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Glucose Uptake During Exercise in Skeletal Muscles Evaluated by Positron Emission Tomography

Hiroyuki Shimada
Section for Health Promotion, Department of Health and Medical Care,
Center for Development of Advanced Medicine for Dementia,
National Center for Geriatrics and Gerontology
Japan

1. Introduction

Traditionally, *in vivo* skeletal muscle function has been investigated with noninvasive techniques such as magnetic resonance (MR) imaging that can characterize the motion and mechanics of contracting skeletal muscle (Axel & Dougherty, 1989; Drace & Pelc, 1994; Pipe et al., 1991). Other techniques include kinetic analyses to examine muscle activity during walking and electromyography (EMG) to evaluate muscle activity as amplitude-based algorithms. However, these techniques are limited because MR cannot be used to measure the metabolic activity of skeletal muscle, and kinetic analyses cannot measure isolated synergistic muscular activities or provide information on the etiology of the metabolic cost of exercise. Moreover, EMG quantification requires normalization of EMG amplitude to the EMG amplitude of maximal voluntary contractions, which some elderly are unable to achieve (Stevens et al., 2003). In addition, surface EMG is inappropriate for evaluating the activities of deep muscles such as the gluteus minimus.

Recently, the use of positron emission tomography (PET) and [^{18}F]fluorodeoxyglucose (FDG) has emerged as a more satisfactory method for investigating cumulative muscle activity during exercise and providing images of the spatial distribution of skeletal muscle metabolism (Fujimoto et al., 2000; Kemppainen et al., 2002; Oi et al., 2003; Shimada et al., 2007; Tashiro et al., 1999). FDG PET analysis is a metabolic imaging modality that involves the detection of intracellular FDG-6-P using gamma ray emission (Phelps et al., 1979). FDG is a glucose analog that is taken up by glucose using cells from the circulation through glucose transporters 1–4. FDG enters the glycolysis pathway and is phosphorylated into FDG-6-phosphate by hexokinase (Sokoloff et al., 1977). Intracellular FDG-6-P accumulates as it is a poor substrate for glucose-phosphate isomerase which converts glucose to fructose, and it therefore escapes dephosphorylation (Bessell & Thomas, 1973). FDG can be used to assess cumulative muscle activity over an extended period of time because the half-life of ^{18}F is relatively long (109.8 min) compared with that of other positron-emitting tracers; however, transient measurements are impossible.

FDG PET is useful for comparing task-specific muscle activity because FDG uptake is closely correlated with exercise intensity (Fujimoto et al., 2003; Kemppainen et al., 2002; Pappas et al., 2001). Results of regression analyses between normalized biceps FDG uptake and the number of repetitions of elbow flexion performed with 2 and 10 lb weights showed statistically significant positive correlations for both the 2 lb and 10 lb weights. The ratio of the slopes of the regression lines for the 10 lb and 2 lb weights was 4.94, indicating an almost fivefold difference between the external forces produced by the elbow flexors for these two loads (Pappas et al., 2001).

In this chapter, we review the findings of previous studies to demonstrate the importance of FDG PET for exercise studies and the development of rehabilitation programs for the elderly.

2. Glucose uptake in skeletal muscles during walking

2.1 Characteristics of gait function in older adults

Healthy elderly people exhibit decreased muscle mass, strength, and power production compared with healthy young people (Gallagher et al., 1997; Klitgaard et al., 1990; Larsson et al., 1979; Lynch et al., 1999; Metter et al., 1997; Porter et al., 1997; Poulin et al., 1992; Thelen et al., 1996). These decreases result in a slower gait speed, shorter step length, shorter swing phase and less range of motion at the hip, knee, and ankle joints during walking (Crowinshield et al., 1978; Elble et al., 1991; Finley et al., 1969; Hageman & Blanke, 1986; Judge et al., 1993, 1996; Kerrigan et al., 1998; Murray et al., 1969; Ostrosky et al., 1994; Winter et al., 1990). Reduced gait function in older people is associated with a decreased ability to undertake the activities of daily living (Brach & VanSwearingen, 2002; Guralnik et al., 2000).

Kinesiological studies show that older adults perform locomotor tasks nearer their maximal torque-producing capabilities than young adults. This greater effort is associated with increased neural drive to the muscles responsible for walking and enhanced coactivation of opposing muscles (Hortobagyi & DeVita, 2000; Hortobagyi et al., 2003). In addition, increased age is associated with a redistribution of joint torques and power as older adults use their hip extensors more and their knee extensors and ankle plantar flexors less when walking than the young. Data suggests that healthy older adults produce 279% more work at the hip, 39% less work at the knee, and 29% less work at the ankle compared with healthy young adults during gait (DeVita & Hortobagyi, 2000). The localized increase in muscular activation in the elderly during sustained walking may cause decreased physical activity, not because of generalized exhaustion, but due to the onset of fatigue in particular muscles. Therefore, localized muscle energy expenditure is more important than global expenditure when considering control of movement in older people (O'Dwyer & Neilson, 2000). The older adults also exposed gait instability due to enhanced coactivation of opposing muscles during walking.

