

AN ABSTRACT OF THE DISSERTATION

Gianni F. Maddalozzo for the degree of Doctor of Philosophy in Human Performance
presented on June 11, 1998. Title: Effects of Two Resistance Training Protocols on
Insulin-Like Growth Factors, Muscle Strength and Bone Mass in Older Adults.

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Abstract approved: _____

Christine M. Snow, Ph.D.

With age, there are marked declines in bone mineral density (BMD), lean mass (LM), muscular strength, and diminished anabolic hormones, specifically growth hormone (GH) and insulin-like growth factor-I (IGF-I). We compared the effects of a moderate-intensity seated resistance training program using machine weights, to a high-intensity training program using free-weight exercises on regional and total body BMD, LM, muscular strength and power, and serum levels of IGF-I and IGFBP-3 in healthy older men and women. Twenty-eight healthy men (54.58 ± 3.20 yr.) and twenty-six healthy non-estrogen replaced women (52.83 ± 3.26 yr.) served as their own control group for 12 weeks, then were randomly assigned to either a moderate (60% of 1 RM) or high (70-90% of 1 RM) intensity resistance training group. Training was conducted 3 days per week for 6-months under the supervision of a personal trainer. Prior to and after the control period and at the conclusion of the 6-month intervention period, BMD at the hip, spine and whole body and body composition were assessed by dual-energy x-ray absorptiometry, muscle strength by isokinetic dynamometry, muscular power by Wingate Anaerobic Power Test, and IGF-I by radioimmunoassay. We report that high intensity, but not moderate intensity resistance training produced regional changes in bone mass at the hip. Specifically, high intensity free weight training produced a significant increase in trochanteric BMD for women (2.0%) and for men (1.3%) and a significant decrease in

femoral neck BMD for both men and women (1.8%). No changes were observed in total hip BMD. At the spine, high intensity training resulted in a significant ($p < .05$) gain in men (1.9%) but not women, whereas, moderate intensity training produced no change at this site. Neither circulating IGF-I nor IGFBP3 were altered by either training regimen, however, both training programs resulted in improvements in peak force, anaerobic power and lean mass ($p < .01-.05$) and were similar in both the high intensity (HIF) and moderate intensity (MIM) groups and were independent of gender. Despite these increases, neither intensity protocol significantly increased serum levels of IGF-I. Results demonstrate that high intensity training produced a shift in mineral at the hip for both men and women, increased spine BMD in men but not women, and maintained whole body BMD in both genders. These improvements were not accompanied by changes in circulating levels of IGF-I, IGFBP3 or IGF-I/IGFBP3. Although resistance training of moderate to high intensity produced similar muscle changes in younger older adults, a higher magnitude is necessary to stimulate osteogenesis. The redistribution at the hip indicates a highly-specific response to mechanical loads at this site. The long-term implication of this response is unclear, but it may confer some protection from trochanteric fractures.

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Effects of Two Resistance Training Protocols on Insulin-Like Growth Factors,
Muscle Strength and Bone Mass in Older Adults

by

Gianni F. Maddalozzo

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~~Gianni F. Maddalozzo, Author~~

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DEDICATION

This dissertation is dedicated in loving memory of my father, Augusto Maddalozzo.

Possibilities must be weighed.
Then priorities must be swayed.
Now plans must be laid and
commitments must be made.
The price must be paid,
the timing may be delayed.
But the course must be stayed,
and the trumpets will be played.

R.H. Schiller

THE EFFECTS OF TWO RESISTANCE TRAINING PROTOCOLS ON INSULIN-LIKE GROWTH FACTORS, MUSCLE STRENGTH AND BONE MASS IN OLDER ADULTS

Chapter I INTRODUCTION

With age, there are marked declines in muscular strength (Larsson, Grimby & Karlsson, 1979), lean mass (Forbes, 1992, Steen, 1988) and bone mineral density (Riggs, Wahner, Melton, Richelson, Judd & Offord, 1986); reproductive and anabolic hormones, specifically growth hormone (GH) and insulin-like growth factor-I (IGF-I) (Copras, Harman & Blackman, 1992; Rudman, Kuter, Rodger, Lubin, Fleming & Bain, 1981, Vermulen, 1987). Diminished muscle mass and strength in the lower extremities are associated with an increased risk of falling in the elderly (Lipsitz, Jonsson, Kelly & Koesmer, 1991). Often, a decline in lean mass is associated with an increase in fat mass which in turn can lead to obesity (Rudman 1985). Presently it is unclear if these declines are a direct result of the aging process, or a reduction in physical activity that accompanies aging (Kelly et al., 1990, Poehlman, Rosen, & Copeland, 1994).

Osteoporotic fractures associated with bone fragility are a major health concern in America today. The loss of trabecular bone (axial skeleton) in women begins in young adulthood and continues linearly throughout life, whereas, the loss of cortical bone (appendicular skeleton) starts around menopause and increases until age 65 when it begins to decelerate (Riggs et al., 1986). Kanis and colleagues (1992) recently reported that the incidence of fractures in men younger than 45 years of age is greater than in similarly aged females. However, after age 45 incidence of fractures in females is greater than in males.

Numerous studies have shown that regional bone mass can be enhanced following periods of physical stress resulting from weight training (Nelson, Fiatarone, Morganti, Trice, Greenberg, & Evans; 1994; Pruitt, Jackson, Bartels & Lehnhard, 1992; Menkes et

al., 1993). Thus, it appears that exercise intervention such as resistance training that produces strains high in magnitude, may induce new bone formation. This, in turn, may strengthen bone by increasing its overall density.

The process of aging is often associated with a decrease in lean body mass and an increase in adipose tissue (Rudman 1985). Lean mass is a very important component of body composition since it plays a central role in energy expenditure through metabolism of fat, and carbohydrate metabolism. Decreases in lean mass (LM) observed with aging have been linked to the development of obesity and diabetes (Copeland et al., 1990). Therefore, interventions aimed at the preservation or increase in lean mass are of considerable medical interest.

Numerous studies have examined the effects of resistance training on lean mass (LM) (Charette et al., 1991, Nelson et al., 1994, Ravussin et al., 1986). Many of these studies have involved previously untrained females ranging in age from 50 to 75 years. Most studies have used machine based programs involving two or three sessions per week and 2 to 3 sets of 8 to 10 repetitions per exercise. Training intensities in these studies have ranged among 60 to 80 percent of 1 repetition maximum (1 RM). Interventions have run for as little as 12 weeks and have lasted up to one year. Most investigators have concluded that progressive weight training can significantly increase strength and lean mass (LM). The average increase in LM has been approximately .9-2.1 kg. However, there is a paucity of information regarding the effects of resistance training on LM in middle aged, non-obese women (50-60 years). Although the rate at which skeletal muscle can adapt to vigorous and constant exercise decreases with age, adaptations such as increases in muscular strength and skeletal muscle hypertrophy are still attainable. However, the potential for a reversal of the declines in strength associated with aging and inactivity remains relatively unexplored.

Although insulin-like growth factor (IGF-I) has been shown stimulate skeletal muscle protein synthesis in humans (Fryberg et al., 1995), very little information exists regarding the interactions of regular, long term weight training and the GH/IGF-I axis in older adults. Evidence of increased IGF-I in skeletal muscles, such as increased messenger RNA (mRNA) for IGF-I, has been associated with compensatory hypertrophy (DeVol et al. 1990) and stretch-induced hypertrophy (Czerwinski et al., 1994; Goldspink et al., 1995) of skeletal muscles in animals, suggesting that IGF-I plays a role in muscular hypertrophy related to the application of increased or altered forces to skeletal muscle. Since IGF-I and GH strongly correlate with lean mass, (LM) (DeVol et al., 1990) it is conceivable that increases in LM, often associated with weight training, could result in a significant increase in basal IGF-I concentrations.

Chronological age does not accurately reflect a person's health or physical capacity, nor is it used to reliably predict how long one will live. Banchet (1990) has reported that in Canada, the life expectancy for a male was 70.3 years and 78.2 years for women. However, disability-free life expectancies were 59 and 60 years, respectively. Among people over 65, the prevalence of disability affecting mobility is phenomenal. Approximately 17% of this population have reported being unable to perform major activities such as walking without assistance; 21% report some limitations, and 7% report physical limitations that do not affect major activities (US Department of Health and Human Services Publication 1980).

Resistance Training and Older Adults

Recently, investigators (Charette et al., 1991; Pyka et al., 1994 and Nelson et al., 1994) have begun to involve older adults to resistance training protocols using higher intensities (80% of 1 RM) similar to those used in resistance training studies involving younger adults. Research findings indicate that muscle hypertrophy and strength gains

will only occur in response to loads greater than 60% of 1 repetition maximum (Schmidtblecher, 1992). The number of repetitions prescribed for resistance training also appears to play a critical role in the development of muscular strength in older adults. Low to moderate intensity (30-50% of 1 RM) resistance training has produced little or no increases in the strength of older adults (Aniansson and Gustafsson 1991; Larsson 1982; and Hagberg et al., 1989). Whereas, higher intensities (60-80% of 1 RM) have produced significant increases in muscular strength (Pyka et al., 1994) in older adults.

Until recently it was hypothesized that strength gains made by older adults reflected improvements in neurological factors rather than actual muscle fiber hypertrophy (Moritani and de Vries, 1979 and 1980). However, several authors (Pyka et al., 1992; Fiatarone et al., 1990; Frontera et al., 1988; Charette et al., 1991; and Nelson et al., 1994) have recently shown that elderly men and women retain the capability for muscle fiber hypertrophy as a result of resistance training. During the last decade, resistance training has become recognized as an important component of overall fitness (American College of Sports Medicine, 1991). Therefore, it would appear that engaging in an active lifestyle can result in slowing of the catabolic effects often associated with aging.

Resistance Training and Bone Density

Individuals who consistently engage in habitual physical activity have greater bone density than less active age and gender matched individuals (Block et al., 1989). Recently, several cross-sectional studies have shown that strength positively correlates with high bone mineral density (BMD) (Snow-Harter et al., 1990, Conroy et al., 1993). Snow-Harter et al. (1990) reported that muscle strength is a significant predictor of BMD. Other cross sectional studies have shown that athletes, especially those who weight train regularly, have higher bone mineral densities than endurance athletes and nonathletes. Nilsson and Westlin (1971) examined the bone density of the lower limb in international

caliber athletes. Their findings suggested that athletes who participated in power events that required repeated high force movements, such as weightlifting and throwing events, had higher bone mineral density than distance runners, soccer players and swimmers. Conroy et al., (1993) recently compared the BMD of elite junior power lifters (17.4 years) to those of a non active group of males of similar age. The authors reported that bone mineral density values for junior weight lifters were significantly greater at the lumbar spine and femoral neck when compared to an age matched control group. In addition to this finding, they reported a significant relationship between bone mineral density at the spine, femoral neck, greater trochanter, and ward's triangle and maximum lifting ability in the snatch, clean and jerk, and total (snatch plus clean and jerk). This suggests that load bearing activities such as weight training may be effective in stimulating bone formation.

Human Growth Hormone

Growth hormone (GH) secretion declines with normal aging, resulting in lower circulating levels of insulin-like growth factor (IGF)-I (Rudman et al., 1985). Decreases in growth hormone (GH) and the insulin-like growth factors are also associated with declines in bone and muscle mass observed with age (Rudman et al., 1985). The activity of the growth hormone releasing hormone (GHRH) and insulin-like growth factor (IGF) axis declines with aging, a phenomenon that is referred to as "somatopause" (Hoffman et al., 1993). Growth hormone and insulin-like growth factors are major regulators of cell division and protein synthesis and secretion decreases with age, particularly after age 50 (Rudman 1985).

The insulin-like growth factors (IGF-I) are anabolic peptides produced in response to growth hormone (GH) secretion (Copeland et al., 1990) The IGF's play an important regulatory role in numerous processes, including cell proliferation, glucose transport,

protein and lipid synthesis (Copeland et al., 1990). The IGF's also mediate the effects of GH on bone, cartilage and skeletal muscle (Jones and Clemmons, 1995). Circulating IGF-I is derived from local synthesis of GH from liver, bone, and muscle in other sites. Although the function of circulating IGF-I is not yet certain, environmental factors such as exercise and nutrition may affect the levels of IGF-I, and therefore, play an important role in determining body composition and bone mass (Jones and Clemmons, 1995). IGF-I is transported to and from target tissues by insulin-like growth factor binding proteins (IGFBP's), six of which can be found in human serum (Coprass et al., 1992, 1993). The IGFBP's also act to enhance or inhibit the biological action of IGF-I (Coprass et al. 1992, & 1993).

The action of growth hormone (GH) on the skeletal system within adults is not well defined. Barnard et al., (1991), has suggested that GH directly stimulates IGF production in osteoblasts, since it has been reported that GH activates cell surface receptors in cultured osteoblast-like cells to increase IGF-I production. Recently, Johansson et al. (1994), investigated the relationship between BMD, strength, body composition, $\dot{V}O_2$ max., IGF-I and IGFBP-3 (the primary binding receptor for IGF-I). The investigators reported that although IGF-I and IGFBP-3 correlated positively with strength and $\dot{V}O_2$, IGFBP-3 had its strongest association with BMD.

The regulation of the IGF's could help explain changes in body composition, bone mineral density and muscular strength, associated with various exercise regimens. Also, through data on the IGF regulatory system, insight may be gained as to the physiologic role of GH during exercise. This may prove important when designing preventive measures to enhance body composition and/or bone mass in this population (i.e., middle-aged adults). Understanding of the IGF regulatory system may prove useful in defining the effects of long-term exercise in middle-aged adults.

Resistance Training Protocols

Recently, in order to offset and/or reduce the physical declines in the muscular system, interest has been devoted to developing exercise programs that will produce optimal increases in strength and lean body mass in older adults. Weight training studies involving older adults have demonstrated that increases in strength and lean mass are possible. Strong evidence exists that weight training in older adults can positively influence muscular strength and lean mass (Fielding, 1995, Charette et al., 1991, Frontera et al., 1988, Fiatarone et al., 1990, Trueth et al., 1994).

