0</td>
<td>39.2 ± 7.6</td>
</tr>
<tr>
<td>(T₃ - T₀)/T₀ (%)</td>
<td>2.5</td>
<td>3.5</td>
<td></td>
<td>7.0 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3.1</td>
</tr>
<tr>
<td>TᵟFU</td>
<td>38.7 ± 4.7</td>
<td>41.1 ± 5.4</td>
<td>41.0 ± 5.6</td>
<td>39.9 ± 4.7</td>
</tr>
<tr>
<td>(TᵟFU - T₀)/T₀ (%)</td>
<td>3.8</td>
<td>3.5</td>
<td></td>
<td>7.6 *</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4.7</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: bP<0.05, *P<0.01 when T₁, T₂, T₃ and TᵟFU were compared with T₀

Among groups: * P<0.05, ** P<0.01 when compared with control group; *P<0.01, *** P<0.01 when compared with PLBO+TRT group; +++P<0.01 when compared with TENS group.
Fig. 5.8 Mean % changes of single support duration (% of gait cycle) in affected leg over time and among groups. *P<0.05, **P<0.01 when compared with control group; †P<0.01, ‡P<0.01 when compared with PLBO+TRT group; ***P<0.01 when compared with TENS group.

comparing with baseline values (Table 5.6), only subjects in the combined TENS+TRT group showed significant within-group increases in single support duration (% of gait cycle) from T1 to T_FU (P<0.01) in the affected leg, and from T2 (P<0.05) to T_FU (P<0.01) in the unaffected leg.

When comparing among groups (Fig.5.8), the combined TENS+TRT group demonstrated significantly greater % increase in single support duration (% of gait cycle) at T2 and T3 when compared with those of the TENS group (P<0.01), and from T1 to T_FU when compared with those of PLBO+TRT and control groups (P<0.05) in the affected leg. The PLBO+TRT also showed significantly greater % increase at T2 and T3 in their affected legs when compared with those of the
control group. In contrast, negligible differences were found among 4 groups in the unaffected leg (Table 5.6).

5.4.2.7 Double Support Duration (% of gait cycle)

The influence of the 4 treatment protocols on double support duration in terms of percentage of gait cycle is shown in Table 5.7. There was no statistically difference in double support duration (% of gait cycle) before treatment. When comparing with baseline values (Table 5.7), subjects in the combined TENS+TRT group showed significant within-group decreases in double support duration (% of gait cycle) from T₁ (P<0.05) to T₂ (P<0.01) in both affected and unaffected legs. Those in the TENS group showed significant decrease from T₃ to T₄ in the affected leg (P<0.05), and at T₃ in the unaffected leg (P<0.05). Subjects in the PLBO+TRT group showed significant decreases at T₄ in both affected (P<0.05) and unaffected legs (P<0.01).

When comparing the affected leg among groups (Fig. 5.9), the combined TENS+TRT group demonstrated significantly greater % decreases in double support duration (% of gait cycle) at T₂ and T₄ when compared with those of the TENS group (P<0.01), at T₂ to T₄ when compared with those of the PLBO+TRT groups (P<0.05), and at T₁ to T₄ when compared with those of control group (P<0.05). For the unaffected leg (Fig. 5.10), the combined TENS+TRT group demonstrated significantly greater % decreases in double support duration (% of gait cycle) at T₂ and T₄ when compared with those of the TENS group (P<0.01), and from T₂ to T₄ when compared with those of the control group (P<0.01). In the TENS group (Fig. 5.10), there was significantly greater % decrease at T₃ in the
unaffected leg when compared with that of the control group ($P<0.01$). In contrast, the PLBO+TRT group achieved negligible among-group changes over the 8 weeks.

Table 5.7 Double support duration (% of gait cycle) and percentage changes from baseline in affected and unaffected leg before treatment ($T_0$), immediately after first treatment ($T_1$), after 2 weeks and 4 weeks of treatment ($T_2$ and $T_3$), and at 4 weeks post-treatment ($T_{FU}$)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS + TRT (n=21)</th>
<th>PLBO + TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Affected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_0$</td>
<td>34.5 ± 9.2</td>
<td>35.6 ± 10.8</td>
<td>36.1 ± 10.9</td>
<td>37.3 ± 14.4</td>
</tr>
<tr>
<td>($T_1 - T_0)/T_0$</td>
<td>0.9</td>
<td>-3.8</td>
<td>-4.9 b**</td>
<td>-0.2</td>
</tr>
<tr>
<td>$T_2$</td>
<td>34.8 ± 11.6</td>
<td>34.6 ± 10.1</td>
<td>31.6 ± 10.7</td>
<td>35.9 ± 14.5</td>
</tr>
<tr>
<td>($T_2 - T_0)/T_0$</td>
<td>1.0</td>
<td>-2.9</td>
<td>-12.6 * * * hashtags</td>
<td>-3.6</td>
</tr>
<tr>
<td>$T_3$</td>
<td>34.9 ± 10.1</td>
<td>32.7 ± 9.1</td>
<td>30.7 ± 9.9</td>
<td>35.3 ± 13.3</td>
</tr>
<tr>
<td>($T_3 - T_0)/T_0$</td>
<td>1.1</td>
<td>-8.3 b</td>
<td>-15.0 * * * hashtags</td>
<td>-5.3</td>
</tr>
<tr>
<td>$T_{FU}$</td>
<td>33.9 ± 8.9</td>
<td>32.8 ± 8.6</td>
<td>29.3 ± 9.0</td>
<td>34.4 ± 14.1</td>
</tr>
<tr>
<td>($T_{FU} - T_0)/T_0$</td>
<td>-1.7</td>
<td>-7.9 b</td>
<td>-18.9 * * * hashtags</td>
<td>-7.8 b</td>
</tr>
<tr>
<td><strong>Unaffected</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_0$</td>
<td>34.4 ± 9.5</td>
<td>35.9 ± 11.1</td>
<td>36.2 ± 10.8</td>
<td>37.6 ± 14.6</td>
</tr>
<tr>
<td>($T_1 - T_0)/T_0$</td>
<td>0.4</td>
<td>-5.1</td>
<td>-5.2 b</td>
<td>-1.2</td>
</tr>
<tr>
<td>$T_2$</td>
<td>34.9 ± 11.4</td>
<td>34.9 ± 10.2</td>
<td>31.8 ± 10.9</td>
<td>35.9 ± 13.8</td>
</tr>
<tr>
<td>($T_2 - T_0)/T_0$</td>
<td>1.4</td>
<td>-2.8</td>
<td>-12.2 * * * hashtags</td>
<td>-4.5</td>
</tr>
<tr>
<td>$T_3$</td>
<td>35.1 ± 10.0</td>
<td>32.8 ± 9.2</td>
<td>30.6 ± 9.8</td>
<td>35.1 ± 13.8</td>
</tr>
<tr>
<td>($T_3 - T_0)/T_0$</td>
<td>2.2</td>
<td>-8.5 b **</td>
<td>-15.4 * * * hashtags</td>
<td>-6.7</td>
</tr>
<tr>
<td>$T_{FU}$</td>
<td>34.1 ± 9.2</td>
<td>33.4 ± 9.3</td>
<td>29.9 ± 9.1</td>
<td>34.4 ± 14.5</td>
</tr>
<tr>
<td>($T_{FU} - T_0)/T_0$</td>
<td>-0.9</td>
<td>-7.1</td>
<td>-17.4 * * * hashtags</td>
<td>-8.7 a</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Within group: b$P<0.05$, b$P<0.01$ when $T_1$, $T_2$, $T_3$ and $T_{FU}$ were compared with $T_0$
Among groups: * $P<0.05$, ** $P<0.01$ when compared with control group; "$P<0.01$, ### $P<0.01$ when compared with PLBO+TRT group; **$P<0.01$ when compared with TENS group
Fig. 5.9 Mean % changes of double support duration (% of gait cycle) in affected leg over time and among groups. *P<0.05, **P<0.01 when compared with control group; †P<0.01, ‡P<0.01 when compared with PLBO+TRT group, ++P<0.01 when compared with TENS group.

Fig. 5.10 Mean % changes of double support duration (% of gait cycle) in unaffected leg over time and among groups. **P<0.01 when compared with control group; ++P<0.01 when compared with TENS group.
5.4.2.8 Correlations Among Outcome Measurements

Relationships between gait velocity on the one hand, and cadence, stride and step length, stance time, single and double support duration on the other are presented in Table 5.8. Pearson correlation analyses revealed that there were significant positive associations between gait velocity, and cadence ($r=0.833$; $P=0.000$), stride and step length of both affected and unaffected legs ($r=0.612$ to $0.895$; $P=0.000$), and single support duration of both affected ($r=0.855$) and unaffected legs ($r=0.356$) ($P=0.000$) (Table 5.9). Significant negative relationships were found between gait velocity, and stance time ($r=-0.337$ to $-0.868$; $P=0.000$) and double support duration ($r=-0.759$ to $-0.764$; $P=0.000$).

Table 5.8 Correlations between gait velocity and other gait variables

<table>
<thead>
<tr>
<th>Gait Variables</th>
<th>$r$</th>
<th>$P$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cadence</td>
<td>0.833**</td>
<td>0.000</td>
</tr>
<tr>
<td>Stride Length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>0.894**</td>
<td>0.000</td>
</tr>
<tr>
<td>Unaffected</td>
<td>0.895**</td>
<td>0.000</td>
</tr>
<tr>
<td>Step Length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>0.758**</td>
<td>0.000</td>
</tr>
<tr>
<td>Unaffected</td>
<td>0.612**</td>
<td>0.000</td>
</tr>
<tr>
<td>Stance time (% gait cycle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>-0.337**</td>
<td>0.000</td>
</tr>
<tr>
<td>Unaffected</td>
<td>-0.868**</td>
<td>0.000</td>
</tr>
<tr>
<td>Single support duration (% gait cycle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>0.855**</td>
<td>0.000</td>
</tr>
<tr>
<td>Unaffected</td>
<td>0.356**</td>
<td>0.000</td>
</tr>
<tr>
<td>Double support duration (% gait cycle)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Affected</td>
<td>-0.759**</td>
<td>0.000</td>
</tr>
<tr>
<td>Unaffected</td>
<td>-0.764**</td>
<td>0.000</td>
</tr>
</tbody>
</table>

$r$ denotes Pearson correlation coefficient, ** $P<0.01$

5.4.3 Influence of the 4 Treatment Protocols on Six-Minute Walk (6 MW) Test
The influence of the 4 treatment protocols on distance covered in 6 MW is shown in Table 5.9. There was no statistically difference in distance covered in 6 MW before treatment. When comparing with baseline values (Table 5.9),