2.2 Differences in glucose metabolism between young and older adults during walking

Shimada et al. (2009b) compared the differences between the glucose uptakes of skeletal muscles during walking in young and older adults using FDG PET. In this study, 10 healthy young and older men walked on a treadmill for 50 min. Walking speed was maintained at 4.0 km/hr for younger subjects and between 1.86 and 3.54 km/h as achievable limits for

older subjects. FDG (360 MBq) was injected 30 min after the start of walking. PET scans of the crista iliaca-planta region were conducted in six overlapping bed positions using a 7-min emission time per position and simultaneous attenuation correction. Glucose metabolism in the regions of interest (ROIs) was evaluated from the standardized uptake value (SUV) for FDG defined as follows:

$$SUV = C/D/w \quad (1)$$

where C (Bq/ml) represents the concentration of radioactivity in the tissue, D (Bq) is the injected dose, and w is body mass (Sadato et al., 1998).

SUV was significantly increased in the semitendinosus, biceps femoris, iliacus, gluteus minimus, gluteus medius, and gluteus maximus muscles of older adults. FDG uptake ratios of older adults to young adults were 3.02 in the semitendinosus, 3.19 in the biceps femoris, 1.66 in the iliacus, 1.64 in the gluteus minimus, 3.68 in the gluteus medius, and 3.05 in the gluteus maximus muscles (Shimada et al., 2009b). The data indicate there was inefficient activity of these muscles during walking in the older adults. Figure 1 shows representative FDG PET images in a young and an older adult.

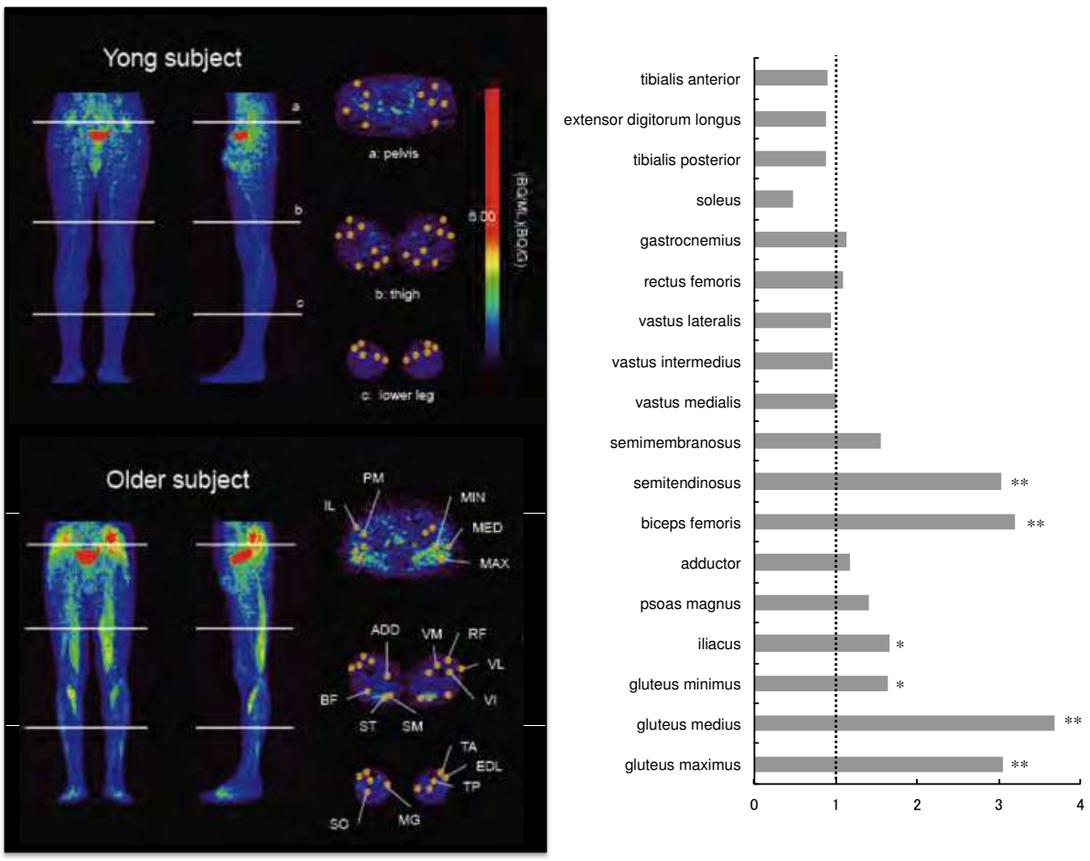

Fig. 1. FDG PET images taken after walking in a young and older subject.

Left panel: Projection and sectional images. The yellow circles indicate the following regions of interest: Section a (pelvis): 30 mm above the femoral head PM, psoas magnus; IL, iliacus; MIN,

gluteus minimus; MED, gluteus medius; MAX, gluteus maximus. Section b (tight): 50% of the distance from the femoral head to the knee joint RF, rectus femoris; VL, vastus lateralis; VI, vastus intermedius; VM, vastus medialis; SM, semimembranosus; ST, semitendinosus; BF, biceps femoris; AD, hip adductor. Section c (lower leg): 30% of the distance from the knee joint to the external malleolus TA, tibialis anterior; EDL, extensor digitorum longus; TP, tibialis posterior; SO, soleus; MG, medial gastrocnemius. The red color at the center of the pelvis resulted from the accumulation of FDG in the bladder. Right panel: Graph showing FDG uptake ratios of older adults to young adults. Significant difference: $*P < 0.05$ and $**P < 0.01$.