Most weight training protocols involving older adults have employed machine based exercises and traditional progressive weight training prescriptions (3 sets of 8-12 reps @ 60-90% of 1 RM) (Fielding, 1995). Strength training experts have stressed the use of athletic type exercises (squats, deadlifts, etc.) to develop maximal strength and power. The combination of free weight exercises and near maximal loads (intensity of 90% of 1 RM) is considered to produce optimal neuromuscular adaptations and maximal power (Schmidtblechier, 1992).

Training studies that have used young athletes have employed some form of change or variation in the exercise program in order to obtain optimal gains in strength and lean mass (Willoughby, 1993, Herrick and Stone, 1996, Ben-Sira et al., 1995; Baker et al., 1994). This method of training is often referred to as periodization (Stone et al., 1981). The periodized model is based on the training protocols of elite power athletes. These protocols are characterized by a large initial training volume at a moderate intensity (60-70% of 1 RM) with a progressive decrease in volume while increasing intensity, working towards a peaking of intensity (95+% of 1 RM) at the conclusion .

Training volume is generally estimated by the multiplying sets x repetitions x weight lifted. It has been hypothesized that the high volume period emphasizes the hypertrophied adaptations, as evidenced by the significant increase in fat free mass during

this phase (Stone et al., 1981). On the other hand, the high intensity low volume phase stresses the neural response, therefore, providing a greater overall training effect for the development of strength and power than the traditional nonperiodized training model (Schmidtblechier, 1992).

The periodization model has been reported to produce greater increases in strength, power, and muscular endurance when compared to more traditional training models involving protocols requiring 3 sets of 6 RM, 3 X 10-12 RM, 1 X 10-12 RM, 5 X 10 RM or 6 X 8 RM (O'Bryant et al., 1988, McGee et al., 1992, Secher, 1975, Stone et al., 1981, Stowers et al., 1983, Willoughby, 1993). Poliquin (1988) hypothesized that short periods of high volume training emphasizing the hypertrophy phase and alternated with short periods of high intensity training emphasizing the neural response would offer a better method of training than the more linear traditional methods of training.

Regular participation in resistance training programs can result in various physiological adaptations, such as: increases in muscle strength and size, greater BMD, increases in lean mass and changes in body composition. Growth hormone has been found to be responsive to resistance training, however, not all resistance exercise protocols demonstrate increased serum growth hormone concentrations. Research has shown that serum increases in growth hormone are differentially sensitive to different resistance training protocols (Kraemer et al., 1992). Therefore, depending on the load, rest, and volume of training, differential GH responses will occur. Several factors have been hypothesized to play a role in many of the catabolic changes seen in the normal aging process such as, osteopenia, muscle atrophy and increased body fat. Some suggest that these declines are a result of a sedentary life-style found in aging populations (Poehlman and Copeland 1990).

Significance of the Study

Aging is associated with declines in lean muscle mass and IGF-I secretion (Rudman, 1985). Since resistance training has been shown to increase GH levels following exercise (Kraemer et al., 1992), and since serum levels of GH reflect IGF-I status (Copeland et al., 1991), it is hypothesized that increases in lean muscle mass and BMD associated with resistance training are due in part to increased serum levels of IGF-I.

Snow-Harter et al., (1995) recently reported that IGF-I is an important predictor of lean body mass. Thus, it is believed that periodization resistance training that varies the intensities, loads, rest periods and repetitions will produce greater gains in strength, lean muscle mass, BMD, and higher serum levels of IGF-I than traditional methods of resistance training.

Statement of the Problem

To date the benefits of a high intensity free weight periodized weight training program on the growth hormone and musculoskeletal systems of older adults have not been examined. The present study was designed to compare the effects of two different weight training protocols over a 6-month weight training intervention period on bone mineral density, lean mass, strength, anaerobic power and circulating levels of GH and IGF-I in older adults (50-60 years of age). In order to answer these questions, we compared a moderate intensity, seated machine, weight resistance training program (MIM), to a high intensity, free weight program, (HIF) using exercises such as standing back-squats and deadlifts. We hypothesized that the HIF training would result in significantly greater improvements in hip and spine bone mineral density and circulating levels of IGF-I, lean mass, strength, and anaerobic power.

Chapter 2

Redistribution of Bone Mineral Density at the Hip from High Intensity Weight Training in Older Adults

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Abstract

Aging is associated with a marked reduction in bone mineral density (BMD), muscle mass, and diminished growth hormone levels. The effects of moderate and high intensity weight training on bone mass in older adults is equivocal. Further, very little is known about the chronic effect of weight training on IGF-I in population. We compared the effects of a moderate-intensity seated resistance training program using machine weights, to a high-intensity training program using free-weight exercises on regional and total body BMD and serum levels of IGF-I and IGFBP-3 in healthy older men and women. Twenty-eight healthy men (54.58 ± 3.20 yr.) and twenty-six healthy non-estrogen replaced women (52.83 ± 3.26 yr.) served as their own control group for 12 weeks, then were randomly assigned to either a moderate (60% of 1 RM) or high (70-90% of 1 RM) intensity resistance training group. Training was conducted 3 days per week for 6-months under the supervision of a personal trainer. Prior to and after the control period and at the conclusion of the 6-month intervention period, bone mass at the hip, spine and whole body and body composition were assessed by dual-energy x-ray absorptiometry, muscle strength by isokinetic dynamometry, muscular power by Wingate Anaerobic Power Test, and IGF-I by radioimmunoassay. Paired t-tests comparing percent change means for greater trochanter and femoral neck revealed that high intensity, but not moderate intensity resistance training produced regional changes in bone mass at the hip. Specifically, high intensity free weight training produced a significant increase in trochanteric BMD for women (2.0%) and for men (1.3%) and a significant decrease in femoral neck BMD for both men and women (1.8%). We observed a similar but non-significant trend at the hip for both women and men in the moderate intensity machine based group. No changes were observed in total hip BMD. At the spine, high intensity training resulted in a significant ($p < .05$) gain in men (1.9%) but not women, whereas,

moderate intensity training produced no change at this site. Neither circulating IGF-I nor IGFBP3 were altered by either training regimen, but both training programs resulted in improvements in total body strength (37.62%), lean mass (males 4.1%, females 2.7%) and leg lean mass (3.3%) regardless of gender. Results demonstrate that high intensity training produced a shift in mineral at the hip for both men and women, increased spine BMD in men but not women, and maintained whole body BMD in both genders. These improvements were not accompanied by changes in circulating levels of IGF-I, IGFBP3 or IGF-I/IGFBP3. Although resistance training of moderate to high intensity produced similar muscle changes in younger older adults, a higher magnitude is necessary to stimulate osteogenesis. The redistribution at the hip indicates a highly-specific response to mechanical loads at this site. The long-term implication of this response is unclear, but it may confer some protection from trochanteric fractures.

Introduction

Aging is associated with a marked reduction in bone mineral density (BMD), muscle mass, and diminished growth hormone (GH) levels⁽¹⁻³⁾. Growth hormone has also been shown to stimulate both systemic and local production of insulin-like growth factor (IGF)-I, a known bone mitogen⁽⁴⁾. Since pathological GH declines and normal aging are both associated with reductions in BMD, it is hypothesized that this age-related decline in BMD may be mediated by age-related reductions in serum IGF-I and IGFBP-3 (the primary binding receptor for IGF-I) levels⁽⁵⁾.

There is evidence that prevention of age-related declines in BMD⁽⁶⁾ and even moderate to significant increases in regional BMD,^(7,8,9) can be enhanced following periods of mechanical stress resulting from resistance training and muscle strengthening exercises. For example, Nelson et al.,⁽⁷⁾ reported a maintenance in femoral neck BMD and an increase of 1.0% at the lumbar spine respectively in estrogen depleted postmenopausal

females after one year of high intensity training on pneumatic resistance machines two times per week. Pruitt et al.,⁽⁸⁾ reported that early postmenopausal women who engaged in a 9-month machine-based resistance intervention study exhibited an increase in lumbar spine BMD of 1.6% compared to a decrease of 3.6% in the non-exercising age matched control group.

Since IGF-I and GH strongly correlate with lean mass, (LM)⁽¹⁰⁾ and IGFBP-3 has been shown to correlate with BMD,⁽¹¹⁾ it is conceivable that increases in LM and to some extent BMD, often associated with weight training, could result in a significant increase in basal IGF-I concentrations⁽¹¹⁾.

There have been few investigations dealing with the interaction between resistance training and the GH/IGF-I axis in older adults⁽¹²⁾. Acute bouts of resistance training in younger adults have produced increases in GH levels^(12,13), whereas, older adults appear to have an attenuated GH response reflected in IGF-I levels, compared with younger adults⁽¹²⁾. However, this lack of an acute response of GH in older adults may be due in part, to lower training intensities and volume of total work performed.

To date there has been no investigation of the effects of resistance training on both BMD and IGF-I in older adults. Further, no study has evaluated the effects on BMD of standing free weight exercises in older adults. Given the higher forces at the hip during standing activity, free weight resistance exercises may prove osteogenic at this site in older adults as has been shown to be the case in younger adults⁽¹⁴⁾. Thus, we conducted a study which compared a moderate-intensity seated-machine-weight-resistance training program (MIM), to a high-intensity training free weight program (HIF) using exercises such as standing back squats and deadlifts. We hypothesized that the HIF training would result in significantly greater improvements in hip and spine BMD and serum levels of IGF-I compared to MIM. In this study, we have defined intensities as follows: Very high 90% of 1 RM, high 70-80% of 1 RM, and moderate 60% of 1 RM.

Materials and Methods

Subject Recruitment and Selection

Two hundred and sixty-three men and women 50-60 years of age responded to a recruitment notice published in newspapers from within Benton County, Oregon. From this pool of inquiries, 54 participants satisfied the selection criteria to participate in the study. Participants were free of heart and metabolic and did not take any medications that may affect bone metabolism. All women were postmenopausal and free of hormone replacement therapy. Participants completed a comprehensive screening process which included a health questionnaire and written release from their family physician allowing them to participate in the training study. Participants were screened for chronic disease, orthopedic problems (significant disability of shoulder, knee, lower back, or hip) and alcohol consumption (>2 drinks per day) by health history questionnaire. Both exercise groups (MIM and HIF) consisted of previously untrained non-exercising adult men and women. The mean ages at the time of laboratory testing were 54.58 years (SD = 3.20) for men, and 52.83 years (SD = 3.26) for women. In order to be enrolled, participants were classified as normally active (not having participated in an exercise or resistance training program for the past two years). This study was approved by the Oregon State University Institutional Review Board.

Study Design and Protocol

This study design was a randomized intervention trial comparing two resistance training protocols (moderate intensity: MIM vs. high intensity: HIF) on IGF-I, and BMD. Fifty-four participants (male = 28; female = 26) selected according to criteria previously

described were randomly assigned to either a high intensity weight training group (n = 27) or a moderate intensity weight training group (n= 27).

Control Group

Participants served as their own control group. The first 12 weeks of the study was a control period, during which time participants were instructed to maintain their normal daily routines and eating habits. Bone mineral density and body composition were assessed at baseline, week 12, and week 36. Muscle strength, hormonal status and anaerobic power were assessed at baseline and weeks 12, 24 and 36 of the study.

Bone Mineral and Body Composition

Bone mass and body composition were determined by dual-energy x-ray absorptiometry (DXA, Hologic QDR-1000/W, Waltham, MA) to measure bone area (cm²), and bone mineral density (BMD, g/cm²) of the lumbar spine (L2-L4), proximal femoral neck, ward's triangle, greater trochanter and the whole body. All scans were performed and analyzed by one trained technician. Scans were analyzed using Hologic software version 6.10.01 Rev A (Hologic, Inc., Waltham, MA) and all follow-up scans were analyzed using the compare mode. The coefficient of variation (CV) for repeated DXA scans at the Oregon State University Bone Research Laboratory are 1.0% for BMD of the hip and lumbar spine.

A whole body DXA scan (Hologic, Inc., Waltham, MA) was performed to quantify lean and fat mass (independent of bone). The percentage of water in lean tissue was assumed to be 73.2%. Validation of this procedure for body composition analysis has recently been conducted in our laboratory ⁽¹⁵⁾. These results demonstrated that DXA is comparable to two and four component body composition models. The CV for body

composition analysis in our laboratory, whole body fat and lean mass with DXA is 1.2% and 1.5% for lean and fat mass of specific regions (i.e., legs, trunk, arms).

Blood Sampling and IGF-I and IGFBP-3

All participants underwent an 8-hour fasting blood draw of approximately 10 to 15 ml. Blood samples were collected at baseline, and weeks 12, 24 and 36 of the study. All blood samples sat at room temperature for 30 minutes, and then were centrifuged for 10 minutes at a speed of 1200 x gravity in order to separate the serum. Serum samples were then frozen at -20°C (and stored at -70°C). Serum samples for determining IGF-I and IGFBP-3 were shipped frozen on dry ice, via an overnight shipping service, to the Maine Center for Osteoporosis Research and Education in Bangor, Maine. Samples for serum IGF-I assay were prepared for analysis by acid ethanol cryoprecipitation as per Breier⁽¹⁶⁾. In this manner, IGF-I is extracted from its binding proteins. Acid ethanol extraction followed by cryoprecipitation has been found to reduce residual IGFBPs to a level that does not interfere with the competitive antigen-antibody binding in radioimmunoassay (RIA) of IGF-I. The recovery of ratio-labeled ^{125}I IGF-I determined by high performance gel chromatography is 98% for AEC-extracted serum⁽¹⁶⁾. Following acid ethanol cryoprecipitation, the samples were analyzed by radioimmunoassay with IGF-I kits from Nicholas Institute Diagnostic (San Juan Capistrano CA). Samples were extracted and analyzed in duplicate. Intra-assay CVs ranged from 1.03% to 7.1%. The inter-assay coefficient of variation (CV) was 4.65%. Serum IGF-I, determined from acid ethanol cryoprecipitation and radioimmunoassay in this manner, has been dissociated from its binding proteins, and represents total (bound and free) IGF-I levels.