Table 5.9 Distance covered in the six-minute walk (6 MW) test and percentage changes from baseline before treatment (T₀), immediately after first treatment (T₁), after 2 weeks and 4 weeks of treatment (T₂ and T₃), and at 4 weeks post-treatment (T₄₉)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T₀ (m)</td>
<td>203.8 ± 74.3</td>
<td>196 ± 83.0</td>
<td>195.9 ± 89.4</td>
<td>161.5 ± 76.2</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>1.8</td>
<td>2.5</td>
<td>7.7 a</td>
<td>1.6</td>
</tr>
<tr>
<td>T₁ (m)</td>
<td>207.5 ± 76.1</td>
<td>201.5 ± 85.5</td>
<td>210.9 ± 98.1</td>
<td>164.1 ± 76.5</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>-2.2</td>
<td>1.4</td>
<td>17.0*** ++</td>
<td>10.5</td>
</tr>
<tr>
<td>T₂ (m)</td>
<td>199.4 ± 67.8</td>
<td>199.3 ± 84.9</td>
<td>229.1 ± 95.0</td>
<td>178.4 ± 86.3</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>-0.1</td>
<td>10.3 b</td>
<td>25.3 *** ++</td>
<td>17.7 a **</td>
</tr>
<tr>
<td>T₃ (m)</td>
<td>203.7 ± 68.9</td>
<td>216.8 ± 92.7</td>
<td>245.5 ± 106.9</td>
<td>109.1 ± 88.9</td>
</tr>
<tr>
<td>(T₄₉-T₀)/T₀ (%)</td>
<td>1.1</td>
<td>8.6</td>
<td>25.4 ***[+++   ]</td>
<td>17.2 a</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Within group: bP<0.05, aP<0.01 when T₁, T₂, T₃ and T₄₉ were compared with T₀
Among groups: ** P<0.01 when compared with control group; ++P<0.01 when compared with TENS group

there was a cumulative within-group increase of 25.3% in the TENS+TRT group, 10.3% in the TENS group and 17.7% in the PLBO+TENS group at T₃ after 4 weeks of treatment. Subjects in the combined TENS+TRT demonstrated earlier improvement (from T₁ on) than those in the TENS (in T₃ only) and the PLBO+TRT groups (in T₃ and T₄₉). Of special interest is that only subjects in the 2 exercise (TEN+TRT and PLBO+TRT) groups maintained such within-group improvement 4 weeks after treatment ended at T₄₉. In contrast, the control group
showed negligible within-group changes in the distance covered in 6MW over the 8-week period.

When comparing among groups (Fig. 5.11), the combined TENS+TRT group showed significantly greater % improvement in distance covered in 6MW from T₂ to T₉ when compared with those of the TENS and control groups (P<0.01). Moreover, subjects in the PLBO+TRT group showed significantly greater % increase than that of the control group at T₃ (P<0.01). Our results showed that the distance covered in the 6MW in the TENS+TRT group at T₉ (245.6 ± 102.5 cm) was significantly increased when compared with that of T₀ (195.9 ± 89.4 cm), but it was still shorter when compared with that of the healthy elderly in our pilot study (416.5 ± 95.2 cm) (see 3.4.2.4, Table 3.8).

![Figure 5.11 Mean % changes of distance covered in the six-minute walk over time and among groups. **P<0.01 when compared with control group; *P<0.01 when compared with TENS group.](image-url)
5.4.4 Influence of the 4 Treatment Protocols on Timed “Up & Go” (TUG) Test

The influence of the 4 treatment protocols on the scores of the TUG is shown in Table 5.10. There was no statistically difference in scores of TUG before treatment. When comparing with baseline values (Table 5.10), there was a cumulative decrease of -25.3% in the TENS+TRT group, of -10.4% in the TENS and PLBO+TENS groups at T3 after 4 weeks of treatment. Subjects in the combined TENS+TRT demonstrated earlier improvement (from T1 on) than those in the PLBO+TRT groups (in T3 and TFU).

When comparing among groups (Fig. 5.12), the combined TENS+TRT group showed significantly greater % decreases in TUG scores at TFU when

Table 5.10: Scores of the Timed “Up & Go” (TUG) test and percentage changes from baseline before treatment (T0), immediately after first treatment (T1), after 2 weeks and 4 weeks of treatment (T2 and T3), and at 4 weeks post-treatment (TFU)

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0 (s)</td>
<td>21.9 ± 13.2</td>
<td>23.6 ± 11.0</td>
<td>24.4 ± 15.3</td>
<td>31.4 ± 23.6</td>
</tr>
<tr>
<td>T1 (s) (T1-T0)/T0 (%)</td>
<td>-2.3</td>
<td>-5.7</td>
<td>-6.6</td>
<td>0.4</td>
</tr>
<tr>
<td>T2 (s) (T2-T0)/T0 (%)</td>
<td>22.1 ± 14.3</td>
<td>22.1 ± 10.6</td>
<td>20.3 ± 11.2</td>
<td>30.1 ± 24.6</td>
</tr>
<tr>
<td>T3 (s) (T3-T0)/T0 (%)</td>
<td>0.7</td>
<td>-6.2</td>
<td>-16.7 ***</td>
<td>-4.1</td>
</tr>
<tr>
<td>TFU (s) (TFU-T0)/T0 (%)</td>
<td>22.0 ± 13.0</td>
<td>21.2 ± 10.5</td>
<td>18.7 ± 9.3</td>
<td>28.1 ± 23.3</td>
</tr>
<tr>
<td></td>
<td>-2.3</td>
<td>-10.4</td>
<td>-23.5 ***</td>
<td>-10.4 b</td>
</tr>
</tbody>
</table>

Values are mean ± SD.
Within group: b P<0.05, *P<0.01 when T1, T2, T3 and TFU were compared with T0
Among groups: ** P<0.01 when compared with control group; ‡‡P<0.01 when compared with TENS group
compared with those of the TENS groups (\(P<0.01\)), and from \(T_2\) to \(T_{FU}\) when compared with those of the control group (\(P<0.01\)). In contrast, the PLBO+TRT group showed significantly greater % decrease than that of the control group only at \(T_{FU}\) (\(P<0.01\)), while the TENS and control groups respectively showed negligible among-group and within-group differences over the 8-week period.

Our results showed that the TUG score in the TENS+TRT group at \(T_{FU}\) (18.5 ± 10.2 s) was significantly reduced when compared with that of \(T_0\) (24.4 ± 15.3 s), but it was still greater when compared with that of the healthy elderly in our pilot study (9.1 ± 1.6 s) (see 3.4.2.5, Table 3.9).

Relationships between the time scores of the timed "Up and Go" (TUG) test and gait velocity and distance covered in the 6-minutes walk (6 MW) test are presented in table 5.11. Pearson correlation analyses revealed that there were

![Graph](image)

Fig. 5.12 Mean % changes of scores of timed "Up & Go" test over time and among groups. \(**P<0.01\) when compared with control group; \(***P<0.01\) when compared with TENS group.
Table 5.11 Correlations between time scores of timed "Up & Go" (TUG) test and gait velocity and distance covered in the 6-minutes walk (6 MW) test

<table>
<thead>
<tr>
<th>Variables</th>
<th>r</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait velocity</td>
<td>-0.747 **</td>
<td>0.000</td>
</tr>
<tr>
<td>Distance covered in the 6 MW</td>
<td>-0.747**</td>
<td>0.000</td>
</tr>
</tbody>
</table>

r denotes Pearson correlation coefficient, ** P<0.01 significant negative associations between TUG scores and gait velocity and distance covered in the 6 MW (both r=-0.747, P=0.000).

5.4.5 Correlations Between Plantarflexor Spasticity, Ankle Muscle Strength, Gait Velocity, Distance Covered in the Six-Minute Walk Test (6MW), and Timed "Up & Go" Test (TUG)

Relationships between the level of plantarflexor spasticity, ankle muscle strength, gait velocity, distance covered in 6MW and TUG scores immediately after the first treatment session, after 2 and 4 weeks of treatment, and at follow-up are presented in Table 5.12 to Table 5.14 respectively. Immediately after the first treatment session, Pearson correlation analyses revealed very low correlation coefficients with no statistically significant relationship between the different outcome measures (Table 5.12).

After 2 weeks of treatment (Table 5.13), the change of composite spasticity scores were found to be mildly but significantly correlated with the change in peak plantarflexion torque of affected leg (r=-0.230, P<0.05), gait velocity (r=-0.333, P<0.01) and distance covered in the 6MW (r=-0.276, P<0.01) in a negative manner. Change in peak dorsiflexion torque was mildly correlated
with the change in peak plantarflexion torque in a positive manner ($r=0.236$, $P<0.05$), while change in peak plantarflexion torque was mildly correlated with change in gait velocity and with change in distance covered in 6MW in a positive manner ($r=0.261$ and $0.262$ respectively, $P<0.05$). The change in gait velocity was mildly correlated with the change in TUG scores ($r=-0.277$, $P<0.01$) in a negative manner, and with the change in distance covered in 6MW ($r=0.371$, $P<0.01$) in a positive manner. The change in TUG scores was mildly correlated with the change in distance covered in 6MW ($r=-0.233$, $P<0.05$) in a negative manner.

Table 5.12 Correlations between the scores of Composite Spasticity Scale, ankle muscle strength, gait velocity, timed “Up & Go” (TUG) scores, and distance covered in the 6-minutes walk test (6 MW) immediately after first treatment session

<table>
<thead>
<tr>
<th></th>
<th>Peak dorsiflexion torque</th>
<th>Peak plantarflexion torque</th>
<th>Gait velocity</th>
<th>TUG scores</th>
<th>Distance covered in 6MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSS</td>
<td>0.072</td>
<td>-0.060</td>
<td>0.076</td>
<td>-0.053</td>
<td>0.020</td>
</tr>
<tr>
<td>Peak dorsiflexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak plantarflexion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>torque</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gait velocity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TUG scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

$r$ denotes Pearson correlation coefficient, all $r$ values were non-significant.
Table 5.13 Correlations between the scores of Composite Spasticity Scale, ankle muscle strength, gait velocity, timed "Up & Go" (TUG) scores, and distance covered in the 6-minutes walk test (6 MW) after 2 weeks of treatment