During walking, the hamstrings are most active from the period just before to just after heel contact. Before heel contact, the hamstrings decelerate knee extension to prepare for the placement of the foot on the ground. The hamstrings are active during the initial 10% of the stance phase in walking to assist with hip extension and to provide stability to the knee through coactivation. Strong activation of the gluteus maximus allows the hip to extend and prevents forward jackknifing of the torso at heel contact. The gluteus maximus remains active from heel contact to mid stance to support the weight of the body and produce hip extension. The iliacus becomes active before toe off to decelerate hip extension. Concentric muscle activation follows eccentric muscle activation to bring the hip into flexion just before toe off and during transition into initial swing. The gluteus medius and minimus, the primary hip abductors, are most active during single-limb support to stabilize the pelvis in the frontal plane (Neumann, 2002).

A previous study showed that hip, knee, and ankle joint muscles produce 44, 5, and 51% and 16, 11, and 73% of the total extensor work during the stance phase in older and younger adults, respectively (DeVita & Hortobagyi, 2000). These data suggest that older adults perform similar amounts of work at the hip and ankle, but young adults perform the majority of work at the ankle (DeVita & Hortobagyi, 2000). In addition, coactivation time of the thigh muscles is higher in older people than in young people, and there is a linear correlation between the coactivation time and the metabolic cost during walking (Mian et al., 2006). The redistribution of joint power during walking in older adults increases glucose metabolism in the hip extensors (gluteus maximus, hamstrings) and coactivation increases glucose metabolism of the hamstrings.

The hip joint is stabilized by the gluteus medius in the initial phase of the gait cycle and by the gluteus minimus during the mid- and late-phases (Gottschalk et al., 1989). However, the degree of activation of the gluteus minimus muscle during walking is unclear because activities of deep muscles such as the iliacus and gluteus minimus cannot be evaluated by EMG. By contrast, FDG PET can measure the activity of deep muscles. FDG PET analyses showed glucose metabolism in the gluteus minimus during walking in young adults was 2.1 times higher than that at rest and higher than that of the gluteus maximus, gluteus medius, and thigh muscles (Oi et al., 2003).

3. Oxygen consumption and FDG uptake in skeletal muscles during exercise

3.1 Physical activity and oxygen consumption in older adults

Many studies have shown that there is an association between restricted outdoor activities and the deterioration of physical function in healthy and frail older people (Bruce & McNamara, 1992; Clarfield & Bergman, 1991; Fujita et al., 2006; Ganguli et al., 1996; Kono &

Kanagawa, 2001; Kono et al., 2004). A two-year prospective study in initially able-bodied older individuals showed an association between a low frequency of baseline outdoor activity and incident disability (Fujita et al., 2006). In older individuals who went outdoors once a week or less, the adjusted risks of incident mobility impairment (odds ratio = 4.02) and disability in instrumental activities of daily living (odds ratio = 2.65) were significantly higher compared with an active group who went outside once a day or more. Outdoor activity may be restricted in individuals who have difficulty walking for extended periods (Simonsick et al., 2005).

Muscle activity during exercise results in a mechanical energy cost, which is reflected by whole body metabolic cost. During physical activity, there is relatively greater muscle activity and increased levels of coactivation of opposing muscles in older people (Hortobagyi & DeVita, 2000; Hortobagyi et al., 2003). Furthermore, oxygen consumption (VO_2), which provides an index of walking efficiency, is greater in older adults even when there are no gait impairments (Malatesta et al., 2003; Martin et al., 1992; McCann & Adams, 2002; Waters et al., 1988). These data suggest that older adults may have difficulties in performing the activities of daily living as they have to work at a higher level of effort relative to their maximum capability (Hortobagyi et al., 2003).

3.2 Muscular activity and oxygen consumption

Unlike other techniques, FDG PET allows the observation of continuous activities such as extended walking and can measure cumulative muscle metabolism during unrestricted physical activities. Furthermore, FDG uptake closely correlates with exercise intensity in healthy adults and can be used to compare task-specific muscle activity (Fujimoto et al., 2003; Kemppainen et al., 2002; Pappas et al., 2001).

3.3 Relationship between FDG uptakes and VO_2

Few studies have investigated the relative contribution of different muscle groups to whole body energy consumption during walking. In one study, 10 community-dwelling older women participated in FDG PET and VO_2 analyses during exercise on separate days within one week (Shimada et al., 2010). VO_2 during walking was determined using an automated open-circuit gas analysis system (Cosmed K4b², Rome, Italy). The gas analyzers were calibrated immediately before each test using ambient air comprising certified standard gases at 15.94% oxygen and 4.97% carbon dioxide (Sumitomo Seika Chemicals Co., Ltd., Osaka, Japan). The subjects walked for 12 min at a comfortable speed on a circular 16 m indoor course and breath-by-breath data were obtained from the gas analyzers during walking, which was stored in the analyzer's memory. The mean VO_2 values from the 3rd to the 12th min were used to assess constant whole body energy metabolism (McArdle et al., 1997). All SUV values were adjusted for the distance walked during the 50 min FDG PET trial as:

$$\text{Adjusted SUV} = x / a \tag{2}$$

where x represents the measured SUV, and a represents the walking distance in km.

The left and right panels show representative projection images of FDG PET uptake taken after walking. The scatterplot shows correlations between VO_2 and adjusted SUV for different muscle groups.