IGFBP-3 was assayed in duplicate using a two site immunoradiometric assay (IRMA) kit (Diagnostic System Laboratories, Inc. Wedster TX), as described in Poehlman⁽¹⁷⁾. The intra CVs ranged from 0.10% to 3.28%, and the inter-assay CV was 2.66%.

IGFBP-3 analyzed in this manner represents total (bound and whole, bound and truncated, and free) serum IGFBP-3.

Block Food Frequency Questionnaire

Participants completed a computer-scored 100-item Block Food Frequency Questionnaire (18) designed for use by the National Cancer Institute. Information regarding average daily calcium intake, caloric, protein, fat, carbohydrate consumption, and grams of protein per kilograms of body weight were obtained using this tool.

Resistance Training Protocols

Participants followed a training program which activated all major muscle groups. The MIM program (a seated machine based program) included 13 exercises: leg extension, leg press, hamstring curls, arm curl, triceps press, chest press, pec deck, shoulder press, side lateral raise, lat pull down, seated row, abdominal crunch, and calf raise. The HIF program (a primarily standing free weight program) consisted of 12 exercises: free weight back squats, deadlifts, biceps curls, sit-ups and triceps extensions and resistance machine exercises (Hammer Strength), chest press, incline chest press, shoulder press, high lat pull down, leg curl, gripper (wrist strength) and calf raise.

Training sessions were conducted 3 times per week for approximately 75 minutes under close supervision of a personal trainer (1 trainer for every 2 subjects) which ensured proper technique, provided motivation and encouragement, and decreased risk of injury. Exercise sessions included a 10 minute dynamic warm-up and cool down period which consisted of 5-7 minutes of cardio exercise and 3-5 minutes of total body stretching. Participants were given a 3 week learning period which focused on proper technique, safety and weight room etiquette prior to beginning the loading phase of the

study. Minimal resistance was used during this phase. All training sessions were conducted at Gold's Gym of Corvallis, OR. Each training session was recorded.

Moderate Intensity Machine Weight Training Group (MIM)

Participants in this group performed 3 sets of 10-13 repetitions for 13 exercises (40-60% of 1 RM; 20-40 seconds rest between stations) for 24 weeks. One repetition maximum (1 RM) was defined as the maximum amount of weight each subject could lift one time with proper technique through a full range of motion for each exercise in the program. Exercise intensities were set at 40% of initial 1 RM for the first 3 weeks. Participants were instructed to execute the concentric phase of each exercise as forcefully as possible and the eccentric phase over 2-3 seconds. After retesting and establishing new individual 1 RM, training loads were adjusted to 50 % of their new 1 RM for 6 weeks. For the remaining 15 weeks, subjects performed at 60% of their newly determined 1 RM values, retesting and load adjustments were conducted every 6 weeks.

High Intensity Free Weight Resistance Training Group (HIF)

Participants in this group performed a staged 25-week high intensity training program. The training period consisted of 3 stages: (I) a 12-week training program, (II) a transitional stage (1 week), and (III) a second 12-week training program. Stages I and III were subdivided into 3 phases which differed in the intensity and volume of training. Volume of work was estimated by: sets X repetitions X weight lifted. Phase I consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 10 repetitions (intensity: 70 % of 1 RM) for each exercise, with 1-minute rest between sets and exercises. Phase II consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 5-6 repetitions (intensity: 80 % of 1 RM) for each exercise, with 3-minute rests between sets. Phase III consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 2-4 repetitions

(intensity: 90+ % of 1 RM) for each exercise, with 3-minute rests between sets. During phase III, repetitions of 2-4 were only performed for the large muscle groups: legs, chest, back and shoulders. Smaller muscle groups, biceps, triceps and calves performed 3 sets of 8 repetitions at 70% of 1 RM. This was done to avoid injury to smaller muscle groups. Participants were instructed to execute the concentric phase of each exercise as forcefully as possible and the eccentric phase over 2-3 seconds. During the transition phase (1 week), participants were engaged in non-resistance training fitness activities involving low intensity cardiovascular exercise, stretching and relaxation. This was done to allow the participant to recover both physically and emotionally from the high intensity work loads. New 1 RM values, retesting and load adjustments were conducted every 6 weeks.

Statistical Analysis

The overall design employed a 2 (group) X 2 (gender) x 2 (time) between/within design with repeated measures (RM) on the last factor. Uni- and multivariate repeated measures techniques were conducted to determine, group by gender and group by time interactions. Baseline values were used as covariates when analyzing bone mineral density (BMD) of the femoral neck, lumbar spine, whole body, and greater trochanter. Repeated measures MANOVAs were employed to determine the effects of the training on IGF-I and its receptor IGFBP3. Repeated measures was used for both within- and between-group comparisons. For multivariate analyses, univariate follow-up procedures were utilized to determine which dependent variables contributed to significant findings.

Subject numbers were determined from formal power calculations. With a power = 0.8, alpha = 0.05, and an expected difference between groups of 1-2 % at the proximal femur, 25 subjects per group were needed in order to determine significance. Data were entered and analyzed using SPSS 7.5 for Windows ⁽¹⁹⁾ for univariate and multivariate

analyses, respectively. All data are presented as mean (\pm SD). The level of significance was set at $\alpha = 0.05$.

Results

Descriptive Statistics

Baseline variables (means \pm SD) were normally distributed and did not differ significantly between the moderate and high intensity exercise groups (Table 2.1).

Attrition and Compliance

Of the 54 participants (28 males and 26 females) recruited, 42 participants completed the 9 month study (24 males and 18 females), representing an attrition of 22%. Those who left the study did so for personal, work related, or family reasons. No subjects stopped participation because of injury resulting from the training program.

Compliance, defined as the percentage of workouts attended and completed was 93% and 94% for men and women respectfully. No significant difference in compliance was observed between the HIF (92%) and MIM (94%) groups. The training programs were well tolerated by all participants. None of the participants developed any overuse or other types of injury sufficient enough to warrant any program modifications, withdrawal or interruption in their training schedules (Table 2.2).

TABLE 2.1. BASELINE DESCRIPTIVE PHYSICAL CHARACTERISTICS: (MEANS \pm SD)

Variable	Moderate Intensity Group		High Intensity Group	
	Males = 13	Females = 14	Males = 15	Females = 12
Age: Years	54.92 \pm 3.25	53.14 \pm 3.13	54.40 \pm 3.35	52.75 \pm 2.59
% Body Fat	23.21 \pm 6.23	33.82 \pm 9.26	21.06 \pm 3.27	32.90 \pm 5.84
Lean Mass: kg	67.29 \pm 8.42	42.79 \pm 4.72	65.99 \pm 7.22	45.17 \pm 3.62
Fat Mass: kg	22.55 \pm 6.70	24.86 \pm 11.17	18.24 \pm 8.27	23.99 \pm 7.12
Weight: kg	92.87 \pm 18.81	69.74 \pm 13.88	85.12 \pm 13.38	71.65 \pm 9.31
BMD				
FnBMD: g/cm ²	0.853 \pm .08	0.731 \pm .11	0.856 \pm .10	0.808 \pm .16
LuBMD: g/cm ²	1.146 \pm .16	0.950 \pm .12	1.035 \pm .12	1.032 \pm .13
WdsBMD: g/cm ²	0.664 \pm .15	0.557 \pm .12	0.598 \pm .11	0.653 \pm .16
WhBMD: g/cm ²	1.239 \pm .08	1.068 \pm .07	1.175 \pm .09	1.136 \pm .10
TrBMD: g/cm ²	0.779 \pm .10	0.631 \pm .08	0.737 \pm .09	0.685 \pm .12
T Scores				
Femoral Neck	-0.909 \pm .91	-1.46 \pm -1.16	-0.977 \pm .91	-0.918 \pm 1.81
Greater Trochanter	-0.147 \pm .99	-1.01 \pm 1.00	-0.456 \pm .69	-0.56 \pm 1.49
Post Men: Mos		46.07 \pm 39.14		54.25 \pm 65.17
IGF-I				
IGF-I: ng/mL	171.00 \pm 63.55	150.29 \pm 38.08	170.60 \pm 47.39	165.33 \pm 34.77
IGFBP3: ng/mL	2548.50 \pm 565.68	3012.62 \pm 628.1	2762.93 \pm 554.39	2888.08 \pm 553.4
IGF-I/BP3	0.0619 \pm .02	0.0497 \pm .01	0.0615 \pm .01	0.0581 \pm .00

TABLE 2.2. REASONS FOR PARTICIPANT WITHDRAWAL FROM STUDY (N = 12)

Reasons given	Baseline to 3 months n = 0	3 months to 6 months n = 5	6 months to 9 months n = 7	Total n = 12
Relocated	0	2	1	3
Personal/family	0	0	2	2
Job related	0	2	1	3
Injury	0	0	0	0
Vacation	0	0	2	2
Auto accident	0	1	1	2

Bone Mineral Density : Control Period

Multiple paired-sample t-tests revealed no significant differences between groups during the control period (baseline to week 12). All variables were highly and significantly correlated for the four bone mineral density (BMD) variables; femoral neck, lumbar spine [L2-L4], greater trochanter and whole body). Correlations ranged from a low of .68 to a high of .99 (mean .95). As a result, a mean value was calculated for the control period for each of the dependent variables. This mean values was subsequently used as a covariate.

BMD Percentage Change

Analysis of covariance (ANCOVA) was performed on percentage change in BMD for each of the following dependent variables separately: Femoral neck, lumbar spine (L2-L4), greater trochanter and whole body for the two training groups. Percentage change was determined as follows (change due to intervention - initial value/ initial value). Data were analyzed while controlling for initial BMD differences (ANCOVA). Comparisons

were performed between males in the MIM and HIF groups. Similar analyses were performed for the women as well. For the men, results revealed a significant difference between groups at the lumbar spine. High intensity training produced a significant increase in spine BMD and whole body BMD $p < .05$. Since the increase in whole body BMD was less than the precision error, we interpret this as a maintenance, rather than a true increase in whole body BMD. No significant differences were observed between groups for femoral neck $p > .11$ or greater trochanter $p > .75$ BMD. Results revealed no significant difference in BMD between groups for women at the lumbar spine $p > .37$, femoral neck $p > .81$, trochanter $p > .38$, or whole body BMD, $p > .52$.

Paired t-tests comparing percent change means for greater trochanter and femoral neck revealed that high intensity, but not moderate intensity resistance training produced regional changes in bone mass at the hip. Specifically, a significant increase in trochanteric BMD for women (2.0%) and for men (1.3%) accompanied by a significant decrease in femoral neck BMD for both men and women (1.8%) in the high intensity free weight training program ($p < .05$). Both women and men in the moderate intensity machine based group showed a similar but non-significant trend at the hip. No changes were observed in total hip BMD. These findings suggest a "shift" in BMD from the femoral neck to the trochanter, given that total hip BMD did not change. These data indicate that resistance training may be dose and exercise specific, and that, at the hip, the effects of low estrogen maybe overridden (Table 2.3).

TABLE 2.3. PERCENT CHANGE BONE MINERAL DENSITY VALUES FOR THE MODERATE AND HIGH INTENSITY GROUP AFTER 6 MONTHS OF TRAINING.

Variable	Females		Males	
	MIM n = 9	HIF n = 9	MIM n = 12	HIF n = 12
FnBMD	- 1.44 ± 3.0	- 1.78 ± 2.7 #	- 0.61 ± 2.3	- 1.76 ± 2.3 #
TrBMD	0.38 ± 2.6	2.00 ± 3.8 #	1.02 ± 2.5	1.24 ± 2.3 #
LuBMD	- 0.81 ± 1.5	0.39 ± 3.1	- 0.52 ± 2.5	1.89 ± 2.9 *
WhBMD	- 0.92 ± 1.4	0.20 ± 0.7	- 0.21 ± 1.6	0.18 ± 1.2 *
TotHipBMD	0.33 ± 2.2	1.66 ± 2.6	0.48 ± 1.2	0.78 ± 1.9

ANCOVA: * level of significance $p < .05$.
 Paired t-tests: # level of significance $p < .05$.

Growth Factor Variables

Baseline correlation's (Pearson product moment, two-tailed) examining the relationship between IGF-I, IGFBP3 and IGF-I/IGFBP3 ratio and age, and measures of bone mineral density, mean strength values and measures of body composition for combined groups and gender were calculated (see Table 2.4). At baseline, higher IGF-I and IGFBP3 levels were significantly ($p < .05$) associated with fat mass (kg), but not with LM, body weight (kg), age, and measures of BMD, or mean strength values. Table 2.4 also shows bivariate correlation's of IGFBP3 and IGF-I/IGFBP3 with age, and measures of BMD, mean strength values and measures of body composition. At baseline, IGF-I/IGFBP3 showed no significant association with any of the variables tested.

TABLE 2.4. BIVARIATE PEARSON CORRELATIONS BETWEEN IGF-I, IGFBP3 AND IGF-I/IGFBP3 RATIO, AGE, BONE MINERAL DENSITY MEAN STRENGTH AND BODY COMPOSITION DURING THE CONTROL PERIOD. GROUPS COMBINED FOR INTENSITY AND GENDER.