<table>
<thead>
<tr>
<th></th>
<th>Peak dorsiflexion torque</th>
<th>Peak plantarflexion torque</th>
<th>Gait velocity</th>
<th>TUG scores</th>
<th>Distance covered in 6MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSS</td>
<td>-0.183</td>
<td>-0.230*</td>
<td>-0.333**</td>
<td>0.107</td>
<td>-0.276*</td>
</tr>
<tr>
<td>Peak dorsiflexion torque</td>
<td>-</td>
<td>0.236*</td>
<td>0.041</td>
<td>-0.204</td>
<td>0.073</td>
</tr>
<tr>
<td>Peak plantarflexion torque</td>
<td>-</td>
<td>-</td>
<td>0.261*</td>
<td>-0.149</td>
<td>0.262*</td>
</tr>
<tr>
<td>Gait velocity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.227*</td>
<td>0.371**</td>
</tr>
<tr>
<td>TUG scores</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.233*</td>
</tr>
</tbody>
</table>

r denotes Pearson correlation coefficient, **P<0.01, *P<0.05

After 4 weeks of treatment (Table 5.14), the change of composite spasticity scores was found to be mildly significantly correlated with the change in peak dorsiflexion torque of the affected leg (r=-0.284, P<0.05), gait velocity (r=-0.310, P<0.01) and distance covered in 6MW (r=-0.297, P<0.01) in a negative manner. Change in peak dorsiflexion torque was mildly correlated with the change in peak plantarflexion torque (r=0.394, P<0.01) and with the change in distance covered in 6MW (r=0.275, P<0.05) in a positive manner, and with the change in TUG scores (r=-0.235, P<0.05) in a negative manner. The change in peak plantarflexion torque was mildly correlated with change in gait velocity and with change in distance covered in 6MW in a positive manner (r=0.316 and 0.491 respectively, P<0.01). The change in gait velocity was mildly correlated with the change in TUG scores (r=-0.246, P<0.05) in a negative manner, and the change in distance covered in 6MW (r=0.654, P<0.01) in a positive manner.
Table 5.14 Correlations between the scores of Composite Spasticity Scale, ankle muscle strength, gait velocity, timed “Up & Go” (TUG) scores, and distance covered in the 6-minutes walk test (6 MW) after 4 weeks of treatment

<table>
<thead>
<tr>
<th></th>
<th>Peak dorsiflexion torque</th>
<th>Peak plantarflexion torque</th>
<th>Gait velocity</th>
<th>TUG scores</th>
<th>Distance covered in 6MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSS</td>
<td>-0.284*</td>
<td>0.198</td>
<td>-0.310**</td>
<td>0.057</td>
<td>-0.297**</td>
</tr>
<tr>
<td>Peak dorsiflexion torque</td>
<td>-</td>
<td>0.394**</td>
<td>0.164</td>
<td>-0.235*</td>
<td>0.275*</td>
</tr>
<tr>
<td>Peak plantarflexion torque</td>
<td>-</td>
<td>-</td>
<td>0.316**</td>
<td>-0.108</td>
<td>0.491**</td>
</tr>
<tr>
<td>Gait velocity</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.246*</td>
<td>0.654**</td>
</tr>
<tr>
<td>TUG scores</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.189</td>
</tr>
</tbody>
</table>

r denotes Pearson correlation coefficient, **P<0.01, *P<0.05

At follow-up (Table 5.15), the change of composite spasticity scores was found to be mildly but significantly correlated with the change in peak dorsiflexion torque of the affected leg (r=-0.360, P<0.01), gait velocity (r=-0.433, P<0.01) and distance covered in the 6MW (r=-0.525, P<0.01) in a negative manner. Change in peak dorsiflexion torque was correlated with the change in peak plantarflexion torque (r=0.387, P<0.01), the change in gait velocity (r=0.409, P<0.01), and the change in distance covered in 6MW (r=0.385, P<0.01) in a positive manner. The change in peak plantarflexion torque was correlated with the change in distance covered in 6MW in a positive manner (r=0.414, P<0.01), and with the change in TUG scores in a negative manner (r=-0.373, P<0.01). The change in gait velocity was correlated with the change in TUG scores (r=-0.313, P<0.01) in a negative manner, and the change in distance covered in 6MW
(r=0.598, \(P<0.01\)) in a positive manner. The change in TUG scores was correlated with the change in distance covered in 6MW (r=-0.247, \(P<0.01\)) in a negative manner.

Table 5.15 Correlations between the scores of Composite Spasticity Scale, ankle muscle strength, gait velocity, timed “Up & Go” (TUG) scores, and distance covered in the 6-minutes walk test (6 MW) at follow-up

<table>
<thead>
<tr>
<th></th>
<th>Peak dorsiflexion torque</th>
<th>Peak plantarflexion torque</th>
<th>Gait velocity</th>
<th>TUG scores</th>
<th>Distance covered in 6MW</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSS</td>
<td>-0.360**</td>
<td>-0.116</td>
<td>-0.433**</td>
<td>0.194</td>
<td>-0.525**</td>
</tr>
<tr>
<td>Peak dorsiflexion torque</td>
<td>0.387**</td>
<td>0.409**</td>
<td>-0.214</td>
<td>0.385**</td>
<td></td>
</tr>
<tr>
<td>Peak plantarflexion torque</td>
<td>-</td>
<td>0.218</td>
<td>-0.373**</td>
<td>0.414**</td>
<td></td>
</tr>
<tr>
<td>Gait velocity</td>
<td>-</td>
<td>-</td>
<td>-0.313**</td>
<td>0.598**</td>
<td></td>
</tr>
<tr>
<td>TUG scores</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-0.247*</td>
<td></td>
</tr>
</tbody>
</table>

r denotes Pearson correlation coefficient, **\(P<0.01\), *\(P<0.05\)

5.5 Discussions

5.5.1 Effects of the 4 Treatment Protocols on Gait Performance

The major finding of the present study was that combining TENS with task-related training increased the gait velocity by 34.9% in chronic stroke survivors at T3 after 4 weeks of treatment (Table 5.1). This was accompanied by significantly greater % increase in cadence at T_FU (Table 5.2) and in stride length of both affected and unaffected legs at T2, T3 and T_FU when compared with those of the other 3 groups (except that of the affected leg in the PLBO+TRT group; Table 5.4). Previous studies have attempted to use task-related training to
improve lower leg functions in patients with chronic stroke. For example, Dean et al. (2000) found that gait velocity was increased by about 13% after 4-weeks of task-related training program in 12 chronic stroke patients. Ada et al. (2003) reported that there was some 21% increase in gait velocity after 4 weeks of a treadmill and overground walking program in 29 subjects with >6 months after stroke. It is interesting that, in the present study, the relative improvements in gait velocity after 4 weeks of PLBO+TRT treatment (18.5%) was similar to that observed by Dean et al. (2000) and Ada et al. (2003) after 4 weeks of similar TRT training. These results support our hypothesis that combining TENS with task-related training would augment motor recovery more than either TENS or TRT alone, even in subjects who had stroke at least one year ago.

We found that gait velocity was strongly correlated with cadence ($r=0.833$, $P=0.000$; Table 5.8), stride length ($r=0.894$ to $0.895$, $P=0.000$) and step length ($r=0.612$ to $0.758$, $P=0.000$) of both affected and unaffected legs. The results indicate that the increase in gait velocity in our subjects was achieved by an increase in cadence, as well as stride and step length of both affected and unaffected legs. Walking velocity is a combination of the distance walked and of the number of steps made. This relationship is described in the equation (Winter 1990):

$$\text{Gait velocity} = \frac{\text{Stride length} \times \text{cadence}}{120}$$

Wagenaar and Beek (1992) have shown that, compared with normal, stroke patients increased gait velocity by increasing their cadence. Subjects in the
TENS+TRT group, on the other hand, increased their velocity by increasing step length of both their affected and unaffected legs earlier (respectively from T₁ and T₂ on) than that of cadence (from T₁ on; Table 5.3) when compared with that of the control subjects.

There may be 2 mechanisms through which increased step length contributed to the increased gait velocity. Relief of plantarflexor spasticity by TENS and stretching of tight plantarflexors by task-related training may provide patients’ leg with less resistance in rolling over the supporting affected leg during its stance phase. This could increase the single support duration on the affected leg, as shown in the TENS+TRT group from T₁ on (Table 5.6). The latter may in turn increase step length of the unaffected side (as shown in Table 5.3 from T₂ on) and hence gait velocity. Despite some controversial findings (Bohannon et al. 1987; De Bujanda et al. 2003; Nadeau et al. 1999), several studies had provided evidence that spasticity in the affected ankle plantarflexors could decrease gait velocity in hemiplegic patients (Hesse et al. 1995; Hesse et al. 1996; Hesse et al. 1994; Reiter et al. 1998). Secondly, task-related training may strengthen the paretic hip flexors, knee extensors and ankle plantarflexors. Stronger hip flexors may contribute to the generation of a larger swing movement and of a greater step length in the affected leg, hence a faster gait speed (Annaswamy et al. 1999; Nene et al. 1999). Stronger knee extensors may stabilize the affected knee joint in the mid-stance of the gait cycle better (Sutherland et al. 1980), which permits the unaffected leg to make a larger step and thus increase the walking speed. Plantarflexor muscles are an important muscle group in regulating gait speed in healthy subjects, because they generate a large part of energy required to move the
limbs forward during the push-off phase (Winter 1983, 1991). This enables the affected leg to make a larger step and hence increases the walking speed.

Perry et al. (1995) developed a classification system which used gait velocity to classify walking disability in stroke patients. When the mean gait velocity data from baseline at T₀ were used to classify the subjects, all subjects in our study with gait velocity from 48.7 to 62.6 cm/s would be classified as least-limited community walker (58 to 80 cm/s). At 4 weeks after treatment ended, the mean gait velocity of the combined TENS+TRT group (72.2 ± 34.0 cm/s; Table 5.1) approached the value set for community walkers (≥ 80 cm/s), but not the other 3 groups. Community walkers were supposed to be independent in all home and moderate community activities, such as being able to walk over uneven terrain and to negotiate a crowded shopping centre with supervision.

5.5.2 Effects of the 4 Treatment Protocols on Six-Minute Walk (6MW) Test

Poor cardiovascular fitness had been reported in persons with chronic hemiparesis (Macko et al. 1997; Potempa et al. 1996). Impairments resulting from stroke, such as pain, spasticity, muscle weakness, and poor balance could result in reduced tolerance to activity. This could in turn lead to a more sedentary life style and poorer cardiovascular fitness. Moreover, the energy expenditure in walking was found to be elevated approximately 1.5 to 2 folds in hemiparetic stroke patients as compared with normal control subjects (Corcoran et al. 1970; Gerston and Orr 1971). Alternations in spasticity, central gait patterning and reduced oxidative capacity in paretic musculature have been hypothesized to explain the elevated energy costs of hemiparetic gait (Macko et al. 2001). In addition,
exercise capacity may also be compromised by comorbid cardiovascular disease (Roth 1993) and age-related declines in cardiorespiratory fitness (Bouchard et al. 1990), which may further deteriorate walking endurance in elderly stroke patients.

Few studies had examined the effects of training on walking endurance in terms of the distance covered in 6MW. In a randomized controlled clinical trial, Dean et al. (2000) showed that there was a 20.2% increase in distance covered in 6 MW after 4 weeks of task-related circuit training in 12 subjects with chronic stroke. In a randomized controlled trial with a placebo group, Ada et al. (2003) demonstrated that there was a 28.01% increase in distance covered in 6MW in 29 subjects with chronic stroke after 4 weeks of treadmill and overground walking program. Results of these 2 studies were comparable with those of the subjects in the two exercise (TENS+TRT and PLBO+TRT) groups in the present study (25.3% and 17.7% respectively). It appears that task-related exercises play a main role in mediating the increase of 6 MW distance in the TENS+TRT group.