The VO_2 during walking was significantly and positively correlated with the adjusted SUV in the biceps femoris, gluteus minimus, gluteus medius, and the pelvis muscle group (Fig. 2; Shimada et al., 2010). This shows that these muscle groups contribute to the increase in VO_2 during walking in older adults. Evidence suggests the hamstrings, including biceps femoris, are most active from a period just before to just after heel contact during walking (Neumann, 2002). Furthermore, older adults display higher levels of antagonist coactivation during gross locomotor tasks (Hortobagyi & DeVita, 2000; Mian et al., 2006). Indeed, there is greater antagonist thigh muscle coactivation during walking in older men than young men and a linear relationship between muscle coactivation and whole body metabolic cost of walking (Mian et al., 2006).

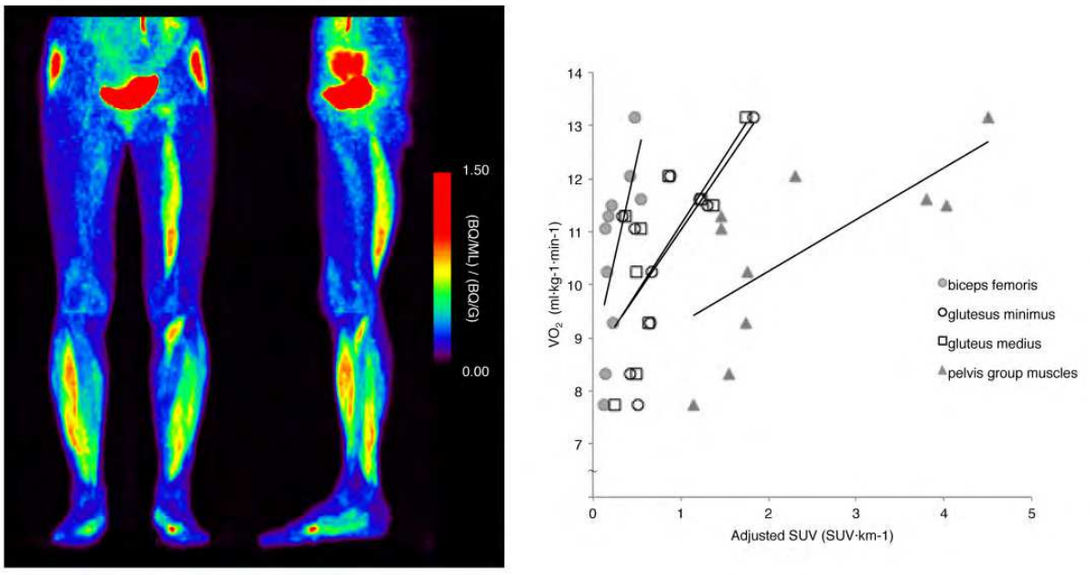

Fig. 2. Relationship between glucose uptake and VO_2 in older subjects.

Gait endurance contributes to the ability to perform the activities of daily living; however, information describing the fatiguing effect of daily activities on gait is limited. Previous studies indicate there is a relationship between muscle fatigue and physical function (Gribble & Hertel, 2004a,b; Helbostad et al.,2007; Kavanagh et al., 2006) as there are changes in gait step width, mediolateral trunk acceleration amplitude, step-length variability, and trunk acceleration variability in the vertical direction following physical fatigue induced by an atypical daily activity (i.e., sit-to-stand task), even in the absence of a change in gait speed (Helbostad et al.,2007). These gait variables are related to the incidence of falling in older people (Hausdroff et al., 2001; Maki, 1997; Mbourou et al, 2003).

The primary hip abductors, the gluteus medius and minimus, stabilize the pelvis in the frontal plane and are important for single-limb support (Neumann, 2002). During walking, the body is unstable for most of the stride cycle as its center of mass is outside the base of support 80% of the time (Winter, 1991). During walking in older people, mediolateral stability is generally reduced resulting in greater activation of the hip abductors compared with the young (Dean et al., 2007). Reduced mediolateral stability in older people can lead to an increased step width to avoid falling while walking at a preferred speed; a wider step

width increases both mechanical work and metabolic energy expenditure (Donelan et al., 2001). A previous study showed older subjects selected a narrower step width when walking at a preferred speed on a treadmill with external lateral stabilization, and the energy cost with lateral stabilization was reduced in a zero step width condition i.e., tandem-like walking, compared with without stabilization (Dean et al., 2007). These findings are supported by observations of a significant relationship between the adjusted SUV in the hip abductors and VO_2.

A previous study showed that FDG uptakes by the biceps femoris, semitendinosus, iliacus, gluteus minimus, gluteus medius, and gluteus maximus muscles were significantly increased in older adults compared with young subjects (Shimada et al. 2009b). However, lower leg muscles such as tibialis anterior, tibialis posterior, and soleus had a ratio of less than one. These results suggest that the excess muscle activity of the larger thigh muscles contributes to the increase in VO_2 during walking in older adults.

Moreover, subjects with proportionally greater activity in their hip muscles had a higher VO_2 while walking compared with those with proportionally lower hip muscle activity. There may be a redistribution of muscle activity with aging; studies show increased work by the hip musculature in older adults is associated with decreased work by the musculature of the more distal joints (e.g. reduced power in plantar flexor) in both healthy older adults (DeVita & Hortobagyi, 2000; Judge et al., 1996) and older adults with a lower extremity disability (McGibbon & Krebs, 2002; McGibbon et al., 2001). FDG PET findings provide further evidence describing increased output by the hip musculature and introduce new information indicating that this increased output increases VO_2 in older adults during walking.