Variable	IGF-I Control	IGF-I/IGFBP3 Control	IGFBP3 Control
Age	-.028	.119	-.075
Lean Mass kg	.042	.168	-.151
Fat Mass kg	-.325*	-.463**	.106
Body Weight kg	-.146	-.122	-.060
Mean Strength N	-.001	.117	-.181
Greater Trochanter BMD	.160	.214	.021
Ward's Triangle BMD	-.041	-.025	-.020
Femoral Neck BMD	.048	.018	.052
Lumbar Spine BMD	-.002	.155	-.100
Whole Body BMD	.068	.185	-.103

*: Correlation is significant at the 0.05 level (2-tailed)

**: Correlation is significant at the 0.01 level (2-tailed)

Effects of Training

IGF-I and IGFBP3 were analyzed using a 2 X 2 X 4 (group by gender by time) MANOVA with RM on last factor. The dependent variables were insulin-like growth factors IGF-I, IGFBP3 and IGFBP3/IGF-I ratio. The RM MANOVA, showed that neither a significant multivariate main effects for group, nor significant univariate group by gender or group by time interactions existed. These findings suggest that neither the HIF or MIM training protocols produced a training effect on any of the dependent variables tested.

No group, gender or training effects existed, thus only total means for each variable over the 4 assessment periods are reported. Overall means and standard deviations for IGF-I, IGFBP3, and IGFBP3/IGF-I ratio are presented in Table 2.5.

TABLE 2.5. VALUES FOR INSULIN-LIKE GROWTH FACTOR I (IGF-I), INSULIN-LIKE GROWTH FACTOR I BINDING PROTEIN (IGFBP3) NG/ML AND IGFBP3/IGF-I RATIO (MEANS \pm SD) DURING AT BASELINE, AFTER CONTROL PERIOD (12 WEEKS) DURING THE INTERVENTION PERIOD (WEEK 24) AND FOLLOWING RESISTANCE TRAINING (WEEK 36).

Measurement Period	IGF-I:ng/mL	IGFBP3: ng/mL	IGFBP3/IGF-I
Baseline	159.54 + 44.84	2755.03 + 592.19	.0061 + .0015
Week 12	163.46 + 44.98	2760.49 + 503.61	.0058 + .0014
Week 24	167.18 + 50.41	2685.67 + 543.58	.0063 + .0016
Week 36	158.51 + 52.98	2686.13 + 564.04	.0059 + .0017

Stability of IGF-I

The stability of IGF-I over the 9-month intervention period was evaluated by two-tailed correlation and revealed that pre and post-training basal serum concentrations were significantly correlated, thus remaining relatively stable over the 9-month period ($r = .87$, $p < .01$, Figure 2.1). These results were similar to those recently reported by Vitiello⁽²⁰⁾ who found that IGF-I values for endurance trained older men and women remained extremely stable over time (6.5 month), ($r = .85$ $p < .001$). Since IGF-I has important autocrine and paracrine activity in muscle, an increase in serum levels of IGF-I may not be needed to produce an anabolic effect within skeletal muscle tissue.

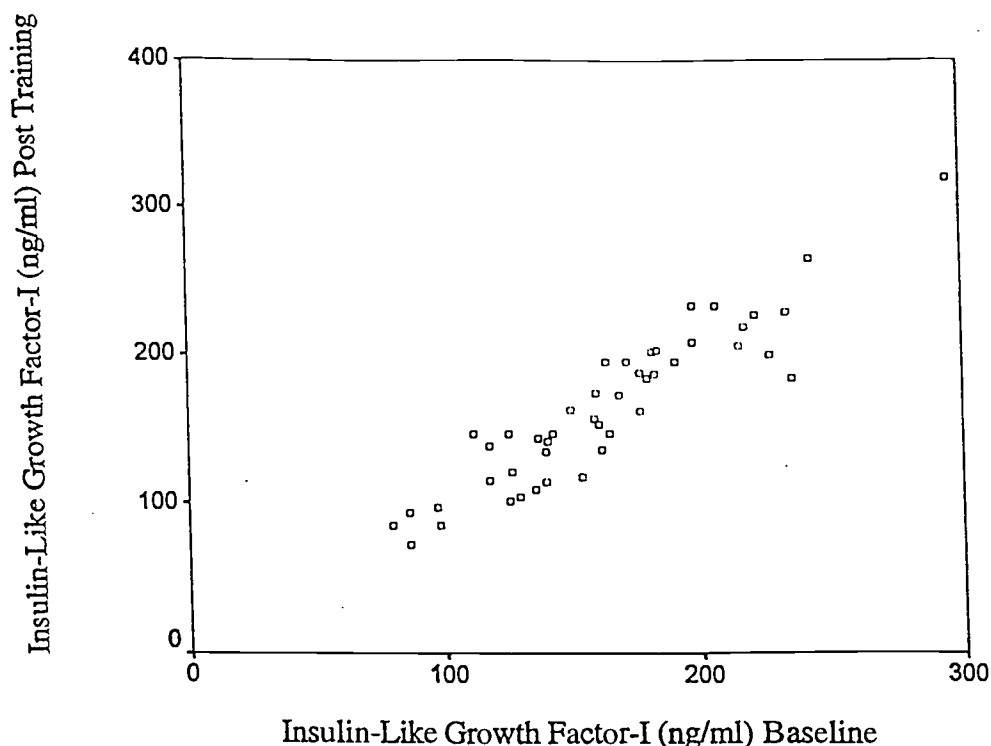


Figure 2.1. Scatter plot of baseline versus post-training insulin-like growth factor-I (IGF-I) levels (ng/ml) for all subjects ($r = .87$).

Mean Total Body Strength:

A mean total score was derived from five strength variables: peak quadriceps force, peak hamstring force, peak hip abduction force, peak pectoral force and peak latissimus dorsi force. The data were analyzed using a 2 X 4 (group by time) repeated measures (RM) ANOVA which showed a significant within component effect for time, $p < .001$ regardless of training group. In the follow-up, the dependent variables were significant for time in the follow-up univariate ANOVA's. During the control period a slight decrease in peak force was observed in both groups. This was followed by an increase in peak force in time period 3 (a training effect) and time period 4 (a continuation of the training effect). Time by group effect $p > .09$ was not significant. Table 2.6 presents means and standard deviations for total mean strength (peak force) for baseline, weeks

12, 24 and 36 of the study. A significant difference $p < .001$ existed for time across all phases of this study (baseline, weeks 12, 24 and 36) regardless of training or gender.

TABLE 2.6. COMBINED TOTAL MEAN STRENGTH (PEAK FORCE (N)): (MEANS + SD) FOR ALL PARTICIPANTS REGARDLESS OF GENDER OR TRAINING INTERVENTION DURING THE CONTROL PERIOD (BASELINE TO WEEK 12) AND THE INTERVENTION PERIOD (WEEK 12 TO WEEK 36).

<u>Time</u>	<u>Mean</u>
Baseline	345.60 \pm 129.57
Week 12	339.63 \pm 124.16
Week 24	425.46 \pm 134.58 *
Week 36	453.69 \pm 143.74 *

$p < .001$: Significant improvement in total strength

Total Leg Lean Mass

Leg lean mass was analyzed using a 2 X 2 (group by time) RM ANOVA. The RM ANOVA, showed a significant within component effect for time, $p < .001$. Focusing on the main effects, the dependent variable was significant for time in the follow-up univariate ANOVA's indicating an increase in leg lean mass due to training. Time by group effect $p > .89$, was not significant. Table 2.7 presents means and standard deviations for total leg lean mass for baseline, weeks 12, 24 and 36 of the study. A significant difference $p < .001$ existed for time across all phases of this study (baseline, weeks 12, 24 and 36) regardless of training or gender.

Block Food Frequency Questionnaire

Participants completed a computer-scored 100-item Block Food Frequency Questionnaire ⁽¹⁸⁾ designed for use by the National Cancer Institute. Information regarding average daily calcium intake, caloric, protein, fat, carbohydrate consumption, and grams of protein per kilograms of body weight were obtained using this tool (Table. 2.8).

TABLE 2.7. TOTAL LEG LEAN MASS (LM) BY GENDER AND TRAINING INTERVENTION PROTOCOL DURING THE CONTROL PERIOD (BASELINE TO WEEK 12) AND THE INTERVENTION PERIOD (WEEK 12 TO WEEK 36).

	<u>Moderate Intensity</u> <u>Group</u>		<u>High Intensity</u> <u>Group</u>	
<u>Time</u>	<u>Males</u> <u>Mean/SD</u>	<u>Females</u> <u>Mean/SD</u>	<u>Males</u> <u>Mean/SD</u>	<u>Females</u> <u>Mean/SD</u>
Baseline	68.41 ± 7.71	42.50 ± 4.70	65.99 ± 7.22	43.83 ± 4.42
Week 12	68.59 ± 7.49	43.06 ± 4.65	66.01 ± 6.70	44.89 ± 4.17
Week 36	70.20 ± 7.89*	44.38 ± 4.96*	68.97 ± 7.51*	46.83 ± 3.99*

* $p < .05$: Significant improvement in lean mass regardless of gender or training program

TABLE 2.8: INFORMATION REGARDING AVERAGE DAILY CALCIUM INTAKE, CALORIC, PROTEIN, FAT, CARBOHYDRATE CONSUMPTION, AND GRAMS OF PROTEIN PER KILOGRAMS OF BODY WEIGHT FOR MALE AND FEMALE PARTICIPANTS.

	Mean ± SD Males	Mean ± SD Females
Calcium (mg/d)	914.69 ± 329.0	889.75 ± 299.95
Protein: g/kg	1.27 ± 0.46	1.28 ± 0.34
Calories (kcal/d)	1829.89 ± 633.21	1269.06 ± 323.59
Carbohydrates (g)	216.86 ± 83.75	107.00 ± 38.39
Fat (g)	60.09 ± 29.91	40.25 ± 16.20

Discussion

At the hip, we observed a significant difference in change in bone mineral density between the femoral neck and trochanter for women and men from high intensity training. At the spine, men, in the high intensity (HIF) group experienced a significant gain in lumbar spine bone mineral density (BMD) (1.9%) while maintaining whole body BMD (.18 %). Males in the moderate intensity (MIM) group observed no change in lumbar spine BMD, however, a significant decline in whole body BMD 0.21% occurred. Both training programs resulted in improvements in total body strength (37.62%) total lean mass (males 4.1%, females 2.7%) and total leg lean mass (3.3%) regardless of gender. Further, these changes occurred over a relatively short period of time (6-months). No

significant increases in lumbar spine BMD in either group were observed in women, nor were there changes in circulating IGF-I or IGFBP3. Possibly, the lumbar spine is influenced to a greater extent by estrogen depletion, and thus less responsive to forces applied by resistance exercises to the lumbar spine .

Of special interest was the redistribution in bone mineral density from the femoral neck to the greater trochanter in both men and women from high intensity training. Femoral neck BMD decreased by 1.76% and trochanter BMD increased by 1.24% in men and by 1.78% and 2% in the women. Also, there was a trend for a similar shift in the men and women in the moderate intensity group, suggesting an exercise and dose response. The principle of specificity of training, would imply that bone remodeling responded to highly specific mechanical strains in regions of the greater trochanter by high intensity training. The greater trochanter serves as the point of origin for the vastus lateralis ⁽²¹⁾ and point of insertion for the gluteus medius and minimus and lateral rotators of the hip joint (piriformis, quadratus femoris, obturator internus and externus, gemellus superior and inferior) muscles which are heavily involved while executing a deadlift and squat exercise. Specific angles of force placed on the trochanter by the deadlift and squat may play a critical role in the increased BMD of the trochanter in the high intensity group. Our data support this hypothesis since no shift of bone mineral density from the femoral neck to the trochanter occurred during the control period. Why bone is robbed from the femoral neck is unclear. However, this shift may be safe guard against trochanteric hip fractures. Greenspan ⁽²²⁾ has demonstrated that relatively low trochanteric BMD or high femoral neck BMD to be associated with trochanteric hip fractures in older adults. It may be that this shift in BMD from the femoral neck to the trochanter is a defensive mechanism to protect against trochanteric hip fractures as adults age.

To our knowledge, this study is the first to use standing multijoint free weight exercises such as back squats and deadlifts involving high intensities up to 90% of 1 RM

in a longitudinal training study with older adults. We have also shown that this age group is capable of tolerating high volumes of work and intensity without injury.

Several limitations of this study design must be noted. While a within subjects design is strong, the control period of 12 weeks prior to training did not match the 6-month exercise period for these subjects. Small samples of both genders limits the power of statistical analysis, a problem often associated with longitudinal exercise intervention studies. In order to achieve a statistical power of 0.80, the number of participants required in each group would have to be 25 males and 25 females respectively. However, even with our limited sample size of 9 females and 12 males in each of the HIF and MIM groups our mean power was 0.55. Further, we did not monitor acute changes in IGF-I a known endocrine and local anabolic factor for bone tissue ⁽²³⁾, which has been shown to increase significantly during intense bouts of weight training ⁽¹³⁾, which in turn may support an increase in BMD. Additionally, since IGFs are secreted proteins which accumulate and circulate within the extracellular space, there is a high probability that a significant amount of mixing occurs between IGFs produced by skeletal muscle and other tissues (e.g. liver, heart, brain). As a result, this most likely inhibits a quantitative assessment of skeletal muscles contribution to the overall mixture. In addition to this, very few studies have reported IGF peptide measurements because of the difficulty involved in extracting free peptides from IGFBPs.

Average calcium intake for both men and women over the course of this study was males (915 + 330 mg/d) and females (900 + 300 mg/d) which is approximately 600 mg/d below the Institute of Medicine, Harvard Guide to Women's Health requirement of 1500 mg/day for Estrogen depleted postmenopausal women and 300 mg/day below the requirement of 1200 mg/day for men age 50-60 years.