The mechanisms underlying the improvement in walking capacity in terms of 6MW appears multifactorial. Firstly, stroke population is physically deconditioned and has a high prevalence of cardiovascular disease risk factors which could be potentially modified by exercise therapy (Hagberg and Brown 1995; Potempa et al. 1995). Secondly, improved gait biomechanics may be one of the reasons in improving the walking endurance in subjects with stroke. TENS plus gait training with rhythmic auditory cues in the combined treatment protocol may improve gait biomechanics. TENS had been found to relieve ankle plantarflexor spasticity in hemiparetic patients (Levin and Hui-Chan 1992; Yan and Hui-Chan 2002), and auditory rhythm had been shown to improve the
temporal stride symmetry and variability of lower limb EMG pattern in hemiparetic gaits (Thaut and McIntosh 1992; Thaut et al. 1993b; Thaut et al. 1997). Thirdly, task-related training may also induce exercise-mediated neuromuscular adaptations which may improve gross motor efficiency in chronic hemiplegic patients. Fourthly, exercise may enhance muscle oxidative capacity in this older sedentary population (Gardner et al. 1989).

However, limitations of the 6MWT outcome measure should be noted. The distance covered in the 6MW reflects the ability to undertake everyday activities, and may be a good indicator of functional capacity required for normal daily activities. However, the 6 MW is not only influenced by cardiorespiratory and cardiovascular fitness, but also by other factors such as motivation, neuromuscular function, and peripheral muscle strength (Fitts and Guthrie 1995). Eng et al. (2002) showed that the 6MW distance and self-selected gait speed were related to balance, spasticity, and muscle strength in persons with stroke.

5.5.3 Effects of the 4 Treatment Protocols on Timed “Up & Go” (TUG) Test

At the end of the treatment program (T3) and at follow-up (TRU), the time taken to complete the timed “Up & Go” test in the TENS+TRT group was shortened by 24% of that recorded at baseline (T0) (Table 5.10). Note that TUG is not a “simple” walking task. It includes a series of motor tasks that also challenge balance control in addition to muscle strength and co-ordination, e.g. when rising up from a chair to take the first step and then turning. The improved performance in the TUG was not surprising in light of the improvement observed in gait velocity, because the TUG test includes walking per se. In fact, a negative
correlation was uncovered between TUG scores and gait velocity in our study on chronic stroke subjects \((r=-0.747, P=0.000; \text{Table 5.11})\). This finding suggests that, in addition to walking faster, subjects were better able to rise from a chair to change direction while walking. As practice is believed to be essential for effective learning of complex tasks (Schmidt 1991), training activities that resemble real-life tasks is supposed to maximize training effects. It may be the reason why the treatment effect was only evident in the 2 exercise groups, but not in the TENS and control groups (Fig. 5.12).

Podsiadlo and Richardson (1991) found that older adults who were able to complete the TUG task in less than 20 seconds were independent in the transfer tasks involved in activities of daily living, while those requiring 30 seconds or longer to complete the task tended to be more dependent in their activities of daily living and required assistive devices for ambulation. In our study, the mean TUG scores ranged from 23.6 to 31.4 seconds at baseline. After 4 weeks of treatment, only subjects in the TENS+TRT group could finish the task in less than 20 seconds at T3 and TFU.

5.6 Conclusion

In conclusion, the present study demonstrated that the home-based rehabilitation program involving TENS and/or task-related training was feasible and acceptable by subjects with stroke at least one year ago. More importantly, the combined TENS+TRT home-based rehabilitation program improved the gait performance, walking endurance and functional mobility in individuals with chronic stroke significantly more than the other two treatment protocols (TENS
alone and PLBO+TRT). These findings provide solid scientific evidence for combining TENS with task-related training into an effective home-based therapeutic regimen, for patients with chronic stroke to obtain more optimal recovery in locomotor functions at a low cost to the society.
Chapter 6

Summary and Conclusions
6.1 Introduction

In the past, it was often believed that most recovery of function occurs in the first 3 months following stroke. However, there is a growing body of evidence demonstrating that with appropriate training, individuals at 6 months or more after stroke can still improve their performance of functional tasks and aerobic capacity (see details in 1.3.1). Despite this evidence, rehabilitation programs appear to be available only to patients during their stay in the hospital or at outpatient units in Hong Kong. The absence of ongoing rehabilitation programs after discharge from hospital could exacerbate disability and handicap, which arise not only from the impairments resulting from stroke, but also from the deleterious neural, muscular, psychological, and cardiovascular adaptations that accompany disuse and use of maladaptive behavior (Hachisuka et al. 1997; Ryan et al. 2000). Home rehabilitation programs are one way to provide ongoing treatment for patients with stroke to maintain and/or improve their performance.

Although TENS has been used in stroke rehabilitation over the last decades, there were only 2 single-blinded randomized clinical trials conducted with placebo groups on the influence of high frequency TENS in stroke patients between 1966 and 2003 (Levin and Hui-Chan 1992; Yan and Hui-Chan 2002). Levin and Hui-Chan (1992) demonstrated that 60 minutes of TENS for 3 weeks over the peroneal nerve decreased clinical spasticity in the spastic ankle plantarflexors, EMG co-contraction ratios, and increased increased vibratory inhibition of the soleus H reflex and voluntary ankle dorsiflexing force up to 820% in 13 subjects with chronic stroke. Similar protocol with TENS applying over 4 acupuncture points of the affected lower extremity: ST 36 (Zusanli), LR 3
(Taichong), GB 34 (Yanglingquan), and UB 60 (Kulun) was found to produce a similar cumulative enhancing effect on motor recovery of the lower extremity in 56 subjects with acute stroke (Yan and Hui-Chan 2002).

Muscle weakness is recognized as a major cause of disability in patients with stroke (Fellows et al. 1994; Gowland et al. 1992; Sahrmann and Norton 1977), but it is not common to include strengthening exercises due to fear of increasing spasticity. However, several preliminary clinical trials using pre- and post-test designs have revealed the positive effects of strength training on muscle strength and functions in subjects with stroke (Sharp and Brouwer 1997; Teixeira-Salmela 2001). Recent research findings showed that strength training should be task-related and specific to the particular movement velocity, muscle length or position in which muscles are being trained, so as to facilitate the regain of muscle strength and pattern of muscle activation necessary to the task and context (Rutherford 1988).

In fact, there has been no study examining the combined use of TENS and contemporary task-related training in a home-based rehabilitation program for subjects with chronic stroke. As TENS and task-related training appear to be capable of separately inducing plastic changes in the nervous system with beneficial consequences (see 1.4.2. and 1.4.3 for details), we hypothesize that their combined applications would augment motor recovery more so than either TENS or TRT alone, even in subjects who had stroke at least one year ago.

The present thesis consists of 3 studies: 1 pilot and 2 main studies. The objectives of these 3 studies are:
Pilot Study

1. To quantify the reliability of the 5 outcome measures used in the main study. They include:
   (i) spasticity of ankle plantarflexors
   (ii) peak torque generated, integrated EMG of agonists and EMG co-contraction ratio during MIVC of ankle dorsi- and plantar-flexion
   (iii) gait performance in terms of temporal-spatial gait parameters
   (iv) walking endurance assessed by the 6-minute walk test
   (v) functional mobility assessed by the timed “Up & Go” test

2. To examine the differences in the above 5 outcome measures between healthy elderly and subjects with chronic stroke

3. To delineate possible associations between the timed “Up & Go” test and the other 4 outcome measures in subjects with chronic stroke.

Main Studies

4. To compare the relative effectiveness of 4 treatment protocols on spasticity of ankle plantarflexors and ankle muscle functions over a 4-week treatment period in subjects with chronic stroke. The 4 treatment protocols include:
   (i) TEN for 60 minutes
   (ii) TENS and task-related training (TRT) for 60 minutes each
   (iii) Placebo TENS (PLBO) and TRT for 60 minutes each
   (iv) Control without active treatment

5. To compare the relative effectiveness of the above treatment protocols on gait performance, walking endurance and functional mobility over a 4-week treatment period in subjects with chronic stroke.
6.2 Summary and Conclusions of Main Findings

6.2.1 Study 1: Reproducibility of Measurement Protocol: A Pilot Study

The pilot study in this thesis documented the spasticity level of ankle plantarflexors and motor dysfunctions in subjects with chronic stroke as compared with healthy elderly. The study addressed the reproducibility of the 5 outcome measures used in the main study; differences of the 5 outcome measures between healthy elderly and subjects with stroke; and possible associations between the TUG scores and the other 4 outcome measures. The main findings showed:

1. There was high test-retest repeatability of the 5 outcome measures between days with ICCs of:

(i) the Composite Spasticity Scale were 0.80 in both left and right legs of healthy elderly, and 0.97 and 0.80 respectively in affected and unaffected legs of stroke subjects (Table 3.3).

(ii) peak torque generated, IEMG of agonists and EMG co-contraction ratio during ankle dorsiflexion and plantarflexion were 0.63 to 0.99 in healthy elderly, and 0.90 to 0.99 in subjects with stroke (Table 3.4).

(iii) gait performance including gait velocity, cadence, step and stride length, single-leg and double-leg support duration were from 0.66 to 0.99 in healthy elderly, and from 0.94 to 0.99 in subjects with stroke (Table 3.6).

(iv) the distance covered in the 6-minute walk test were 0.91 in healthy elderly and 0.98 in stroke subjects (Table 3.8).
(v) the timed “Up & Go” scores were 0.97 in healthy elderly and 0.95 in subjects with stroke (Table 3.9).

2. Significant differences were found in the 5 outcome measures between healthy elderly and subjects with stroke.

(i) The mean scores of the Composite Spasticity Scale for the affected leg in subjects with stroke (11.6 ± S.D. 1.4; Table 3.3) were significantly higher than those of the left and right legs of healthy elderly (5.8 ± 0.4 and 5.8 ± 0.3 respectively), and the unaffected legs in subjects with stroke (6.2 ± 0.4 ) (P<0.004 for all).

(ii) For muscle functions, subjects with stroke had significantly weaker plantarflexors in terms of decreased peak torque generated (11.2 ± 3.5 Nm; Table 3.5), decreased IEMG of medial gastrocnemius (0.01 ± 0.004 mV.s), and increased EMG co-contraction ratio during ankle plantarflexion (53.7 ± 15.8 %) when compared with those of healthy elderly (respective values for the left side: 25.1 ± 12.1 Nm, 0.09 ± 0.05 mV.s, 25.3 ± 13.4 % with similar values for the right leg) and the unaffected leg of stroke subjects (respective values: 23.7 ± 8.5 Nm, 0.05 ± 0.03 mV.s, 27.6 ± 11.4 %) (P<0.004 for all). During dorsiflexion, subjects with stroke had significantly weaker dorsiflexors in terms of the IEMG of tibialis anterior (0.05 ± 0.03mV.s), when compared with those of healthy elderly (0.13 ± 0.06 mV.s for the left side and 0.14 ± 0.06 mV.s for the right side), and smaller torques (11.1 ± 4.6 Nm) when compared with that of the
unaffected leg of stroke subjects (respective values: 19.3 ± 4.7 Nm) 

(P<0.004).