4. Evaluation of a walking aid using FDG PET

4.1 Importance of walking aids in older adults

Physical function is associated with the ability to perform the activities necessary for independent living without substantial risk of injury (Guralnik & Simonsick, 1993). Evidence suggests that impaired gaits in the elderly strongly affect their ability to perform daily activities (Brach & VanSwearingen, 2002; Guralnik et al., 2000); therefore, evaluation of gaits is an essential part of geriatric health and intervention programs. Kinesiological and epidemiological studies have shown that changes in gait scores such as decreased walking speed and stride length are associated with advanced age (Elble et al.,1991; Judge et al., 1996; Murray et al., 1969; Nagasaki et al., 1996; Nigg et al., 1994; Ostrosky et al., 1994; Winter et al., 1990). The age-related change in gait is characterized by a reduction in ankle power output during the terminal stance phase probably due to an age-related impairment in the power-generating capacity of the ankle which limits walking speed and stride length (McGibbon, 2003). In addition, the metabolic cost of walking is greater for the elderly than for young adults, even when there are no gait impairments (Malatesta et al., 2003; Martin et al., 1992; McCann & Adams, 2002; Waters et al., 1988). The increased metabolic cost of walking can impair the activity and quality of life of elderly people as a decrease in physical activity rapidly degrades physical and psychological functions (Backmand et al., 2006; Young et al., 1995).

There are many interventions that improve gait performance in non-disabled and disabled elderly people. Almost all these interventions include exercise programs to improve muscle strength or balance (Gillespie et al., 2003; Latham et al., 2003). Endurance in elderly people can also be improved by assisted devices such as canes or braces which affect gait speeds, stride lengths, and stability (Alexander, 1996; Joyce & Kirby, 1991; Kuan et al., 1999; Roomi et al., 1998; Van Hook et al., 2003). Shimada et al. developed an automated stride assistance system (Shimada et al., 2009a) (SAS) (Honda R & D Co. Ltd., Wako, Japan) (Figure 3), which uses robotic engineering to control walk ratios (stride length/cadence) and add supporting power to the thigh during walking. The SAS weighs 3.5 kg and it was developed to teach walking efficiency and improve gait endurance in elderly people with age-related short stride length. However, the SAS is limited because it supports movement of the hip joint during walking, which can lead to deterioration of muscle activity in the lower extremities during long-term intervention studies or practical applications.

Fig. 3. Stride assistance system that can control walk ratios (stride length/cadence) and support the thigh during walking.

4.2 Muscular metabolism during walking using a robotic stride assistance system

FDG PET has been used to evaluate muscular activity during exercise with a stride assistance system (Shimada et al., 2007, 2008). In this research, 10 healthy younger men (mean age, 24.1 years) and 7 healthy older men (mean age, 76.0 years) completed FDG PET measurements twice after walking with and without the SAS. The sequence of the experiments was randomized to negate the confounding effect of prior experience of walking on a treadmill. Subjects were asked to walk for 50 min at 4.0 km/h on a treadmill (MAT-5500; Fukuda Denshi Co. Ltd., Tokyo, Japan). All young subjects walked at the target speed of 4.0 km/h. The speed of the treadmill was adjusted to 2.89–3.82 km/h without the SAS and 3.03–4.03 km/h with the SAS for the older subjects who could walk at a constant speed.

Figure 4 shows representative FDG PET images taken in young and older subjects after walking with or without the SAS. Glucose utilization in the lower-extremity muscles was evident after walking. In young subjects, walking with the SAS significantly increased FDG uptakes by the tibialis posterior and the medial gastrocnemius compared with walking without it (Shimada et al., 2007). FDG uptake ratios (SUV after walking with the SAS: SUV after walking without the SAS) of the tibialis posterior and medial gastrocnemius were 2.13 and 2.36, respectively. Walking with the SAS did not have significant effects on any other muscles. In older adults, there were no significant differences between the SUVs with and without the SAS in all lower-extremity muscles. However, walking speeds (mean walking speed without SAS, 3.46 km/h; mean walking speed with SAS, 3.56 km/h) and stride lengths (mean stride length without SAS, 54.9 cm, mean stride length with SAS, 58.2 cm) were