Our findings lend support to the benefits of high intensity standing free weight training (90% of 1 RM) as we report a 1.9% increase in lumbar spine BMD in the HIF

group (men only). Granhed,⁽²⁴⁾ demonstrated that among elite male power lifters (mean age 28.6 yr.) lumbar vertebral bone mineral density was highly correlated ($r=0.82$) with the total poundage lifted over the period of one year. Mathematical modeling demonstrated that compression forces applied to L3 ranged from 18 to 36.4 kN (1877 - 3694 kg) during the deadlift exercise, concluding that weight training may stimulate bone formation through the direct action of muscle pulling on bone or the increased effect of gravity acting on bone when heavy weights are supported by the skeleton. The authors also reported that individuals who lifted more than 1000 tons annually using the deadlift exercise had significantly higher BMD in the lumbar spine. In our laboratory, Adams⁽²⁵⁾ investigated two groups of weight lifters, competitive (43.2 ± 6.8 yr.) and recreational (46.2 ± 7.4 yr.) and categorized subjects by squatters and non-squatters. They found that the squatting group had significantly higher femoral neck BMD (14%) and lumbar spine (12%) BMD than non-squatters, concluding that exercise selection maybe a primary factor in increasing regional BMD. It would have however, been interesting if the two groups were categorized into deadlifters and non-deadlifters to see if the deadlift exercise had the same out comes as the squat regarding higher neck and spine BMD. To date, there is no known 3D dynamic analysis of the forces acting on the hip joint during a repeated free weight back squat. Hattin,⁽²⁶⁾ has reported peak forces on the knee joint at 30% of 1 RM as high as 7 times body weight during knee flexion. However, one can only postulate that there may be an increase in contraction forces at the hip while executing the squat exercise. Thus, at this time, we must conclude that forces at the hip while squatting are probably not high enough to result in an increase in BMD at the femoral neck.

We hypothesized that higher training intensities would result in an increase in BMD at the lumbar spine and femoral neck and in some cases our results support this hypothesis.

To date only a few studies have shown that bone can be enhanced following periods of physical stress resulting from weight training in older adults (7,8,9).

Recently, Menke (9) reported a $3.8\% \pm 1$ (mean \pm SD) increase in femoral neck BMD in a 16-week non randomized exercise group consisting of 11 healthy males volunteers and 7 controls (50-70 yr.) while only doing 1 set of 15 repetitions to failure for each exercise. With only 11 subjects completing the exercise intervention one must question these findings based on the relatively small sample size. However, since baseline values for the exercise group for both the spine and femoral neck appear to be lower than the control group, it may be reasonable to conclude that the increase in femoral BMD may be attributed to the lower initial BMD values in the exercise group. Further, Lohman, (14) reported an increase in spine BMD (2.8%) compared with controls, 5 months into an 18 month free weight training program and a (2%) increase in trochanter BMD after 18 months in premenopausal women (28-39 yr.).

Nelson (7) and Pruitt (6,8) have focused their attention primarily on older women (50-80 yr.). These studies used mostly prone or seated exercises using low to moderate and high intensities (40-80% of 1 RM) sets of 1-3 and repetitions of 8-15 while training either 2 or 3 days per week. Nelson, (7) reported a maintenance in BMD of the hip (0.9%) and an increase of 1.1% of the lumbar spine in estrogen depleted postmenopausal females after one year of training on pneumatic resistance machines two times per week (3 sets of 8 reps, 80% of 1 RM). Pruitt, (8) reported that early postmenopausal women who engaged in a 9-month machine based resistance intervention study exhibited an increase in lumbar spine bone mineral density (1.6%) compared to a decrease of -3.6% in the non exercising age matched control group. The training intensities used in this study were relatively light, exercising three times per week, while performing one set of 8-12 repetitions per exercise (50-60% of 1 RM). Since these studies have reported either a

maintenance or improvement in regional BMD, is it possible that this population responds favorably to this type of exercise protocol.

Thus, it would appear that an exercise intervention such as weight training must be considered as a viable mode for inducing new bone formation, which in turn may lead to the strengthening of bone by increasing its overall density. This would be especially true for exercises programs with lifts which will specifically load the spine and femoral neck would significantly increase bone mass in these regions. The high intensity group did both deadlifts and back squats exercises which we hypothesized would placed heavy mechanical loading (stress) on the lumbar spine and hip area.

Recently, Menkes, ⁽⁹⁾ and Nelson, ⁽⁷⁾ have both reported increases in femoral neck BMD of 3.8% in men and 0.9% in women respectively, as a result of weight training. Further, Lohmanet ⁽¹⁴⁾ reported an increase in BMD at the femoral neck from free weight training in young females. Nelson ⁽⁷⁾ reported a maintenance in BMD of the hip (0.9%) and an increase of 1.0% of the lumbar spine in estrogen depleted postmenopausal females after one year of training on pneumatic resistance machines two times per week (3 sets of 8 reps, 80% of 1 RM). Pruitt, ⁽⁸⁾ reported that early postmenopausal women who engaged in a 9-month machine based resistance intervention study exhibited an increase in lumbar spine bone mineral density (1.6%) compared to a decrease of -3.6% in the non exercising age matched control group. The training intensities used in this study were relatively light. Although the participants exercised three times per week, they only performed one set of 8-12 repetitions per exercise. Both Pruitt ⁽⁸⁾ and Nelson, ⁽⁷⁾ reported significant increases at the lumbar spine BMD (1.6% and 1.1% respectively). Since their programs exercised all of the major muscle groups, it is reasonable to speculate that these exercises produced forces high enough at the spine to cause an increase in spine BMD.

The majority of studies to date are few and varied in the types of exercise programs and intensities employed. This lack of homogeneity between studies prevents any strong conclusions from being made regarding optimal training protocols and intensities as well as efficacy. For example, intervention studies such as Nelson, Pruitt and Menkes used seated machine based weight training exercises yet they have reported increases in lumbar spine or femoral neck BMD. In this present study we found no increases in femoral neck BMD in either the moderate or high intensity group. The MIM program involved machine based leg press, leg extension and leg curl exercises, whereas, the HIF group performed standing and seated free weight exercises. Although we report a significant increase in spine BMD in the high intensity group for males, no changes occurred in the women in either the high or moderate intensity group. Further, 6-months of training employed by our study may not be long enough for older women to show a response at the hip. Pruitt's group trained for 9-months whereas, Nelson trained their subjects for 12-months. Further, if we would have had a larger sample, we may have detected significant changes in our female subjects. Clearly, either the forces or duration of the study were not sufficient enough to increase femoral neck BMD in our group of older women..

Estrogen therapy for postmenopausal women is routinely prescribed to prevent the development of osteoporosis. A number of cross-sectional studies have shown a significantly greater decline in bone mass following menopause (27,28). Cann (29) has reported that trabecular bone decreases significantly during the first 5 postmenopausal years. As a result we cannot overlook the effects of estrogen on bone or in our case the lack of estrogen in our estrogen depleted postmenopausal subjects. Lack of response at the lumbar spine in either the MIM or HIF female participants regardless of training intensity or exercise protocol may be due to low estrogen and calcium intake. Thus,

decreased serum circulating levels of estrogen may in part account for the lack of an increase in regional BMD in this group of women.

On the basis of the findings of a few well-designed high-impact exercise studies, is it possible that the type of loading needed to effectively increase hip BMD may need to be of an "impact" nature. Bassey and Ramsdale ⁽³⁰⁾ have recently reported that high impact jumping exercises produced a significant increase in BMD of the trochanter (3.9%), but no change in either spine or femoral neck BMD in premenopausal women. Kohrt ⁽³¹⁾ recently reported an increase in BMD at the femoral neck at the conclusion of an 11 month training study comparing stress to the skeleton through ground reaction forces (jogging) and joint reaction forces (weight lifting) in older, sedentary women (60-74 years). The investigators reported an increase of 3.5% in bone mineral density of the femoral neck but not the greater trochanter in the ground reaction force trained group. These findings suggest that the magnitude and rate of loading may be more important to induce new BMD changes at the femoral neck.

We expected IGF-I serum levels to increase as a result of weight training since IGF-I and its receptor, IGFBP3, are highly correlated with lean mass and bone mineral density ⁽¹¹⁾. Although we clearly demonstrate that 6-months of resistance training resulted in a significant increase in lean mass, lumbar spine BMD, muscular strength and declines in body fat, these changes do not appear to result from chronically increased insulin-like growth factors. However, given that IGF-I stimulates proliferation and differentiation in both bone and muscle cells ⁽³²⁾, we speculate that local secretion of IGF-I may have played a role in producing the musculoskeletal changes we observed.

Limited data exist on the relationship between weight training and the GH/IGF-I axis. Pyka ⁽¹²⁾ have reported that participation in a longitudinal weight training intervention study produced no changes in basal IGF-I and IGFBP3 levels which may have been due to a lower intensity program. Especially since participants strength in the Pyka ⁽³³⁾ study

plateaued after 3 months of training. We designed a weight training intervention program which compared a high intensity (mostly free weight exercises) regimen to a moderate intensity training (machine based) program, but even then we did not observe IGF-I changes. Our findings are similar to those of Hakkinen ^(34,35) who studied elite power lifters over a period of two years of training and observed that basal levels of growth hormone did not increase as a result of training. These investigators concluded that alterations in resting levels of growth hormone are not a plausible mechanism of chronic adaptations to intense resistance training even though increases in lean mass and strength were observed. Our data corroborate these findings in older adults. However, since IGF-I is a known mediator for the actions of growth hormone ⁽³⁶⁾, and is considered both an endocrine and local anabolic factor for bone tissue ⁽²³⁾, it may be possible that weight training could be associated with an anabolic effect at the bone/tissue level without an observed increase in basal serum levels. Further, acute changes in IGF-I in response to weight training have been observed in young adults ^(8,12). Thus, it is plausible that this mechanism could have in part, produced the musculoskeletal changes we observed in this present study.

Recently, Vitiello ⁽²⁰⁾ reported that in a group of healthy endurance trained males (mean age 66.9 yr) and females (mean age 67.1 yr) no relationship existed between age and IGF-I over a 7 month training period. This lack of an age/IGF-I correlation was also observed in this study. In fact the basal IGF-I concentrations of our participants (mean age 53.6 yr.) remained quite stable over the 9-month intervention period. Vitiello ⁽²⁰⁾ suggests that although IGF-I levels decline continually across the life span, the anabolic status of healthy older adults, as indexed by IGF-I, remain relatively stable across short periods of time (i.e. 9 months).

Our results are the first to demonstrate that high muscle forces produces by high intensities free weight training result in a shift in regional hip bone mineral. The specific

bone strains caused from these forces are not known, nor is the potential protection against trochanteric fractures. High intensity training produced significant increase in spine BMD in the males while maintaining whole body BMD.

Further, we have shown that older adults can tolerate regular participation in a free weight resistance training program which uses high intensities without incurring injury. Thus, resistance training may help offset musculoskeletal declines associated with aging and allow continued participation in recreational activities as well as maintain function well into their senior years.

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Chapter 3

Effects of Exercise on Lean Mass, Strength and Insulin-Like Growth Factors in Older Adults

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Abstract

With age, there are marked declines in lean mass, muscular strength, and anabolic hormones, specifically growth hormone (GH) and insulin-like growth factor-I (IGF-I). To evaluate intensity of training in older adults, we studied the effects of two different resistance training protocols on lean mass, IGF-I levels, muscle strength, and anaerobic power in older adults (50-60 years), we compared a moderate intensity seated machine weight resistance training program (MIM), to a high intensity training free weight program (HIF) using exercises such as standing back squats and deadlifts. Twenty-eight healthy older men (54.58 ± 3.20 yr., mean \pm SD) and twenty-six healthy older women (52.83 ± 3.26 yr., mean \pm SD) were randomized to either a 3d/wk, 6-month moderate intensity (60% of 1 RM) or high intensity (70-90% of 1 RM) resistance training protocol. HIF consisted of two 12 week cycles of upper and lower extremity free weight exercises (intensity: 70-90% of 1 RM) while the MIM program utilized variable resistance machine exercises (intensity: 60% of 1 RM). Before and after training, body composition was assessed by dual-energy x-ray absorptiometry, muscle strength by isokinetic dynamometry, muscular power by modified Wingate Anaerobic Power Test, and IGF-I by fasting blood sampling. Participants served as their own control group for 12 weeks prior to the start of the training intervention ($n = 54$) and no changes in any variables occurred during this period. A (group \times gender \times time) MANOVA was performed on all dependent variables. We report gains in peak force, anaerobic power and lean mass ($p < .01-.05$) in older adults, following a control period (12 weeks) where no significant changes occurred, regardless of gender as a result of 6 months of resistance training. Despite these increases, neither intensity protocol significantly increased serum levels of IGF-I. Further, the changes in strength, power, and body composition were similar in

both the high intensity (HIF) and moderate intensity (MIM) groups and were independent of gender.

Introduction

With age, there are marked declines in muscular strength (33), lean mass (64), and anabolic hormones, specifically growth hormone (GH) and insulin-like growth factor-I (IGF-I) (9,57,69). It is unclear if these declines are a direct result of the aging process, or a reduction in physical activity which accompanies aging (30,50). To offset and/or reduce the physical declines in the muscular system, interest has been devoted to developing exercise programs which will produce optimal increases in strength and lean body mass in older adults.

Strong evidence exists that weight training in older adults can positively influence muscular strength and lean mass (7,16,17,19,68). It has been demonstrated that men have greater absolute strength and power than do women and this difference is in part attributed to the larger muscle fibers (type I & II) reported in males (29,41,59) than in females. However, when strength is expressed per unit of lean mass, most of the absolute strength differences between genders are eliminated (29). Recently, Miller (41) and Castro (5) concluded that both men and women respond similarly to strength training programs and that no evidence exists suggesting that women should train differently than men.

Currently, most weight training programs for older adults have employed machine based exercises and traditional progressive weight training prescriptions, i.e. 3 sets of 8-12 reps 2-3 times per week @ 60-90% of 1 RM, (14). However, strength training experts have stressed the use of free weight exercises (squats, deadlifts, etc.) to develop maximal strength and power. The combination of free weight exercises at near maximal loads (intensities of 90% of 1 RM) are assumed to produce optimal neuromuscular

adaptations and maximal power compared to lower intensity training (61), but, this has not been substantiated. In addition to training with high intensities, it is also important to vary the mechanical stress throughout the workout. This is accomplished by cycling the intensities from moderate to high throughout the training intervention, which is often referred to as periodization (65). This type of cyclic training provides the body with the variation in mechanical stress loads, while preventing overtraining, undertraining and reducing the possibility of injury and burnout (65).