(iii) Patients with stroke walked significantly slower (mean gait velocity, 48.7 ± 22.1 cm/s; Table 3.7) than that of healthy elderly (125.6 ± 23.8 cm/s), with significantly reduced cadence (84.3 ± 20.7) than that of healthy elderly (114.9 ± 9.7). Moreover, subjects with stroke had significantly shorter step and stride length on both affected and unaffected sides, and shortened single-leg support duration on the affected side, as well as lengthened stance time and double-leg support duration on the unaffected side when compared with those of their healthy counterparts (P<0.004 for all).

(iv) For the distance covered in the 6-minute walk test, the stroke subjects walked a significantly shorter distance (202.3 ± 88.0 m; Table 3.8) than that of the healthy elderly (416.5 ± 95.2 m), showing a decrease of slightly more than twofold (P<0.004 for all).

(v) To complete the timed “Up & Go” test, the stroke subjects (22.6 ± 8.6 s; Table 3.9) required significantly longer time than that of the healthy elderly (9.1 ± 1.6 s), a decrease of more than twofold (P<0.004).

3. Spearman correlation analyses revealed that:

(i) there were no significant associations between spasticity of ankle plantarflexors of both affected and unaffected legs and TUG scores (Table 3.10).
(ii) the peak plantarflexion torque generated by MIVC of the affected and unaffected plantarflexors were moderately to strongly correlated with TUG scores in a negative manner \( r=-0.91 \) and \( -0.57 \) respectively; \( P<0.01 \), while the IEMG of tibialis anterior muscle on the affected side was moderately correlated with the TUG scores \( r=-0.50 \); Table 3.10 \( P<0.05 \).

(iii) the gait velocity and cadence were moderately to strongly correlated with the TUG scores in a negative manner \( r=-0.86 \) and \( -0.61 \) respectively; Table 3.10 \( P<0.01 \).

(iv) the step and stride length of both affected and unaffected legs were significantly associated with the TUG scores in a negative manner \( r=-0.60 \) to \( -0.77 \); Table 3.10 \( P<0.05 \).

(v) the stance time (\% of gait cycle) of the unaffected leg and double-leg support duration (\% of gait cycle) of both affected and unaffected legs were moderately associated with the TUG scores in a positive manner \( r=0.45 \) to \( 0.57 \); Table 3.10 \( P<0.05 \), while single-leg support duration of the affected leg was strongly correlated with the TUG scores in a negative manner \( r=-0.6 \); Table 3.10 \( P<0.01 \).

(vi) the distance covered in the 6-minute walk test was strongly correlated with the TUG scores in a negative manner \( r=-0.93 \); Table 3.10 \( P<0.01 \).
6.2.2 Study 2: A Comparison of the Relative Effectiveness of Four Treatment Protocols on Spasticity and Muscle Functions in Subjects with Chronic Stroke

Subjects in the present study had moderate to severe level of spasticity in their affected ankle plantarflexors, which may or may not affect the force-generating capacity of the paretic muscles. Hence, one of the main studies examined the effect of the 4 treatment protocols applied over a 4-week period on the spasticity of ankle plantarflexors and muscle functions during MIVC of ankle dorsiflexors and plantarflexors. The main findings were:

1. Subjects in both TENS (TENS and TENS+TRT) groups demonstrated significantly greater % decrease in the CSS scores (-6.6%; Table 4.2) after 2 weeks of treatment (T2) when compared with those of the PLBO+TRT group (-2.5%) and control groups (-0.9%). At the end of the 4-week treatment (T3) and at follow-up (TFU) 4 weeks after treatment stopped, all 3 intervention groups had significantly greater decreases in CSS scores when compared with that of the control group (P<0.01).

2. Subjects in the 2 TENS (TENS and TENS+TRT) groups showed significant increases in peak dorsiflexion torques in the affected leg earlier (from T1 on; Table 4.3) than those in the PLBO+TRT group (from T3 on) when compared with that of the control. Interestingly, only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the significant increases at follow-up (TFU). The increase in the TENS group was not maintained at TFU and was significantly lower than that of the 2 exercise groups.
3. The TENS+TRT group demonstrated significant increases in peak plantarflexion torques earlier than those in the PLBO+TRT group, when compared with those of the control group in both affected (from T₁ and T₂ on respectively in the TENS+TRT and PLBO+TRT groups; Table 4.3) and unaffected legs (from T₂ on and from T₃ on respectively; Table 4.4). Moreover, the TENS+TRT group showed significantly greater % increases in peak plantarflexion torques when compared with those of the TENS group at T₂ and Tᵢₑₑ (P<0.01) in the affected leg, and at T₃ and Tᵢₑₑ in the unaffected leg. In contrast, the control group showed negligible within- and among-group changes over the 8 weeks.

4. The 3 intervention (TENS, TENS+TRT and PLBO+TRT) groups showed significantly greater % increases in IEMG of tibialis anterior muscle at T₃ when compared with that of our control group during ankle dorsiflexion (P<0.01 for all; Table 4.5).

5. During ankle plantarflexion, the TENS+TRT group showed significantly greater % increases in IEMG of medial gastrocnemius when compared with those of the TENS group at T₂ (P<0.01; Table 4.5) and T₃ (P<0.05), of the PLBO+TRT group at T₂ (P<0.01), and of the control group at T₂ and T₃ (P<0.01)

6. The 2 TENS (TENS and TENS+TRT) groups showed significant decreases in the EMG co-contraction ratios during dorsiflexion at T₂ and T₃ (P<0.01; Table 4.6) and at T₃ (P<0.01) respectively, when compared with those of the control group. In contrast, negligible changes were found in the PLBO+TRT and control groups over the 8-week period.
7. The TENS+TRT group demonstrated significantly greater % reductions of EMG co-contraction ratios during plantarflexion when compared with those of the TENS group from $T_2$ to $T_{FU}$ ($P<0.05$; Table 4.6), and with those of the control group at $T_3$ and $T_{FU}$ ($P<0.01$). The PLBO+TRT group also showed significantly greater % reductions of EMG co-contraction ratios when compared with that of the TENS group at $T_3$ to $T_{FU}$, and the control group at $T_3$ and $T_{FU}$ ($P<0.01$ for all).

In summary, this study revealed that the 2 TENS (TENS and TENS+TRT) groups produced significantly earlier reduction of plantarflexor spasticity and increase of peak dorsiflexion torque over the 20 treatment sessions than the PLBO+TRT group when compared with that of the control group. However, only the 2 exercise (TENS+TRT and PLBO+TRT) groups maintained the increase in peak dorsiflexor torque 4 weeks after treatment ended. For plantarflexion, only the 2 exercise (TENS+TRT and PLBO+TRT groups) but not the TENS group had significant % increases in peak torque, iEMG of the MG muscle and reduction of EMG co-contraction ratio after 4 weeks of treatment when compared with those of the control.

In conclusion, patients from the 3 treatment groups had reduced spasticity of ankle plantarflexors at $T_3$ and $T_{FU}$, and aspects of muscle functions improved during MIVC of the affected ankle dorsiflexors at $T_3$ after 4 weeks of treatment. In contrast, negligible changes were found in the control group over the 8-week period. More specially, 4 weeks of TENS treatment alone decreased spasticity of ankle plantarflexors, increased peak dorsiflexion torque on the affected side,
increased IEMG of the affected TA muscle with reduced EMG co-contraction ratio during dorsiflexion. Four weeks of exercise alone (PLBO+TRT group) produced similar effects as those of TENS over time, except for the reduction of EMG co-contraction ratio during ankle dorsiflexion which had not yet to reach a significant level. Besides, exercise alone also improved ankle plantarflexor function, as shown by increased peak plantarflexor torque, increased IEMG of MG muscle and reduced EMG co-contraction ratio during plantarflexion at T3, except for the IEMG of MG muscle, the significant changes were maintained even 4 weeks after treatment ended. Interestingly, combining TENS and task-related training together (TENS+TRT group) was found superior to TENS or TRT alone in reducing plantarflexor spasticity and improving muscle functions of ankle dorsi- and plantar-flexors. The combined TENS+TRT group had decreased plantarflexor spasticity earlier than that of the PLBO+TRT and control groups, and showed earlier and/or greater muscle function improvement during MVIC of ankle dorsiflexion as well as plantarflexion. Most importantly, the TENS+TRT group maintained more of the treatment effects 4 weeks after the treatment ended than the other 2 treatment groups.

6.2.3 Study 3: A Comparison of the Relative Effectiveness of Four Treatment Protocols on Locomotor Capacities in Subjects with Chronic Stroke

This study examined the relative treatment effectiveness of the 4 treatment protocols on the locomotor capacities in patients with chronic stroke. The findings revealed the following changes:
1. The combined TENS+TRT group showed significantly greater % increase in gait velocity, when compared with those of the other 3 groups. Significant differences from those of PLBO+TRT and control groups were noted as early as T1 after the first treatment, and from all the other 3 groups from T2 on till 4 weeks after treatment ended (T_{FU}; Table 5.1). In contrast, the other 2 treatment (TENS and PLBO+TRT) groups did not achieve significant among-group differences over the entire 8-week period.

2. The combined TENS+TRT group was the only group showing significantly greater cumulative increase of cadence when compared with the other 3 groups at T_{FU} (P<0.01) and with the control group at T3 (P<0.01) (Fig. 5.2). In fact, there were negligible within- and among- group changes in the other 3 groups over the 8 weeks.

3. The combined TENS+TRT group demonstrated significantly greater % increase in step length of the affected leg from T2 to T_{FU} when compared with those of the TENS group, and from T1 to T_{FU} when compared with those of PLBO+TRT and control groups (P<0.01) (Table 5.3). For the unaffected leg, the combined TENS+TRT group also showed significantly greater % increase in step length at T_{FU} when compared with those of the TENS and PLBO+TRT groups (P<0.01), and from T2 to T_{FU} when compared with that of the control group (P<0.01). In contrast, the PLBO+TRT group showed significantly greater % increase in step length only at T_{FU} in the affected leg (P<0.05), and only at T3 in the unaffected leg (P<0.01) when compared with those of the control group. The TENS group without TRT achieved even more negligible among-group differences over the entire 8 week period.
4. The combined TENS+TRT group demonstrated significantly greater % increase in stride length of the affected leg from $T_2$ to $T_{FU}$ when compared with those of the TENS group ($P<0.01$), at $T_1$, $T_2$ and $T_{FU}$ when compared with those of the PLBO+TRT group, and from $T_1$ to $T_{FU}$ when compared with those of control group ($P<0.01$) (Table 5.4). For the unaffected leg, the combined TENS+TRT group again showed significantly greater % increase in stride length from $T_2$ to $T_{FU}$ when compared with those of the TENS group ($P<0.01$), and from $T_1$ to $T_{FU}$ when compared with those of the PLBO+TRT and control groups ($P<0.01$). Again, the TENS group did not achieve significant among-group differences over the 8 weeks.