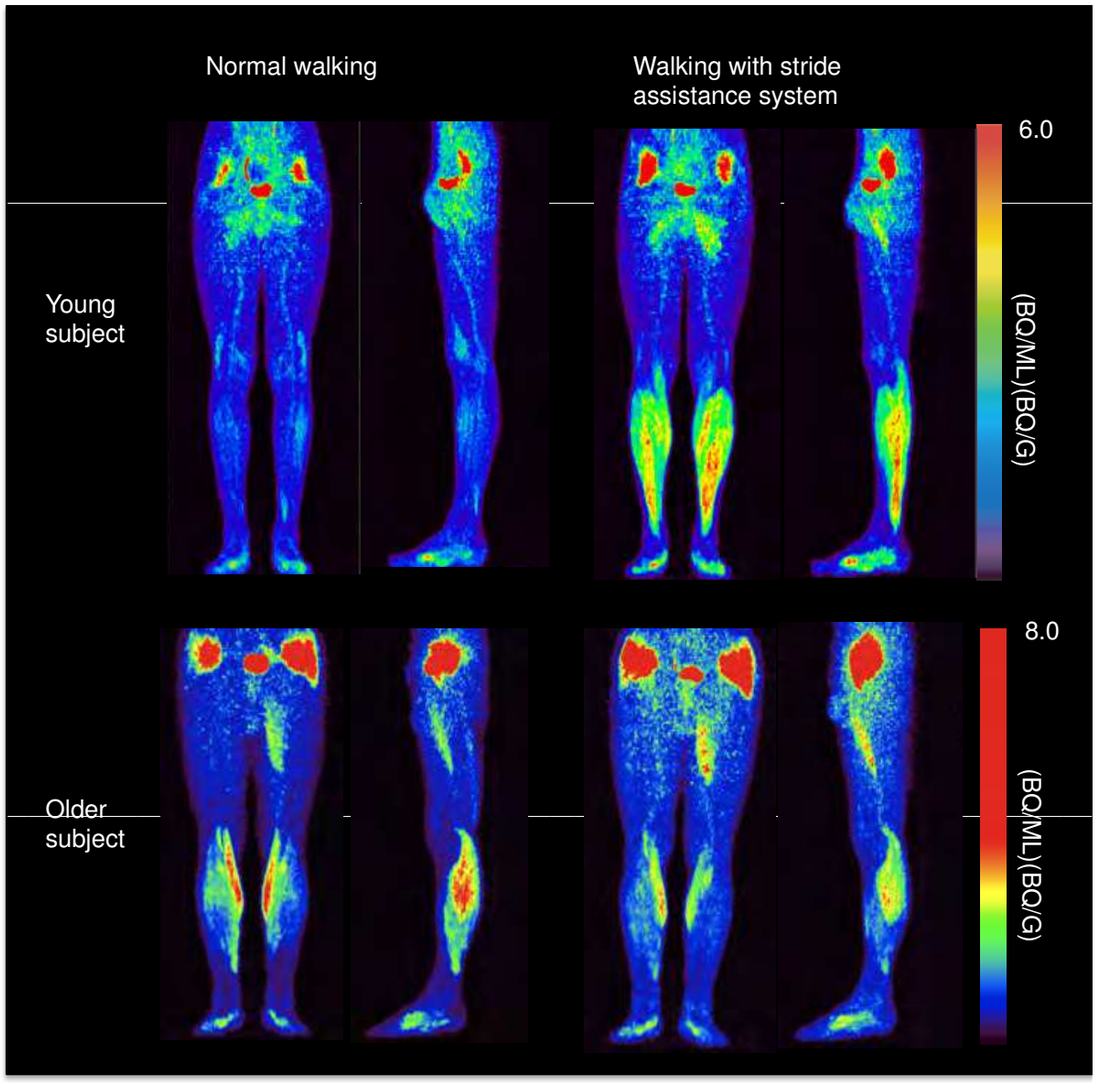

Fig. 4. FDG PET images taken after walking without or with the SAS.
The left and right panels show projection images taken after walking without or with the SAS, respectively.

significantly increased when walking on the treadmill with the SAS in the older subjects. These results suggest that the SAS can facilitate efficient walking patterns irrespective of muscle activity. The SAS may have provided assistance to the thigh and increased the torque of the hip of the older subjects resulting in improved walking scores. Therefore, stride length and walking speed increased without activating lower-extremity muscle activity.

5. Evaluation of exercise intervention using FDG PET

5.1 Effects of exercise in older adults

Older people enjoy walking exercise because it is familiar and more convenient than many other sports and recreational activities (Morris & Hardman, 1997; Mutrie & Hannah, 2004). Intervention studies show that strength or endurance training in older people can improve measures of gait such as walking speed (Binder et al., 2004; Brown & Holloszy, 1993; Buchner et al., 1997a; Ettinger et al., 1997; Judge et al., 1993). Endurance training also improves physical fitness, particularly cardiovascular fitness, as well as cognitive functions (van Uffelen et al., 2008). The development of targeted exercise programs may be facilitated by exercise intervention studies that allow a better understanding of the effects of muscle activity during walking. However, results from previous intervention studies investigating the effects of strength or endurance training on walking speed and gait are inconclusive (Buchner et al., 1997b; Ettinger et al., 1997). Walking is a near-perfect exercise for healthy and frail older people (Morris & Hardman, 1997); therefore, if walking induces walking-specific adaptations, interventions involving walking may be an efficient and appropriate means of improving walking function in older people (Shimada et al., 2003). However, knowledge of the effects of walking exercise on the physical performance of older people is limited. Most walking exercise interventions are prescribed in combination with exercises aimed at increasing muscle strength, neuromuscular coordination, and balance (Morris et al., 1999), and physical performance is not always assessed in intervention studies (Ebrahim et al., 1997).

5.2 Comparison of FDG uptakes in skeletal muscles before and after intervention

The functionality of walking may be improved by increasing the stride length of older people, which in turn may result in benefits such as improved walking efficiency. These benefits may supersede those derived from improved aerobic fitness alone. Shimada et al. (2009a) assessed the effects of a walking program for the elderly using the SAS. Fifteen subjects participated in a three-month walking program of two 90-min supervised sessions per week using the SAS. For FDG PET analysis, subjects walked for 50 min at a comfortable speed on a circular indoor walking track without the SAS. Figure 5 shows representative FDG PET images taken before and after the exercise intervention (Shimada et al., 2009a). FDG uptakes by the gluteus minimus, gluteus medius, and rectus femoris were significantly lower after the intervention than before, although walking speed during FDG PET measurements increased after the intervention. In contrast, the medial gastrocnemius and soleus (the lower distal muscles) showed higher FDG uptakes after the intervention than before, although the difference was not statistically significant.