The interactions of regular, long term weight training and the GH/IGF-I axis in older adults is not well documented. It has been demonstrated that acute IGF-I infusions, at megadose levels, stimulate skeletal muscle protein synthesis in humans (20). Evidence of increased IGF-I in skeletal muscles, such as increased messenger RNA (mRNA) for IGF-I, has been associated with compensatory hypertrophy (13) and stretch-induced hypertrophy (12,21) of skeletal muscles in animals, suggesting IGF-I as a mechanism for muscular hypertrophy related to the application of increased or altered forces to skeletal muscle. Since IGF-I and GH strongly correlate with lean mass (LM) (13), it is conceivable that increases in LM often associated with weight training could result from chronically increased basal IGF-I concentrations.

To date, the benefits of a high intensity free weight periodized weight training program on the muscular and endocrine systems in older adults have not been evaluated. Thus, we compared the effects of moderate and high intensity weight training over a 6-month period on lean mass, serum IGF-I levels, muscle strength, and anaerobic power in older adults (50-60 years).

Materials and Methods

Subject Recruitment and Selection

Two hundred and sixty-three men and women 50-60 years of age responded to a recruitment notice published in newspapers from within Benton County, Oregon. From this pool of inquiries, 54 participants satisfied the selection to participate in the study. Both exercise groups (MIM and HIF) consisted of previously untrained non exercising adult men and women. The mean ages at the time of laboratory testing were 54.58 years ($SD = 3.20$) for men, and 52.83 years ($SD = 3.26$) for women. In order to be enrolled, participants were classified as normally active (not having participated in an exercise or resistance training program for the past two years). All participants were free of heart disease and screened for hormone therapy and medications that may affect bone metabolism. All participants completed a comprehensive screening process which included a health questionnaire and written release from their family physician allowing them to participate in the training study. Participants were screened for chronic disease, orthopedic problems (significant disability of shoulder, knee, lower back, or hip) and alcohol consumption (>2 drinks per day) by health history questionnaire. Women and men on medications known to alter bone metabolism were excluded. All participants were Caucasian and came from middle to upper class backgrounds. Participants were informed of the purpose, procedures, and potential risks of the study before signing an informed consent approved by the Oregon State University Institutional Review Board.

Study Design

This study design was a randomized intervention trial comparing two resistance training protocols (moderate intensity: MIM vs. high intensity: HIF) on IGF-I, muscular

strength (peak force N), anaerobic power (W), gender comparisons, and changes in body composition. Fifty-four participants (male = 28; female = 26) selected according to criteria previously described were randomly assigned to either the HIF exercise group (n = 27) or the MIM exercise group (n= 27).

Control Group

Participants served as their own control group. The first 12 weeks of the study was a control period, during which time participants were instructed to maintain their normal daily routines and eating habits. Body composition was assessed at baseline, week 12, and week 36. Muscle strength, hormonal status and anaerobic power were assessed at baseline and weeks 12, 24 and 36 of the study.

Methods: Measurement

Muscle Strength

Peak force (N) was measured by isokinetic dynamometry (KinCom 500H, Chattex Corp.) in the following muscle groups: hip abductors, knee extensors and flexors, chest and upper back muscles by isokinetic dynamometry (KinCom 500H, Chattex Corp.). All tests were conducted at a speed of 30 degrees per second and were gravity corrected. After a demonstration of procedures, each subject was positioned to isolate the muscle group being tested and instructed to perform 10-12 trials of each exercise at an intensity well below maximum which served as the warm-up activity prior to maximum strength assessment. After the warm-up, subjects performed 3-5 maximal efforts in order to determine peak force and torque. Each maximal effort was separated by approximately 60 seconds of rest. Strength assessment protocols were programmed into the

dynamometer to set parameters for testing (i.e., start and stop angles and speed of contraction), and therefore ensure consistency. Protocols employed previously in our laboratory have revealed good reliability within this population ($CV = 68\%$)

Muscle Strength by 1-RM

One repetition maximum (1 RM) was equal to the maximum amount of weight that could be lifted one time with proper technique through a full range of motion. 1 RM was determined for exercises involving each of the following major muscle groups; legs, arms and trunk. For the MIM group, 1 RM was obtained for each of the following exercises: chest press, pec dec, shoulder press, leg press, leg extension, leg curl, lat pull down, seated row, biceps curl, and triceps extension. For the HIF group, 1 RM was obtained for the following exercises: chest press, incline chest press, back squats, deadlifts, leg curl, barbell biceps curl, triceps press down, high lat pull down, calf raise, shoulder press and wrist curls. Two of the exercises in each group proved to be unreliable and therefore were not considered (wrist curls and calf raises). For each assessment period, one repetition maximum (1 RM) was determined over the course of three testing sessions, with one day of complete rest between testing sessions. For each of the 1 RM testing sessions 1 RM was obtained for the following exercises: HIF group, day one: Chest press, high lat pull and leg curl. Day two: Squats, shoulder press and biceps curl. Day three: Incline chest press, deadlifts, and triceps extension. MIM group, day one: Chest press, high lat pull and leg curl. Day two: leg press, shoulder press and biceps curl. Day three: Pec deck, leg extension, and triceps extension. For each exercise, participants rested 3 minutes between sets and 5 minutes between exercises in an attempt to allow each participant maximum recovery. After two warm-up sets of 10-12 repetitions using light weights, each participant performed a single repetition with a weight he or she could lift through a complete range of motion. All machines and participant limb positions were

adjusted to ensure proper technique and complete range of motion. Each lift began in the bottom position and was deemed successful when the limbs were fully extended. At the conclusion of each successful lift, 5 to 20 lb. was added for the next attempt. This procedure was repeated until the participant could no longer lift the weight, and the highest weight lifted successfully was recorded as the 1-RM. This was generally achieved in 4 to 6 attempts. Assessment of 1 RM was conducted during weeks 1, 8, 16 and 24 of exercise intervention. Purpose of 1-RM assessment was to reassess strength and adjust training intensity. These values were not used to evaluate differences between groups.

Muscular power

Muscular power of the lower extremities was assessed by the Wingate Anaerobic Power Test (WAPT) for older individuals (2). The test involves maximal pedaling against high resistance for 15 seconds. An optical sensor was mounted close to the fly wheel of a Monark 814E (Monark AB, Varberg, Sweden) to detect reflective markers on the fly wheel. The optical sensor was interfaced with an IBM-PC with software from Sports Medicine Industries, Inc. (St. Cloud, MN) to calculate maximal power.

Subjects performed a 5 minute warm-up consisting of pedaling against very light resistance (1 kg) at 60-70 rpm. During the warm-up, subjects were instructed to pedal as fast as they could with no resistance for 5-7 seconds, with the goal to reach 100 rpm. This was performed twice in order to practice increasing the speed of pedaling, a requirement for the test. The two practice sprints were spaced approximately one minute apart. The resistance for the 15-second trial was a relative workload representing 9.5% of whole body lean mass, as determined by the whole body DXA scan. The range of workloads was determined to optimize power output during an in-house pilot study. Subjects were instructed to pedal as fast as possible, and upon exceeding 100 rpm, the

basket was released and the weight engaged on the fly wheel. The 15 second trial began the moment the weight was engaged. At the end of 15 seconds, the weight was released from the fly wheel and the subject continued pedaling at a reduced rate for 3-5 minutes. Measures obtained from the WAPT included absolute (watts) and relative (watts/kg leg lean mass) maximum power. The CV for maximal power on the WAPT in our laboratory in older adults is 4.4%.

Body Composition

A whole body DXA scan (Hologic, Inc., Waltham, MA) was performed to quantify lean and fat mass (independent of bone). The percentage of water in lean tissue was assumed to be 73.2%. Validation of this procedure for body composition analysis has recently been conducted in our laboratory (71). These results demonstrated that DXA is comparable to two and four component body composition models. The CV for body composition analysis in our laboratory, whole body fat and lean mass with DXA is 1.2% and 1.5% for lean and fat mass of specific regions (i.e., legs, trunk, arms).

Blood Sampling and IGF-I and IGFBP-3

All participants underwent an 8 hour fasting blood draw of approximately 10 to 15 ml. Blood samples were collected at baseline, and weeks 12, 24 and 36 of the study. All blood samples sat at room temperature for 30 minutes, and then were centrifuged for 10 minutes at a speed of 1200 x gravity in order to separate the serum. Serum samples were then frozen at -20°C (and stored at -70°C). Serum samples for determining IGF-I and IGFBP-3 were shipped frozen on dry ice, via an overnight shipping service, to the Maine Center for Osteoporosis Research and Education in Bangor, Maine. Samples for serum IGF-I assay were prepared for analysis by acid ethanol cryoprecipitation as per Breier

(4). In this manner, IGF-I is extracted from its binding proteins. Acid ethanol extraction followed by cryoprecipitation (has been found to reduce residual IGFBPs to a level that does not interfere with the competitive antigen-antibody binding in radioimmunoassay (RIA) of IGF-I. The recovery of ratio-labeled 125 IGF-I determined by high performance gel chromatography is 98% for AEC-extracted serum (4). Following acid ethanol cryoprecipitation, the samples were analyzed by radioimmunoassay with IGF-I kits from Nicholas Institute Diagnostic (San Juan Capistrano CA). Samples were extracted and analyzed in duplicate. Intra-assay CVs ranged from 1.03% to 7.1%. The inter-assay coefficient of variation (CV) was 4.65%. Serum IGF-I, determined from acid ethanol cryoprecipitation and radioimmunoassay in this manner, has been dissociated from its binding proteins, and represents total (bound and free) IGF-I levels.

IGFBP-3 were assayed in duplicate using a two site immunoradiometric assay (IRMA) kit (Diagnostic System Laboratories, Inc. Webster TX), as described in Poehlman (51). The intra CVs ranged from 0.10% to 3.28%, and the inter-assay CV was 2.66%. IGFBP-3 analyzed in this manner represents total (bound and whole, bound and truncated, and free) serum IGFBP-3.

Resistance Training Protocols

Participants followed a training program which activated all major muscle groups. The MIM program (a seated machine based program) included 13 exercises: leg extension, leg press, hamstring curls, arm curl, triceps press, chest press, pec deck, shoulder press, side lateral raise, lat pull down, seated row, abdominal crunch, and calf raise. The HIF program (a primarily standing free weight program) consisted of 5 free weight and 7 Hammer Strength resistance exercises: Free weight back squats, deadlifts, biceps curls, sit-ups and triceps extensions and resistance exercise machines (Hammer

Strength), chest press, incline chest press, shoulder press, high lat pull down, leg curl, gripper (wrist strength) and calf raise.

Training sessions were conducted 3 times per week for approximately 75 minutes under close supervision of a personal trainer (1 trainer for every 2 subjects) which ensured proper technique, provide, and decreased risk of injury. Exercise sessions included a 10 minute dynamic warm-up and cool down period which consisted of 5-7 minutes of cardio exercise and 3-5 minutes of total body stretching. Participants were given a 3 week learning period which focused on proper technique, safety and weight room etiquette prior to beginning the loading phase of the study. Minimal resistance was used during this phase. All training sessions were conducted at Gold's Gym of Corvallis, OR. each training session was recorded.

Moderate Intensity Machine Weight Training Group (MIM)

Participants in this group performed 3 sets of 10-13 repetitions for 13 exercises (40-60% of 1 RM; 20-40 seconds rest between stations) for 24 weeks. One repetition maximum (1 RM) was defined as the maximum amount of weight each subject could lift one time with proper technique through a full range of motion for each exercise in the program. Exercise intensities were set at 40% of initial 1 RM for the first 3 weeks. Participants were instructed to execute the concentric phase of each exercise as forcefully as possible and the eccentric phase over 2-3 seconds. After retesting and establishing new individual 1 RM, training loads were adjusted to 50 % of their new 1 RM for 6 weeks. For the remaining 15 weeks, subjects performed at 60% of their newly determined 1 RM values, retesting and load adjustments were conducted every 6 weeks.

High Intensity Free Weight Resistance Training Group (HIF)

Participants in this group performed a staged 25 week high intensity (HIF) training program. The training period consisted of 3 stages: (I) a 12 week training program, (II) a transitional stage (1 week), and (III) a second 12 week training program. Stages I and III were subdivided into 3 phases which differed in the intensity and volume of training. Volume of work was estimated by: sets X repetitions X weight lifted. Phase I consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 10 repetitions (intensity: 70 % of 1 RM) for each exercise, with 1-minute rest between sets and exercises. Phase II consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 5-6 repetitions (intensity: 80 % of 1 RM) for each exercise, with 3-minute rests between sets. Phase III consisted of 1 warm-up set of 10-12 repetitions and 3 working sets of 2-4 repetitions (intensity: 90+ % of 1 RM) for each exercise, with 3-minute rests between sets. During phase III, repetitions of 2-4 were only performed for the large muscle groups: legs, chest, back and shoulders. Smaller muscle groups, biceps, triceps and calves performed 3 sets of 8 repetitions at 70% of 1 RM. This was done to avoid injury to smaller muscle groups. Participants were instructed to execute the concentric phase of each exercise as forcefully as possible and the eccentric phase over 2-3 seconds. During the transition phase (1 week), participants were engaged in non-resistance training fitness activities involving low intensity cardiovascular exercise, stretching and relaxation. This was done to allow the participant to recover both physically and emotionally from the high intensity work loads. New 1 RM values, retesting and load adjustments were conducted every 6 weeks.

Statistical Analysis

The overall design employed a 2 (group) X 2 (gender) x 4 (time) repeated measures (RM) format. Uni- and multivariate repeated measures techniques were conducted to

determine time by group, group by gender and group by time interactions. Analysis of covariance (ANCOVA's) evaluated differences in peak force (N), anaerobic power (W) and body composition. Repeated measures (RM) MANOVA's were employed to analyze the effects of the training on IGF-I and its receptor IGFBP3. For multivariate analyses, univariate follow-up procedures were utilized to determine which dependent variables contributed to significant findings.