5. There were negligible differences in stance time on the affected leg among the 4 groups (Table 5.5). However, the combined TENS+TRT group demonstrated significantly greater % decrease in stance time (in % of gait cycle) on the unaffected leg from $T_2$ to $T_{FU}$ when compared with those of the TENS group ($P<0.01$), at $T_3$ and $T_{FU}$ when compared with those in the PLBO+TRT group ($P<0.01$), and from $T_1$ when compared with those of the control group ($P<0.01$). The PLBO+TRT group was the only other treatment group showing significantly greater % decrease of stance time on their unaffected leg when compared with those of the control group at $T_2$ and $T_3$.

6. The combined TENS+TRT group demonstrated significantly greater % increase in single support duration (in % of gait cycle) at $T_2$ and $T_3$ when compared with those of the TENS group ($P<0.01$), and from $T_1$ to $T_{FU}$ when compared with those of PLBO+TRT and control groups ($P<0.05$) in the affected leg (Table 5.6). Again, the PLBO+TRT was the only other
treatment group showing significantly greater % increase in single support duration in their affected legs when compared with those of the control group at T2 and T3. In contrast, negligible differences were found among the 4 groups in the unaffected leg.

7. The combined TENS+TRT group demonstrated significantly greater % decrease in double support duration (in % of gait cycle) at T2 and T_FU when compared with those of the TENS group (P<0.01), from T2 to T_FU when compared with those in the PLBO+TRT groups (P<0.05), and at T1 to T_FU when compared with those of control group (P<0.05). For the unaffected leg (Fig. 5.10), the combined TENS+TRT group demonstrated significantly greater % decrease in double support duration at T2 and T_FU when compared with those of the TENS group (P<0.01), and at T2 to T_FU when compared with those of the control group (P<0.01). In the TENS group, there was significantly greater % decrease at T3 in the unaffected leg when compared with that of the control group (P<0.01). In contrast, the PLBO+TRT group achieved negligible among-group changes over the 8 weeks.

8. Pearson correlation analyses revealed that there were significant positive associations between gait velocity on the one hand, and cadence (r= 0.833; P=0.000), stride and step length of both affected and unaffected legs (r=0.612 to 0.895; P=0.000), and single support duration of both affected (r=0.855) and unaffected legs (r=0.356) (P=0.000) on the other in those stroke patients (Table 5.8). Significant negative relationships were found between gait velocity, and stance time (r= -0.337 to -0.868; P=0.000), as well as double support duration (r= -0.759 to -0.764; P=0.000).
9. The combined TENS+TRT group further demonstrated significantly greater % increase of the distance covered in 6 MW than those of the TENS and control groups \((P<0.01)\) (Table 5.9). In contrast, the PLBO+TRT group was the only other treatment group showing significantly greater % increase when compared with that of the control group \((P<0.01)\), but much later at \(T_{FU}\) only.

10. The combined TENS+TRT group also demonstrated significantly greater % decrease in TUG scores at \(T_{FU}\) when compared with those of the TENS groups \((P<0.01)\), and from \(T_2\) to \(T_{FU}\) when compared with those of the control group \((P<0.01)\) (Table 5.10). Again, the PLBO+TRT group was the only other treatment group showing significantly greater % decrease than that of the control group only at \(T_{FU}\) \((P<0.01)\).

In summary, this study revealed that the TENS+TRT group demonstrated significantly greater % of increase in gait velocity toward the end of the 4-week treatment when compared with the TENS, PLBO+TRT and control groups (all \(P<0.01\)). Accompanying the increase in gait velocity, significant among group increases in cadence, step and stride length, stance time, single-leg support duration and decrease of double-leg support duration were also found. Furthermore, the TENS+TRT group also demonstrated significantly greater % increase of walking endurance assessed by the distance covered in 6 MW and % decrease of the TUG scores than that of the TENS and/or control groups.

To conclude, this thesis demonstrated that a home-based rehabilitation program involving TENS and/or task-related training is feasible. More importantly, it is effective in improving locomotor capacities in patients who had
stroke at least one year ago. The results further demonstrated that 20 sessions of combined TENS+TRT treatment was superior to either TENS alone or PLBO+TRT, in enhancing the recovery of locomotor and related abilities in chronic stroke survivors. This is the first randomized controlled trial which shows that combining a passive (TENS) and an active (TRT) treatment was more effective than either treatment strategy alone, in improving gait performance, walking endurance and functional mobility of patients with a mean of 5.3 years after stroke.

6.3 Implications for Stroke Rehabilitation

The findings of this study directly challenge the assumption that improvement in function following stroke is mainly due to spontaneous recovery (Dombovy and Bachy-Rita 1988). In addition, the outcome is consistent with the increasing evidence that patients following stroke can improve their performance on specific tasks if those tasks are practiced repeatedly over time (Ada et al. 2003; Dean et al. 2000; Dean and Shepherd 1997, Monger et al. 2002). The results of this thesis further suggest that stroke rehabilitation needs to be continued long after the first 3 months post-stroke when most patients in Hong Kong may not be able to gain ready access to rehabilitation services.

The present study provided detailed guidelines for a 4-week home-based rehabilitation program targeting in improving locomotor functions in patients with chronic stroke. The frequent application of the program (5 times a week) was sufficient to induce improvements after a relatively short period of time of 4 weeks. Moreover, the home-based program is not prohibitively complex. We
predicted that it was feasible to be implemented in a home-environment by many patients under the supervision of a physiotherapist on an intermittent basis only. As such, it is cost-effective.

6.4 Limitations of the Study

There are certain limitations of the present study. First, not all subjects were blinded to their “treatment”, because the 2 exercise groups were aware that they were receiving exercise intervention. It is possible that part of the improvement found in these 2 groups may have been the result of increased motivation. Moreover, subjects in the control group participated in 5 assessment sessions only. The frequency of therapist-patient contacts was less than that of the other 3 treatment groups. The therapists’ enthusiasm, drive, and empathy may have affected treatment outcome in an unspecified manner by as yet unexplained mechanisms (Langhorne and Dennis 1998). The fact that the control group received less attention than the active treatment groups might have by itself affected the results in trials of specific rehabilitation interventions. Nevertheless, possible placebo effect had been addressed in part by our research design. Briefly, the PLBO+TRT group made less and/or more belated gains than the combined TENS+TRT group when all the outcome measures were considered together. In other words, while psychological (placebo) factors cannot be totally ruled out, (the combined TENS+TRT) active treatment was shown to be more effective overall.

Generalization of the results is confined to chronic stroke patients with certain walking ability i.e. walking independently with or without walking aids.
Besides, in assessing the MIVC of ankle muscles, non-normalized EMG areas were compared across subjects and days. Moreover, the present study did not set out to address more global functional outcomes e.g. quality of life. We had predefined important end points at the level of motor impairments and functional limitations, with sample size calculation based on the power to detect important differences in the relevant outcomes, e.g. the muscle strength of affected lower extremity. In order to detect differences in more global outcomes such as quality of life, a large, multisite trial is needed.

Due to time constraints in a PhD thesis, the effects of the treatment protocols were examined up to 4 weeks after cessation of training only. Whether or not improvements in performance can be maintained more than 4 weeks remains unknown. There is evidence that benefits of training are not always maintained (Engardt et al. 1993; Ricahrads et al. 1993). Wolf and colleagues (1989) and Taub and associates (1993, 1994) found that stroke patients were able to maintain the improvement in their affected upper limb for up to two years, after two-week period of restraint of the unaffected arm. They attributed this positive finding to the ability of the patients to use the reacquired skills of their affected upper limb throughout their daily life. If so, the daily requirement for the patients to walk would also help to maintain the functional gains achieved as a result of our home-based rehabilitation program longer. This would be a subject matter for further research.
6.5 Indications for Future Research

As a result of the positive findings from the present study, is the efficacy of TENS with task-related training on locomotor functions should be examined in the acute phase. It may be possible to achieve greater improvements in functional performance during this early phase, when the potential for neural plasticity is known to be greater (see section 1.5 for details), and before the individuals have a chance to learn adaptive behaviors that may interfere with functional recovery.

Another important area of future research concerns hemiparetic subjects with greater motor deficits. In our study, all subjects can walk independently for 10 meters with or without walking aids. Those who cannot fulfill these criteria are the ones who may also have higher risks in developing deleterious cardiovascular and musculoskeletal adaptations due to immobility. Our results strongly suggest that a training program based on an understanding of neurophysiology, neuroplasticity and motor learning may also be effective in improving locomotor functions in the more severely affected patients. Addressing this issue in future studies could expand the applicability of TENS and task-related training across a broader severity spectrum of chronic stroke.

Our training protocol demonstrates that gains can be attained over a relatively short training period, i.e. 4 weeks or 20 treatment sessions in all. However, it is possible that longer training periods or other advanced task-related training, including progressive or incremental resistive components, could result in greater and/or more prolonged motor or functional gains.
Above all, more basic research studies are needed to establish the manner in which improvements in lower extremity functions in chronic hemiparetic patients are mediated by central neural plastic processes.
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Appendices
Appendix Ia: The Informed Consent Form (English Version)

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences

Research Project Informed Consent Form

Project entitled: Effectiveness of an Innovative Home-Based Rehabilitation Program on Performance of Lower Extremity Functions in Patients with Chronic Stroke: A Randomized, Controlled Trial.

Investigators: Ms. Shamay S.M. Ng, Professor Christina W.Y. Hui-Chan.

Purpose:
Using an innovative home-based rehabilitation program with transcutaneous electrical nerve stimulation (TENS) and task-related training to improve motor recovery in the lower extremity of patients with chronic stroke.

Methods:
All subjects will be randomly assigned to 4 groups: (1) treatment group having high-intensity TENS and task-related training, (2) treatment group having low-intensity TENS and task-related training and, (3) treatment group having TENS only and, (4) non-treatment group. If you involve in the first group, you will receive high-intensity electrical stimulation (TENS) for 60 minutes and task-related training for lower extremity for 60 minutes, 5 days a week for 4 weeks. If you involve in the second group, you will receive low-intensity electrical stimulation (TENS) for 60 minutes and task-related training for lower extremity for 60 minutes, 5 days a week for 4 weeks. If you involved in the third group, you will receive only TENS treatment for lower extremity for 60 minutes, 5 days a week for 4 weeks. If you involve in the fourth group, you will not receive any specific treatment.
In any group, you will be assessed on improvement of lower extremity functions and functional abilities at a monthly basis for 5 occasions. You will be required to attend the Department of Rehabilitation Sciences Research Laboratory of the The Hong Kong Polytechnic University for approximately two hours on each occasion. Measurements include level of spasticity of ankle plantarflexor, maximal isometric voluntary contraction of ankle dorsiflexors and plantarflexors, walking performance, walking endurance and performance of timed “Up & Go” test.