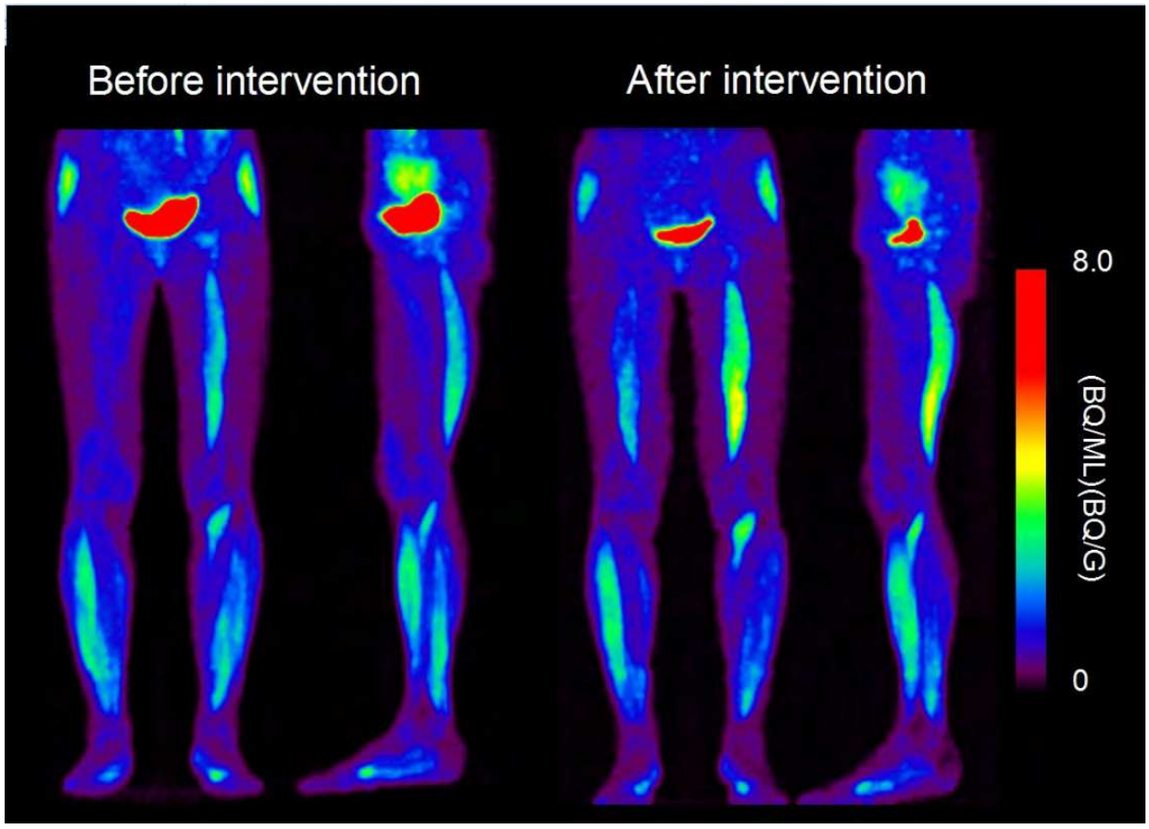

Fig. 5. FDG PET images of an older woman before and after the intervention.
The left and right panels show before and after intervention images, respectively. FDG uptakes by the gluteus minimus, gluteus medius, rectus femoris and pelvic muscles after the intervention were significantly lower than before.

The gluteus medius and gluteus minimus are the two primary hip abductors. They are most active during the first 40% of the gait cycle and they stabilize the pelvis in the frontal plane (Neumann, 2002). It is possible that the activity of the hip abductors decreases to improve mediolateral stability during long-distance walking. Further studies must be carried out using kinematic and kinetic analyses to fully understand the mechanisms involved in the change in cumulative muscle activity during prolonged walking.

Previous data indicate that the activity of hip-related muscles and hamstrings is greater than that of other lower extremity muscles in elderly people during walking. Shimada et al. 2009a found a significant decrease in the activity of the pelvic muscles (iliacus and gluteus muscles) during intervention with the SAS. However, the intervention did not increase FDG uptake of the soleus and gastrocnemius muscles, suggesting that the walking intervention improved the efficiency of muscle activity but did not redistribute muscular effort. This indicates that a walking intervention with the SAS has potential to increase walking endurance in the elderly. Indeed, the distance walked in 50 min after the intervention (median, 3579.0 m) was greater than that before the intervention (median, 3051.0 m); however, this difference was not statistically significant.

The quadriceps femoris controls knee flexion and acts as a shock absorber after heel contact; it then supports the weight of the body in mid-stance. The rectus femoris differs from that of other knee extensors as it is a hip flexor and its activity increases immediately after the toe-off phase (Neumann, 2002). A previous study showed that antagonist thigh muscle coactivation (e.g., activation of the vastus medialis, vastus lateralis, and biceps femoris) is 31% greater in older than in younger adults, and coactivation is moderately correlated with the metabolic cost of walking (Mian et al., 2006). The SAS automatically lends horizontal force to the thigh to facilitate an optimal walk ratio and may teach elderly people to use their muscles more efficiently. The consecutive stimuli provided by the SAS may help elderly people adopt an efficient walking pattern.