Subject numbers were determined from formal power calculations. With a power = 0.8, alpha = 0.05, and an expected difference between groups of 4% increase in lean mass (LM), 25 subjects per group were needed in order to determine significance. Data were entered and analyzed using SPSS 7.5 for Windows (63) for univariate and multivariate analyses, respectively. All data are presented as mean (\pm SD). An alpha level of 0.05 was used for all statistical tests.

Results

Baseline Measures

Participants baseline characteristics across groups and gender (means \pm SD) are summarized in Table 3.1. Multiple t-tests revealed that at baseline all variables were normally distributed and did not differ significantly between the two exercise groups (HIF, MIM). Thus, randomization resulted in a distribution of subject baseline characteristics which were comparable across training groups.

Table 3.1: Baseline Characteristics for Males and Females: Mean \pm SD

Variable	Moderate Intensity Group		High Intensity Group	
	Males = 13	Females = 14	Males = 15	Females = 12
Age: Years	54.92 \pm 3.25	53.14 \pm 3.13	54.40 \pm 3.35	52.75 \pm 2.59
% Body Fat	23.21 \pm 6.23	33.82 \pm 9.26	21.06 \pm 3.27	32.90 \pm 5.84
Lean Mass: kg	67.29 \pm 8.42	42.79 \pm 4.72	65.99 \pm 7.22	45.17 \pm 3.62
Fat Mass: kg	22.55 \pm 6.7	24.86 \pm 11.17	18.24 \pm 8.27	23.99 \pm 7.12
Weight: kg	92.87 \pm 18.81	69.74 \pm 13.88	85.12 \pm 13.38	71.65 \pm 9.31
Leg Flex.: N	332.46 \pm 93.84	165.14 \pm 54.16	08.07 \pm 99.37	182.92 \pm 42.22
Leg Ext.: N	621.77 \pm 159.79	363.93 \pm 96.66	613.27 \pm 166.85	399.92 \pm 78.06
Hip Abd.: N	397.77 \pm 108.78	212.74 \pm 71.37	396.60 \pm 93.81	260.50 \pm 49.17
Chest: N	399.08 \pm 85.05	186.93 \pm 48.83	374.67 \pm 131.11	191.08 \pm 53.17
Back: N	437.62 \pm 83.34	209.14 \pm 37.76	460.80 \pm 138.77	221.25 \pm 50.55
Maxpw: Watts/kg	632.23 \pm 83.76	301.42 \pm 75.11	614.20 \pm 142.01	357.66 \pm 81.22
Post Men: Mos		46.07 \pm 39.14		54.25 \pm 65.17

Attrition and Compliance

Of the 54 participants (28 males and 26 females) recruited, 42 participants completed the 9 month study (24 males and 18 females), representing an attrition of 22 %. Those who left the study did so for personal, work related, or family reasons. No subjects stopped participation because of injury resulting from the training program.

Compliance, defined as the percentage of workouts attended and completed was 93% and 94% for men and women respectfully. No significant differences in compliance was observed between the HIF (92%) and MIM (94%) groups. The training programs were well tolerated by all participants. None of the participants developed any overuse or

other types of injury sufficient enough to warrant any program modifications, withdrawal or interruption in their training schedules.

Strength: Peak Force

The data were analyzed using a 2 X 2 X 4 (Group by Gender by Time) repeated measures (RM) MANOVA. The dependent variables were peak quadriceps force, peak hamstring force, peak hip abduction force, peak pectoral force and peak latissimus dorsi force. The RM MANOVA, showed a significant within component effect for time, [F(18, 20) = 21.12; $p < .001$] and between component effect for gender, [F(6, 32) = 25.95; $p < .001$].

Focusing on the main effects, each dependent variable was significant for time and gender in the follow-up univariate ANOVA's. During the control period a non significant decrease in peak force for all dependent variables was observed. This was followed by an increase in peak force in time period 3 (a training effect) and time period 4 (a continuation of the training effect). Group effect $p > .248$ and group by gender effect $p > .74$ were not significant. Table 3.2 present means and standard deviations for strength (peak force), gender differences in peak force and comparisons between the two training protocols MIM and HIF for baseline, weeks 12, 24 and 36 of the study.

For all of the dependent variables measured (peak quadriceps force, peak hamstring force, peak hip abduction force, peak pectoral force and peak latissimus dorsi force) significant differences $p < .001$ existed between genders across all phases of this study (baseline, weeks 12, 24 and 36) regardless of training (Table 3.3).

Table 3.2: Values for peak force (N) in response to training by gender (means + SD). Groups were collapsed by gender since there were not significant differences in peak force due to training protocols.

Measurement Period	Males: n = 24	Females n = 18
Back: Lat Pull		
Baseline	453.61 ± 125.53	215.11 ± 44.56 *
Week 12	448.74 ± 126.16	211.72 ± 45.23 *
Week 24	561.87 ± 156.58	272.39 ± 64.90 *
Week 36	633.30 ± 156.74	317.83 ± 83.36 *
Chest: Chest Press		
Baseline	402.65 ± 113.10	192.28 ± 50.38 *
Week 12	395.35 ± 110.40	187.39 ± 50.50 *
Week 24	535.47 ± 100.67	271.22 ± 53.46 *
Week 36	569.52 ± 110.35	298.61 ± 54.90 *
Quadriceps: Leg Extension		
Baseline	636.57 ± 162.95	366.78 ± 88.20 *
Week 12	583.61 ± 151.25	344.94 ± 86.32 *
Week 24	697.91 ± 161.47	433.94 ± 79.46 *
Week 36	722.09 ± 159.21	440.50 ± 70.94 *
Hamstrings: Leg Flexion		
Baseline	330.78 ± 98.56	174.28 ± 53.78 *
Week 12	307.87 ± 78.01	162.50 ± 47.17 *
Week 24	368.49 ± 71.35	217.83 ± 35.18 *
Week 36	383.00 ± 72.85	226.33 ± 44.26 *
Hip Abductors: Abduction		
Baseline	400.04 ± 97.46	239.72 ± 70.31 *
Week 12	399.43 ± 82.77	236.78 ± 77.62 *
Week 24	453.13 ± 81.15	306.11 ± 67.75 *
Week 36	480.96 ± 87.13	321.39 ± 57.42 *

* $p < .001$: Significant gender differences

Table 3.3: Values for combined group strength peak force (N) regardless of gender (means \pm SD) based on training protocols.

	Moderate Intensity Group n = 21	High Intensity Group n = 21
Measurement Period		
Back: Lat Pull		
Baseline	339.76 \pm 131.48	358.50 \pm 178.50
Week 12	337.29 \pm 134.34	352.45 \pm 176.05
Week 24	405.91 \pm 162.34 *	465.10 \pm 216.94 *
Week 36	463.38 \pm 184.87 *	527.80 \pm 222.13 *
Chest: Chest Press		
Baseline	309.53 \pm 129.67	311.10 \pm 151.31
Week 12	304.71 \pm 127.23	303.35 \pm 149.45
Week 24	399.24 \pm 149.82 *	440.70 \pm 163.86 *
Week 36	428.95 \pm 147.41 *	473.30 \pm 178.51 *
Quadriceps: Leg Extension		
Baseline	507.28 \pm 197.60	529.50 \pm 187.14
Week 12	462.24 \pm 197.60	496.25 \pm 170.69
Week 24	565.67 \pm 185.10 *	599.20 \pm 190.26 *
Week 36	555.57 \pm 185.10 *	643.50 \pm 200.87 *
Hamstrings: Leg Flexion		
Baseline	265.81 \pm 119.13	258.15 \pm 108.47
Week 12	241.14 \pm 101.25	247.10 \pm 097.26
Week 24	305.38 \pm 101.64 *	299.15 \pm 090.38 *
Week 36	311.19 \pm 097.74 *	317.40 \pm 104.24 *
Hip Abductors: Abduction		
Baseline	319.33 \pm 129.74	340.50 \pm 105.45
Week 12	312.81 \pm 123.65	344.00 \pm 103.76
Week 24	363.90 \pm 113.86 *	414.50 \pm 103.76 *
Week 36	388.53 \pm 117.25 *	434.40 \pm 098.31 *

* $p < .001$: Significant increase in peak strength: An overall training effect

Strength: Peak Force: Gender Differences

Analysis of covariance (ANCOVA) was performed between males and females on each of the five strength (peak force) dependent variables: peak quadriceps force, peak hamstring force, peak hip abduction force, peak pectoral force and peak latissimus dorsi. The covariates consisted of mean baseline values for lean mass and peak force. Results,

(Table 3.4) revealed significant gender differences at baseline and week 12 (control period) for quadriceps force, $[F(1,53) = 51.66; p < .001]$, hamstring force, $[F(1,53) = 52.41; p < .001]$ hip abduction force, $[F(1,53) = 49.56; p < .001]$, pectoral force, $[F(1,53) = 79.46; p < .001]$ and latissimus dorsi force, $[F(1,53) = 100.18; p < .001]$. However, at the conclusion of the training intervention no significant gender differences existed for any of the five dependent variables, quadriceps force, $[F(1,41) = .74; p > .39]$, hamstring force, $[F(1,41) = 3.14; p > .09]$ hip abduction force, $[F(1,53) = .30; p > .59]$, pectoral force, $[F(1,41) = 1.59; p > .22]$ and latissimus dorsi force, $[F(1,41) = .451; p > .51]$.

Strength: Percentage Change Over Time

A 2 X 2 X 4 (Group by Gender by Time) repeated measures (RM) MANOVA was conducted on the dependent variables for percent change. Percent change was defined as the percentage of strength change observed from baseline to week 12 (control period), week 12 to week 24, and week 24 to week 36. The dependent variables consisted of: peak quadriceps force, peak hamstring force, peak hip abduction force, peak pectoral force and peak latissimus dorsi force. For strength, there was a significant within component effect for Time, Wilks' Lambda = $[F(15, 23) = 12.22; p < .001]$.

In the follow-up univariate analysis ANOVA's, a slight decrease in percentage change in peak force was observed in the control period for quadriceps force, hamstring force, pectoral force, and latissimus dorsi force. This was followed by an increase in peak force in time period 3 (a training effect) and time period 4 (a continuation of the training effect).

There was no statistical significance for group ($p > .40$, gender ($p > .43$) or group by gender interaction ($p > .31$). Thus, regardless of training protocol or gender, participants overall strength significantly improved over the 24 week training period.

Mean strength percent change values and standard deviations for all dependent variables comparing training protocols MIM vs. HIF for Time 1, Time 2 and Time 3 (Table 3.5).

Table 3.4: Values for absolute peak force (N) at baseline and after 6-months of training by gender. Training groups were collapsed since no significant differences were observed between training protocols. Post-test values were covaried for initial values of lean mass and peak force.

Variable	Males n = 24	Females n = 18
Back: Lat Pull		
Baseline	416.53 \pm 79.79	250.82 \pm -85.92 *
Post	231.91 \pm -12.01	212.45 \pm -11.12
Chest: Chest Press		
Baseline	334.43 \pm .43.36	244.38 \pm -46.69 *
Post	470.28 \pm 21.92	419.92 \pm -29.43
Quadriceps: Leg Extension		
Baseline	534.51 \pm 31.23	469.61 \pm -33.65 *
Post	621.87 \pm 24.21	565.61 \pm -32.15
Hamstrings: Leg Flexion		
Baseline	283.83 \pm 35.87	210.71 \pm -37.25 *
Post	343.33 \pm 29.72	277.02 \pm -37.98
Hip Abductors: Abduction		
Baseline	379.14 \pm 60.04	254.30 \pm -64.66 *
Post	419.26 \pm 9.20	398.04 \pm -12.27
Anaerobic Power		
Baseline	513.71 \pm 30.95	448.10 \pm -34.67 +
Post	662.41 \pm 49.55	546.79 \pm -66.06 **

* $p < .001$: Significant gender difference at baseline

** $p < .001$: Significant gender difference at conclusion of training

+ $p < .001$: No Significant gender difference at baseline

Table 3.5: Percent change in peak force (\pm SD) increase over time from resistance training. Since no group by gender interactions existed, both the MIM and HIF groups were collapsed to include both genders.

	Moderate Intensity Group n = 21	High Intensity Group n = 21
Variable		
Back: Lat Pull		
Control Period	-01.11 \pm 03.94	-01.69 \pm 03.40
Intervention Wk. 1-12	22.58 \pm 24.61 *	34.95 \pm 25.06 *
Intervention Wk. 12-24	15.79 \pm 22.54 *	16.15 \pm 14.48 *
Chest: Chest Press		
Control Period	-00.57 \pm 05.01	-03.93 \pm 02.33
Intervention Wk. 1-12	31.89 \pm 27.89 *	64.03 \pm 54.59 *
Intervention Wk. 12-24	13.78 \pm 16.51 *	8.045 \pm 14.38 *
Quadriceps: Leg Ext		
Control Period	-06.38 \pm 19.97	-04.46 \pm 18.05
Intervention Wk. 1-12	30.43 \pm 35.13 *	23.82 \pm 23.43 *
Intervention Wk. 12-24	00.27 \pm 22.59 *	8.87 \pm 16.46 *
Hamstrings: Leg Flexion		
Control Period	-04.37 \pm 25.45	-00.89 \pm 24.73
Intervention Wk. 1-12	42.75 \pm 47.61 *	28.18 \pm 27.94 *
Intervention Wk. 12-24	00.34 \pm 16.69 *	06.12 \pm 14.31 *
Hip Abductors: Abduct.		
Control Period	04.93 \pm 41.80	03.28 \pm 24.06
Intervention Wk. 1-12	24.17 \pm 31.78 *	25.64 \pm 26.96 *
Intervention Wk. 12-24	08.90 \pm 20.86 *	05.04 \pm 09.16 *

* $p < .001$:

Muscular Power

In a 2 X 2 X 4 (Group by Gender by Time) repeated measures ANOVA of muscular power (unadjusted for lean mass) revealed a significant between subjects component interaction for time, $[F(3\ 36) = 57.61; p < .001]$, and gender $[F(3\ 36) = 57.61; p < .001]$. However, there were no significant differences between groups (Tables 3.6 & 3.7). These findings reveal that over time both groups (MIM & HIF) significantly

increased their maximum power regardless of gender or training protocol. Secondly, a significant difference existed in muscular power between genders.