Benefits and Risks:

The major benefit from participating in this study is that you may have the opportunity to know your own level of spasticity, muscle strength of ankle muscles, walking endurance, performance of walking and functional tasks. The results may also be beneficial for planning an intensive home rehabilitation for recovery of lower extremity functions in patients with stroke.

The electrical stimulation and testing procedures have been well proved to be safe and used with negligible side effects, both clinically and experimentally. A few subjects may feel some exhaustion during assessment and therefore rest will be allowed between assessment procedures. Some subjects may have temporary mild skin irritation from the conducting gel where the electrodes of electrical stimulation are applied. This should be cured with anti-irritation cream in one or two days.

Confidentiality:

Your participation in the research study is strictly voluntary, and you may withdraw at any time without penalty. The Ethical Committee of The Hong Kong Polytechnic University has approved this study. The results of this study will provide information about the reproducibility of the measurement protocol.
and the effectiveness of the home-based program in improving the lower extremity functions. Any personal information obtained from me through this study will be confidential and you will not be identified in any communication concerning this study.

Enquiries:

Questions about this study will be answered by Ms. Shamay Ng and/or Professor Christina Hui-Chan who can be reached at the Department of Rehabilitation Sciences, the Hong Kong Polytechnic University located at Hung Hom, Kowloon, or by telephone at 2766-7092 and 2766-6704 respectively. You may also contact Ms. Michelle Leung by telephone at 2766-5397.
Informed Consent

I, ________________________________, have been explained the details of this study. I voluntarily consent to participate in this study. I understand that I can withdraw from this study at any time without giving reasons, and my withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential risk in joining this study. I also understand that my personal information will not be disclosed to people who are not related to this study and my name or photograph will not appear on any publications resulted from this study.

I can contact the chief investigator, Professor Christina Hui-Chan at telephone 2766-6704 for any questions about this study. If I have complaints related to the investigators, I can contact Ms. Michelle Leung, secretary of Departmental Research Committee, at 2766-5397. I know I will be given a signed copy of this consent form.

Signature (subject): ________________________________
Date: ______________

Signature (Witness): ________________________________
Date: ______________
Appendix Ib: The Informed Consent Form (Chinese Version)

香港理工大學康復治療學系
中風康復治療研究病人參加研究同意書

項目名稱: 家居復康治療 (包括透皮神經電刺激及康復運動) 對晚期中風病人下肢功能恢復的影響。

研究目的: 採用透皮神經電刺激及康復運動治療晚期中風病人，幫助中風病人恢復偏癱下肢的活動功能。

負責人: 伍尚美女士，許陳雲教授

研究方法: 所有參與此項研究之中風病人將隨機分成四組，分別接受: (1) 高量透皮神經電刺激治療及下肢康復活動; (2) 微量透皮神經電刺激治療及下肢康復活動; (3) 高量透皮神經電刺激治療; (4) 及毋須接受任何治療。若閣下參加第一及第二組治療，則須接受每星期五天之電療及下肢康復活動，每次電療及運動時間均為一小時，即每次治療共須兩小時。若閣下參加第三組，則須接受每星期五天之高量透皮神經電刺激治療。若閣下參加第四組，則毋須接受任何治療及活動。整個研究及治療將持續四個星期。

所有參與人士治療期間，須定時到香港理工大學康復治療學系之研究實驗室，接受共四次，每次為時約兩小時之有關下肢功能恢復的檢查，內容包括量度參與人士之下肢經喚、小腿肌肉力量、步行狀況、運動耐力、活動功能及腦電波等數據。

若能參與此研究，參與人士除了解自己下肢經喚、小腿肌肉力量、步行狀況、運動耐力、活動功能及腦電波等狀況外，並能
提供重要數據，幫助研究家居康復治療對晚期中風病人下肢功能恢復的影響。整個檢查及治療過程十分安全，唯期間小部份參與人士可能會感到少許疲倦，參與人士可按需要於測試期間作中段休息。亦有小部份參與人士可能會於透皮神經電刺激治療的電極擺放處有輕微的皮膚過敏反應，只須在患處塗上抗敏的藥膏，二至三天便能自行痊癒。是項研究並已獲得香港理工大學的安全審批。

所有參與人士均屬自願性質，並於療程中段可隨時退出此項研究。所有個人資料均絕對保密。

參與人士若對是項研究如有任何疑問，可致電康復治療學系博士研究生伍尚美女士（電話：2766 7092）及許陳雲影教授（電話：2766 6704）查詢。若對研究人員有任何投訴，本人可聯絡康復治療科學系研究委員會秘書梁小姐（電話：2766 5397）。
中風康復治療研究病人參加研究同意書

本人________________________(香港身份證號碼:__________)

現聲明自願參加此中風康復治療之研究項目。本人明白是項研究的目的及程序，並證明負責人已將是次項目解釋清楚。本人也明白在此項研究中，所有個人資料會絕對保密，本人並可以隨時退出此項研究，而不會受到任何處罰。本人亦明白此項研究的一切有關風險。

簽名:____________________________________

見證人簽名:____________________________________

日期:_________________________________________

本人________________________現聲明，本人已把是項研究的目的、程序、好處及風險，向上列有關人士解釋清楚。

研究負責人簽署:_____________________________

日期:_________________________________________
Appendix II: Guidelines for Composite Spasticity Scale

1. **Achilles Tendon Jerks**
   Subject will be in the supine position with the hip abducted and knees flexed.
   The examiner will tap the Achilles tendon with the broad end of a reflex hammer.
   
   0: no tendon reflex
   1: minimal tendon reflex
   2: normal tendon reflex
   3: moderately hyperactive tendon reflex
   4: maximally hyperactive tendon reflex.

2. **Resistance to Full-Range Passive Ankle Dorsiflexion**
   Subject will be in the supine position with the leg in extension. The examiner will dorsiflex the foot and feel the resistance.
   
   0: no resistance (flaccidity)
   2: decreased resistance (hypotonia)
   4: normal resistance
   6: mild to moderate resistance
   8: maximally increased resistance

3. **Ankle Clonus**
   Subject will be in the supine position with the leg in the extension. The examiner will dorsiflex the foot quickly (just once) and feel the ankle clonus.
   
   1: clonus not elicited
   2: one to two beats of clonus
   3: greater than two clonus but unsustained clonus
   4: sustained clonus in number of beats per minute (lasting for more than 30 seconds).
Appendix III: Abbreviated Mental Test (Chinese Version)

簡易記憶測試 (AMT)  

1. 你今年幾歲 ? (+/- 5 歲)  
   分數 0/1

2. 現在是什麼時間 ?  
   (約幾點鐘，上午 / 下午，夜晚)  
   分數 0/1

3. 在測試最後，請覆述“上海街 42 號”  
   分數 0/1

4. 今年是一九九幾年 ? (+/-1 年)  
   (或今年是什麼生肖年)  
   分數 0/1

5. 這裏是什麼地方 ?  
   分數 0/1

6. 試認出任何兩人。 (護士或 )  
   分數 0/1

7. 你幾時生日 ? ( 月 日)  
   分數 0/1

8. 中秋節是幾月幾日 ?  
   分數 0/1

9. 現任港督是誰或现任中國領導人是誰 ?  
   分數 0/1

10. 試由 20 倒數至 1。  
    分數 0/1

8 – 10 分  你的認知能力正

4 – 7 分  你的認知能力麻麻

0 – 3 分  你的認知能力好差
Appendix IV: Definitions of Temporal and Spatial Parameters According to the GAITRite Walkway System

Temporal Parameters

(1) Velocity
Velocity is obtained after dividing the distance by the ambulation time.

(2) Stance Time
Stance time is the period of time when the foot is in contact with the ground.

(3) Duration of Single Support
Duration of single support is the time elapsed between the last contact of current footfall to the first contact of the next footfall of the same foot. This is equal to the swing time of the opposite foot.

(4) Duration of Double Support
Duration of double support is the time elapsed between first contact of the current footfall and the last contact of the previous footfall, added to the time elapsed between the last contact of the current footfall and the first contact of the next footfall. As illustrated in Fig 6.1, it is the sum of the initial double support DS1 and the terminal double support DS2.

![Diagram of GAITRite Walkway System](image)

Fig. 6.1 Temporal parameters of the GAITRite Walkway System
Spatial Parameters

(1) Step Length

Step length is measured along the horizontal axis, from the geometric heel centre of the current footfall to the geometric heel center of the previous footfall on the opposite foot. In Fig. 6.2, (AX) is the step length of the right foot, and (YG) the step length of the left foot.

(2) Stride Length

Stride length is measured on the line of progression between the heel points of two consecutive footfalls of the same foot (left to left, right to right). In Fig. 6.2, (GA) is the stride length of the left foot.

Fig. 6.2 Spatial parameters of the GAITRite Walkway System. Points (A), (D) and (G) are the geometric centers of the heel for each of the three footprints. Point (M) is the mid-point of line (AD) and point (N) is the mid-point of (DG). The line of progression can be found by connecting the two midpoints (M) and (N). The length of line (AX), along the horizontal axis, is the step length of the right foot, while the length of line (YG) is the step length of the second left footprint. The length of line (AG) is the stride length of the left foot.
Appendix V: Tables of Data on the Unaffected Leg (Chapter 4)

Table 4.6  Peak torque in maximum isometric voluntary contraction of unaffected ankle muscles before treatment (T₀), immediately after first treatment session (T₁), after 2 weeks and 4 weeks of treatment protocol (T₂ and T₃), and 4 weeks post-treatment (T₅₀₅₅)