6. Functional FDG PET imaging as evaluating of frailty

Frail elderly people are particularly vulnerable for developing disabilities (Boyd et al., 2005; Gill et al., 2004; Hardy et al., 2005) and are at an increased risk for falls, disabilities, hospitalization, institutionalization and death, compared with their age-matched non-frail counterparts (Espinoza & Walston, 2005). Disability is closely related to medical spending; therefore, prevention of disability can lead to reduced health care costs (Cutler, 2001). Physical frailty indicators include mobility, strength, endurance, nutrition, physical inactivity, balance, and motor processing (Ferrucci et al., 2004). Gait disorder is a particularly important indicator of frailty and an independent predictor of disability. The findings of research using FDG PET has revealed a cycle of gait disorder (Figure 6).

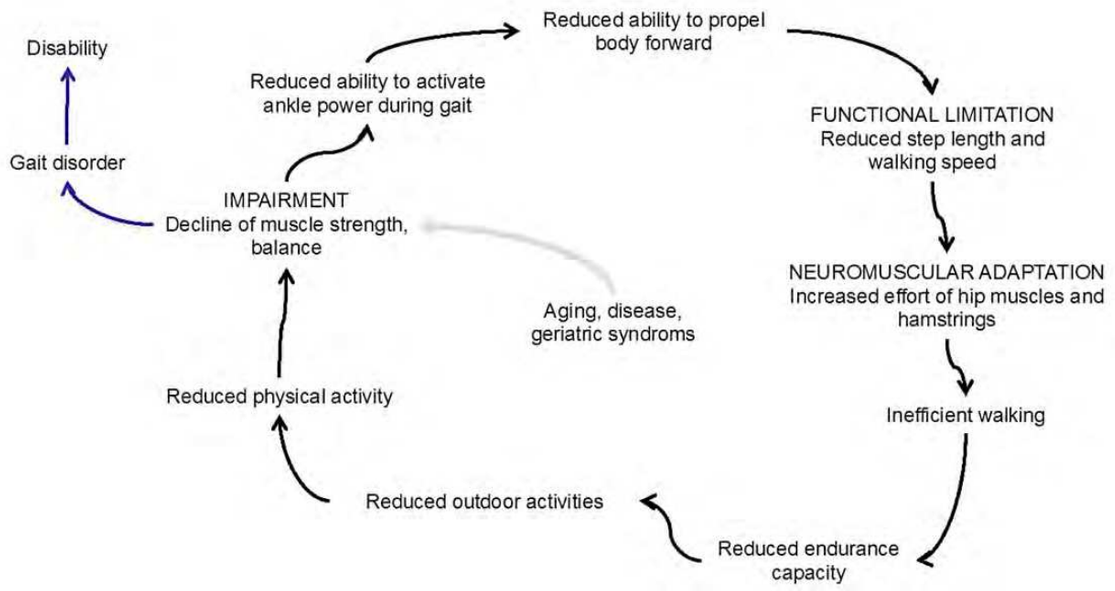

Fig. 6. Schematic diagram of the incidence of gait disorder in older adults.

Aging results in impaired muscle strength and balance, which reduces the ability to activate the ankle plantar muscles during gait and propel the body forward. These impairments manifest as functional limitations including reduced step length and walking speed, which are compensated for by neuromuscular adaptations such as increased effort of the hip

muscles and hamstrings. Walking becomes inefficient and there is reduced endurance capacity. This leads to decreased involvement in outdoor activities and therefore physical activity, which worsens the impaired muscle strength and balance. Ultimately, the cycle can lead to gait disorder and disability.

7. Conclusions

FDG PET has proved useful for understanding the ability of older adults to perform physical activities. Because FDG uptake is closely correlated with exercise intensity, it can be used for comparing task-specific muscle activity. FDG PET and VO_2 analyses indicate that older adults may have difficulties in performing the activities of daily living as they have to work at a higher level of effort relative to their maximum capability due to a redistribution of muscle activity with aging. Automated exercise intervention, such as the automated stride assistance system (SAS), may help slow the cycle of events that ultimately can lead to gait disorder and disability. FDG PET evaluation of glucose metabolism in the muscles of the elderly following intervention with the automated SAS indicates that the SAS has the potential to increase walking endurance. We suggest that FDG PET is a useful method to evaluate the effects of interventions and therefore develop rehabilitation programs.

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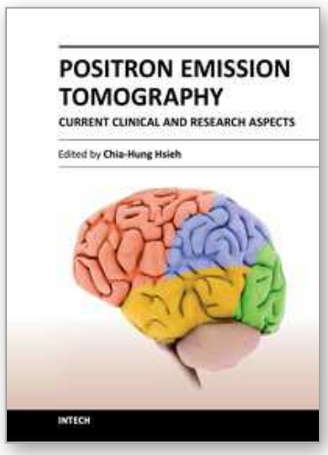

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This book's stated purpose is to provide a discussion of the technical basis and clinical applications of positron emission tomography (PET), as well as their recent progress in nuclear medicine. It also summarizes current literature about research and clinical science in PET. The book is divided into two broad sections: basic science and clinical science. The basic science section examines PET imaging processing, kinetic modeling, free software, and radiopharmaceuticals. The clinical science section demonstrates various clinical applications and diagnoses. The text is intended not only for scientists, but also for all clinicians seeking recent information regarding PET.

InTech Europe
University Campus STeP Ri
Slavka Krautzeka 83/A
51000 Rijeka, Croatia
Phone: +385 (51) 770 447
Fax: +385 (51) 686 166
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中国上海市延安西路65号上海国际贵都大饭店办公楼405单元
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