<table>
<thead>
<tr>
<th></th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
<th>Control (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (Nm)</td>
<td>26.3 ± 9.5</td>
<td>25.9 ± 8.4</td>
<td>25.6 ± 7.1</td>
<td>26.0 ± 10.4</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>5.21</td>
<td>5.0</td>
<td>4.8</td>
<td>3.2</td>
</tr>
<tr>
<td>T₂ (Nm)</td>
<td>27.6 ± 9.5</td>
<td>28.5 ± 8.5</td>
<td>27.2 ± 7.1</td>
<td>26.5 ± 10.0</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>5.1</td>
<td>10.0</td>
<td>6.2</td>
<td>1.9</td>
</tr>
<tr>
<td>T₃ (Nm)</td>
<td>30.0 ± 10.2</td>
<td>29.6 ± 8.5</td>
<td>29.1 ± 7.6</td>
<td>27.3 ± 10.3</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>14.1</td>
<td>14.3</td>
<td>13.8</td>
<td>5.2</td>
</tr>
<tr>
<td>T₅₀₅₅ (Nm)</td>
<td>28.2 ± 8.9</td>
<td>29.5 ± 7.9</td>
<td>28.3 ± 7.1</td>
<td>26.8 ± 9.9</td>
</tr>
<tr>
<td>(T₅₀₅₅-T₀)/T₀ (%)</td>
<td>7.3</td>
<td>14.1 ** a</td>
<td>10.7</td>
<td>3.4</td>
</tr>
<tr>
<td><strong>Plantarflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (Nm)</td>
<td>34.5 ± 13.2</td>
<td>32.0 ± 8.0</td>
<td>29.8 ± 9.0</td>
<td>32.8 ± 12.1</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>0.8</td>
<td>4.3</td>
<td>3.4</td>
<td>1.8</td>
</tr>
<tr>
<td>T₂ (Nm)</td>
<td>35.3 ± 13.6</td>
<td>35.1 ± 9.5</td>
<td>31.9 ± 10.0</td>
<td>33.2 ± 12.5</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>2.4</td>
<td>9.7 ** a</td>
<td>7.2</td>
<td>1.1</td>
</tr>
<tr>
<td>T₃ (Nm)</td>
<td>37.3 ± 14.3</td>
<td>38.0 ± 9.1</td>
<td>35.4 ± 11.1</td>
<td>32.9 ± 12.1</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>8.0</td>
<td>18.6 ** + a</td>
<td>18.8</td>
<td>0.4</td>
</tr>
<tr>
<td>T₅₀₅₅ (Nm)</td>
<td>35.1 ± 13.9</td>
<td>38.1 ± 11.6</td>
<td>34.0 ± 10.0</td>
<td>33.2 ± 12.4</td>
</tr>
<tr>
<td>(T₅₀₅₅-T₀)/T₀ (%)</td>
<td>3.8</td>
<td>18.9 ** + + a</td>
<td>14.4</td>
<td>1.1</td>
</tr>
</tbody>
</table>

Values are mean ± SD in Nm.

Within group: bP<0.05, aP<0.01 when  T₁, T₂, T₃  and T₅₀₅₅  when compared with T₀
Among groups:  * P<0.05, ** P<0.01 when compared with control group;  a,b P<0.01 when compared with PLBO+TRT group;  a,P<0.05,  a,b P<0.01 when compared with TENS group
Table 4.7  Integrated EMG of agonists developed in maximum isometric voluntary contraction of the unaffected ankle muscles before treatment \( (T_0) \), immediately after first treatment session \( (T_1) \), after 2 weeks and 4 weeks of treatment protocol \( (T_2 \text{ and } T_3) \), and 4 weeks post-treatment \( (T_{FU}) \)

<table>
<thead>
<tr>
<th></th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
<th>Control (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>TA in Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( T_0 ) (mVs)</td>
<td>0.126 ± 0.052</td>
<td>0.128 ± 0.045</td>
<td>0.132 ± 0.051</td>
<td>0.125 ± 0.056</td>
</tr>
<tr>
<td>( (T_1-T_0)/T_0 ) (%)</td>
<td>2.4</td>
<td>1.6</td>
<td>-0.8</td>
<td>3.2</td>
</tr>
<tr>
<td>( T_2 ) (mVs)</td>
<td>0.132 ± 0.063</td>
<td>0.135 ± 0.041</td>
<td>0.131 ± 0.044</td>
<td>0.137 ± 0.056</td>
</tr>
<tr>
<td>( (T_2-T_0)/T_0 ) (%)</td>
<td>4.8</td>
<td>4.7</td>
<td>-8.0</td>
<td>9.6</td>
</tr>
<tr>
<td>( T_3 ) (mVs)</td>
<td>0.143 ± 0.066</td>
<td>0.142 ± 0.043</td>
<td>0.139 ± 0.044</td>
<td>0.137 ± 0.060</td>
</tr>
<tr>
<td>( (T_3-T_0)/T_0 ) (%)</td>
<td>13.5</td>
<td>10.9</td>
<td>5.3</td>
<td>9.6</td>
</tr>
<tr>
<td>( T_{FU} ) (mVs)</td>
<td>0.141 ± 0.056</td>
<td>0.135 ± 0.041</td>
<td>0.141 ± 0.047</td>
<td>0.135 ± 0.060</td>
</tr>
<tr>
<td>( (T_{FU}-T_0)/T_0 ) (%)</td>
<td>11.9</td>
<td>5.5</td>
<td>6.8</td>
<td>8</td>
</tr>
<tr>
<td><strong>MG in Plantarflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>( T_0 ) (mVs)</td>
<td>0.077 ± 0.070</td>
<td>0.072 ± 0.037</td>
<td>0.059 ± 0.036</td>
<td>0.068 ± 0.043</td>
</tr>
<tr>
<td>( (T_1-T_0)/T_0 ) (%)</td>
<td>13.0</td>
<td>4.2</td>
<td>6.8</td>
<td>1.5</td>
</tr>
<tr>
<td>( T_2 ) (mVs)</td>
<td>0.082 ± 0.079</td>
<td>0.075 ± 0.034</td>
<td>0.063 ± 0.037</td>
<td>0.069 ± 0.039</td>
</tr>
<tr>
<td>( (T_2-T_0)/T_0 ) (%)</td>
<td>6.5</td>
<td>4.2</td>
<td>6.8</td>
<td>0.7</td>
</tr>
<tr>
<td>( T_3 ) (mVs)</td>
<td>0.086 ± 0.072</td>
<td>0.079 ± 0.029</td>
<td>0.070 ± 0.035</td>
<td>0.070 ± 0.043</td>
</tr>
<tr>
<td>( (T_3-T_0)/T_0 ) (%)</td>
<td>11.7</td>
<td>9.7</td>
<td>18.6</td>
<td>2.9</td>
</tr>
<tr>
<td>( T_{FU} ) (mVs)</td>
<td>0.077 ± 0.064</td>
<td>0.078 ± 0.038</td>
<td>0.065 ± 0.032</td>
<td>0.067 ± 0.034</td>
</tr>
<tr>
<td>( (T_{FU}-T_0)/T_0 ) (%)</td>
<td>0.4</td>
<td>8.3</td>
<td>10.2</td>
<td>-1.5</td>
</tr>
</tbody>
</table>

Values are mean ± SD in mVs. Within group: \(^a\)P<0.05, \(^b\)P<0.01 when \( T_1, T_2, T_3 \) and \( T_{FU} \) when compared with \( T_0 \).

Among groups: \(^+\)P<0.05, \(^++\)P<0.01 when compared with control group; \(^\#\)P<0.01 when compared with PLBO+TRT group; \(^*\)P<0.05, \(^{++*}\)P<0.01 when compared with TENS group.
Table 4.8  Mean values and the percentage change of the EMG co-contraction ratios in the unaffected ankle muscles before treatment (T₀), immediately after first treatment session (T₁), after 2 weeks and 4 weeks of treatment protocol (T₂ and T₃), and 4 weeks post-treatment (Tᵢᵣ).

<table>
<thead>
<tr>
<th></th>
<th>TENS (n=19)</th>
<th>TENS+TRT (n=21)</th>
<th>PLBO+TRT (n=20)</th>
<th>Control (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dorsiflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (%)</td>
<td>7.6 ± 2.9</td>
<td>7.1 ± 3.7</td>
<td>7.3 ± 2.9</td>
<td>6.5 ± 2.7</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>12.0</td>
<td>1.8</td>
<td>-9.7</td>
<td>0.4</td>
</tr>
<tr>
<td>T₂ (%)</td>
<td>8.3 ± 6.1</td>
<td>7.9 ± 3.8</td>
<td>6.7 ± 2.3</td>
<td>6.4 ± 2.4</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>8.9</td>
<td>10.5</td>
<td>-9.3</td>
<td>-1.8</td>
</tr>
<tr>
<td>T₃ (%)</td>
<td>7.2 ± 3.2</td>
<td>7.0 ± 3.4</td>
<td>7.4 ± 4.0</td>
<td>7.6 ± 7.8</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>-4.9</td>
<td>-1.9</td>
<td>0.9</td>
<td>17.5</td>
</tr>
<tr>
<td>Tᵢᵣ (%)</td>
<td>8.0 ± 6.2</td>
<td>6.8 ± 3.6</td>
<td>7.9 ± 7.2</td>
<td>7.6 ± 7.7</td>
</tr>
<tr>
<td>(Tᵢᵣ-T₀)/T₀ (%)</td>
<td>4.8</td>
<td>-4.9</td>
<td>8.0</td>
<td>16.6</td>
</tr>
<tr>
<td><strong>Plantarflexion</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T₀ (%)</td>
<td>21.5 ± 9.1</td>
<td>22.9 ± 11.8</td>
<td>27.3 ± 13.4</td>
<td>25.0 ± 13.0</td>
</tr>
<tr>
<td>(T₁-T₀)/T₀ (%)</td>
<td>18.9 ± 6.6</td>
<td>20.7 ± 8.3</td>
<td>27.6 ± 12.2</td>
<td>24.5 ± 13.1</td>
</tr>
<tr>
<td>T₂ (%)</td>
<td>21.2 ± 9.9</td>
<td>21.5 ± 6.8</td>
<td>27.7 ± 14.0</td>
<td>23.4 ± 13.3</td>
</tr>
<tr>
<td>(T₂-T₀)/T₀ (%)</td>
<td>-1.5</td>
<td>-6.1</td>
<td>1.4</td>
<td>-6.4</td>
</tr>
<tr>
<td>T₃ (%)</td>
<td>19.6 ± 9.2</td>
<td>18.6 ± 8.1</td>
<td>23.6 ± 11.0</td>
<td>22.2 ± 13.8</td>
</tr>
<tr>
<td>(T₃-T₀)/T₀ (%)</td>
<td>-9.0</td>
<td>-18.7</td>
<td>-13.7</td>
<td>-11.3</td>
</tr>
<tr>
<td>Tᵢᵣ (%)</td>
<td>22.2 ± 9.8</td>
<td>21.3 ± 8.3</td>
<td>24.9 ± 12.0</td>
<td>23.3 ± 11.0</td>
</tr>
<tr>
<td>(Tᵢᵣ-T₀)/T₀ (%)</td>
<td>3.1</td>
<td>-7.1</td>
<td>-8.8</td>
<td>-7.1</td>
</tr>
</tbody>
</table>

Values are mean ± SD.

Within group: bP<0.05, *P<0.01 when T₁, T₂, T₃ and Tᵢᵣ when compared with T₀.

Among groups: * P<0.05, ** P<0.01 when compared with control group; "" P<0.01 when compared with PLBO+TRT group; +P<0.05, ++P<0.01 when compared with TENS group.