Analysis of covariance (ANCOVA) was performed between males and females for muscular power. The covariates consisted of mean baseline values for lean mass and maximal muscular power. Results, revealed that gender differences at baseline and week 12 (control period) approached significance [$F(1,52) = 2.95$; $p < .09$] (Table 3.6). However, at the conclusion of the training intervention significant gender differences existed for muscular power, [$F(1,41) = 40.96$; $p < .001$]. Although both males and females significantly improved their lean mass, the results of these data do not support the contention that power differences are a function of body size. Our findings demonstrate that significant differences in muscular power still exist between genders after accounting for differences in lean mass using a covariance analysis in this population.

Table 3.6: Differences in maximum anaerobic power (Watts/kg) between genders regardless of training group: Gender Differences. (means \pm SD)

Measurement Period	Males n = 24	Females n = 18
Baseline	643.37 \pm 104.88 *	333.66 \pm 83.22 *
Week 12	679.33 \pm 133.19 *	334.77 \pm 63.61 *
Week 24	685.71 \pm 080.19 *	367.28 \pm 44.68 *
Week 36	771.33 \pm 097.32 *	434.89 \pm 57.02 *

* $p < .001$ indicates significant gender differences

Table 3.7: Group Comparisons maximum anaerobic power (Watts/kg) (means \pm SD). In order to determine if a training effect existed between the two training protocols, both the MIM and HIF groups were collapsed to include both genders.

	Moderate Intensity Group n = 21	High Intensity Group n = 21
Measurement Period		
Baseline	496.95 \pm 186.83	524.33 \pm 180.46
Week 12	531.33 \pm 203.45	532.00 \pm 208.57
Week 24	532.43 \pm 174.44	566.05 \pm 173.82
Week 36	598.57 \pm 198.73	627.14 \pm 188.73
No significant differences between groups		

Body Composition

A 2 X 2 X 3 (Group by Gender by Time) repeated measures MANOVA was performed on four dependent variables: Lean mass (LM), fat mass (FM), percent body fat (% BF) and body weight (kg). There was a significant between component effect for gender, $[F(4, 35) = 68.89; p < .001]$, and time, $[F(8, 31) = 16.36; p < .001]$. Univariate follow-up analyses revealed that significant differences existed between genders for LM ($p < .001$), FM ($p < .001$) and Percent body Fat ($p < .001$). Examination of the means showed that males had greater amounts of LM than females as well as lower amounts of FM and percent body fat. There was also a significant increase in lean mass for all participants regardless of gender or training program over time ($p < .001$). Paired samples t-tests were performed comparing baseline and post intervention body weight. This analysis revealed no significant change in total body weight for group or gender. Gender and group means and standard deviations are presented in Tables 3.8 & 3.9.

Table 3.8: Lean mass (kg) and body fat (kg) comparisons between males and females during the control period (baseline to week 12) and post 6-month intervention training (means \pm SD).

Variable	Time	Males n = 24	Females n = 18
Lean Mass kg	Baseline	67.20 \pm 7.41	43.83 \pm 4.43 *
	Week 12	67.30 \pm 7.07	43.98 \pm 4.39 *
	Week 36	68.97 \pm 7.51	45.61 \pm 4.55 *
Fat Mass: kg	Baseline	21.65 \pm 8.06	23.91 \pm 8.81 *
	Week 12	22.24 \pm 7.83	23.94 \pm 9.31 *
	Week 36	20.62 \pm 8.10	22.49 \pm 7.65 *
Body Weight:kg	Baseline	92.86 \pm 14.54	71.64 \pm 09.87
	Week 12	92.55 \pm 14.33	69.39 \pm 13.27
	Week 36	92.59 \pm 14.95	70.41 \pm 11.25

* $p < .001$.

Table 3.9: The effects of moderate (MIM) and high intensity (HIF) resistance training on lean mass (kg) for both males and females during the control period (baseline to week 12) and post 6-month intervention training (means \pm SD).

Measurement Period	MIM Females n = 9	HIF Females n = 9	MIM Males n = 12	HIF Males n = 12
Baseline	42.50 \pm 4.70	43.83 \pm 4.42	68.41 \pm 7.71	65.99 \pm 7.22
Week 12	43.06 \pm 4.65	44.90 \pm 4.17	68.59 \pm 7.50	66.01 \pm 6.70
Week 36	44.38 \pm 4.96 *	46.83 \pm 4.10 *	70.20 \pm 7.89 *	68.97 \pm 7.51 *

* $p < .05$ Significant increase in lean mass over time: An overall training effect

Block Food Frequency Questionnaire

Participants completed a computer-scored 100-item Block Food Frequency Questionnaire designed for use by the National Cancer Institute. Information regarding

average daily calcium intake, caloric, protein, fat, carbohydrate consumption, and grams of protein per kilograms of body weight were obtained using this tool (Table. 3.10).

Table 3.10: Average daily calcium intake, caloric, protein, fat, carbohydrate consumption, and grams of protein per kilograms of body weight.

	Males n = 24	Females n = 18
Calcium (mg/d)	914.69 \pm 329.0	889.75 \pm 299.95
Protein: g/kg	1.27 \pm 0.46	1.28 \pm 0.34
Calories (kcal/d)	1829.89 \pm 633.21	1269.06 \pm 323.59
Carbohydrates (g)	216.86 \pm 83.75	107.00 \pm 38.39
Fat (g)	60.09 \pm 29.91	40.25 \pm 16.20

Mean Training Volumes

Total mean training volumes of work among both exercise groups and genders were calculated by multiplying the amount of weight lifted by the number sets and repetitions performed for each exercise, and then summed for each workout. These were then averaged over intervals of six week periods. Since it is difficult to compare volumes of work performed on machine based exercises to free weight exercises due to a very poor correlation between how much someone can lift on a weight machine exercise versus a free weight exercise, no comparisons were made between the two group means.

Insulin Like Growth Factor I (IGF-I)

At baseline IGF-I and IGF-I/IGFBP3, but not IGFBP3 levels were positively ($p < .05$) associated with fat mass (kg), but not with LM, body weight (kg), age, or measures of maximal muscular power (W), and mean strength values (N).

IGF-I and IGFBP3 were analyzed using a 2 X 2 X 4 (group by gender by time) repeated measures MANOVA. In multivariate analysis, no significant findings were revealed for main effects, nor were there significant univariate group by gender or group by time interactions. Thus, neither the HIF or MIM training protocols produced a training effect on any of the dependent variables tested.

No group, gender or training effects existed, thus only total means for each variable over the 4 assessment periods are reported in Table 3.11.

Table 3.11: Insulin-Like Growth Factor I (IGF-I), Receptor for Insulin-Like Growth Factor I (IGFBP3): ng/mL and IGFBP3/IGF-I Ratio (means \pm SD). Since no group, gender or training effects existed, total means \pm SD for each variable over the 4 assessment periods are reported.

Measurement Period	IGF-I:ng/mL	IGFBP3: ng/mL	IGFBP3/IGF-I
Baseline	159.54 + 44.84	2755.03 + 592.19	.0061 + .0015
Week 12	163.46 + 44.98	2760.49 + 503.61	.0058 + .0014
Week 24	167.18 + 50.41	2685.67 + 543.58	.0063 + .0016
Week 36	158.51 + 52.98	2686.13 + 564.04	.0059 + .0017

Stability of IGF-I

The stability of IGF-I over the 9-month intervention period was evaluated by two-tailed correlation and revealed that pre and post-training basal serum concentrations were significantly correlated, thus remained stable over the 9-month period ($r = .87$, $p < .01$, Figure 3.1). These results were similar to those recently reported by Vitiello ⁽²⁰⁾ who found that IGF-I values for endurance trained older men and women remained extremely stable over time (6.5 month), ($r = .85$ $p < .001$). Since IGF-I has important autocrine and paracrine activity in muscle, an increase in serum levels of IGF-I may not be needed to produce an anabolic effect within skeletal muscle tissue.

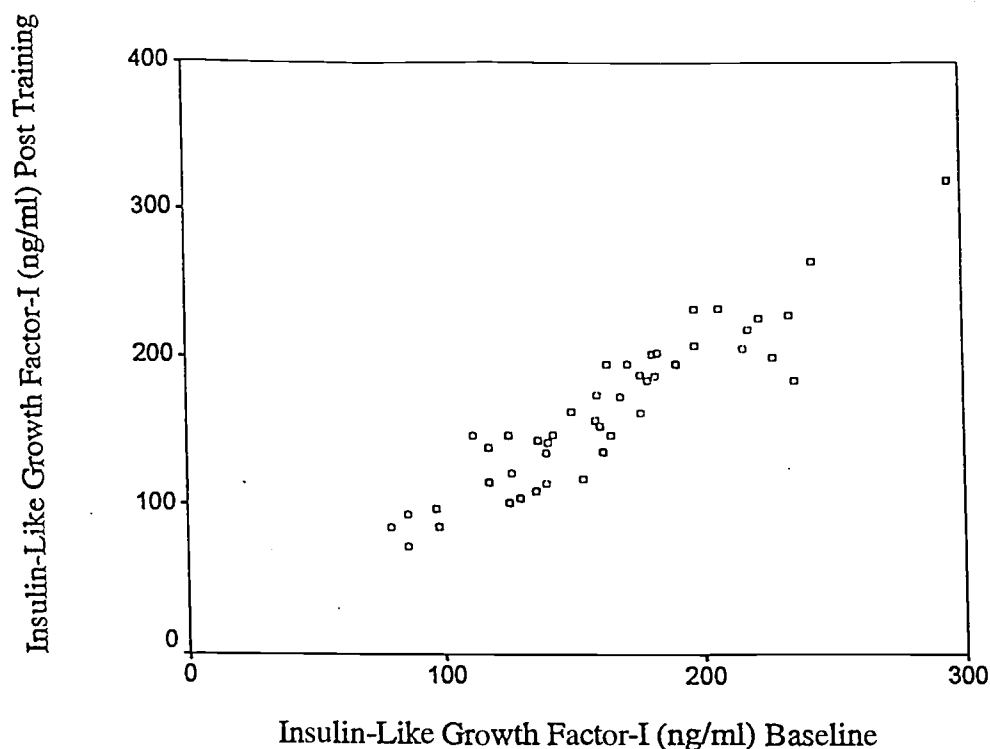


Figure 3.1. Scatter plot of baseline versus post-training insulin-like growth factor-I (IGF-I) levels (ng/ml) for HIF (n=21) and MIM (n=21) training groups (both genders are included).

Discussion

We report significant gains in strength, maximum power and lean mass in older adults regardless of gender as a result of 6 months of resistance training. While the changes were not statistically significant between groups, there was a trend across all muscle variables for the high intensity participants to have greater values than the moderate intensity group. Despite increases in the muscle system, neither weight training program significantly increased basal levels of IGF-I. To our knowledge, this is the first study to train older adults to these types of free weight multijoint exercises and high intensities for this length of time.

Improvements in lean mass were statistically significant for both training groups regardless of gender or training protocols. These results did not support our hypothesis that high intensity training would produce significantly greater muscle changes. Males and females in the high intensity group had a mean increase in lean mass of 2.96 and 3.0 kilograms respectively, whereas, males and females in the moderate intensity groups increased their lean mass (LM) 1.80 and 1.88 kilograms respectively. Although increases in LM were higher for males and females in the high intensity group, these differences were not statistically different and most likely due to a type II error. In order to achieve a statistically significant difference between groups with a power of 0.80, the number of participants required in each group would have to be 25 males and females in each group. Thus, with higher numbers, it appears that our hypothesis would be supported. Regardless of initial gender differences or training protocols, percent change in strength was similar in men and women. We were surprised, yet encouraged by this finding which suggests that not only can older women (50-60 years) significantly increase their strength by weight training three days per week, but that they can also achieve similar gains in strength as do males. Although not statistically significant, all muscle groups except the hamstrings showed more improvement in the high intensity group than the moderate group, likely due to a type II error.

Participants in the current study subject were not supplemented with protein or other nutrients in order to produce gains in lean mass. Although we did not expect the participants to make any changes to their diets during the study period, the limited dietary data obtained at the conclusion of the study revealed that both men (1.27 g/kg) and women (1.28 g/kg) exceeded the RDA recommendations for protein of 0.8 g/kg/day (42). Thus, we concluded that all participants received ample protein to produce increases in lean mass in response to resistance training.

Several limitations of this investigation should be noted. Inclusion of both genders in this intervention without a sufficient increase in subject numbers limits the statistical power, a problem often associated with exercise intervention studies. In order to achieve a statistical power of 0.80, the number of participants required in each group would have to be 25 males and females respectively. However, even with our limited sample size of 9 females and 12 males in each of the HIF and MIM groups our mean power was 0.59. Second, participants were their own controls during the first 12 weeks prior to training and while we did not observe changes during this period, a randomized control group followed during the 6-month intervention would have strengthened the design. Third, since IGF's are secreted proteins which accumulate and circulate within the extracellular space, it is probable that a significant amount of mixing occurs between IGF's produced by skeletal muscle and other tissues (e.g. liver, heart, brain, bone) (26). Thus, local changes in skeletal muscle IGF-I may be masked by this method of measurement. In addition to this, very few studies have reported IGF peptide measurements because of the difficulty involved in extracting free peptides from IGFBP's (26). Finally, since the exercises were different between groups (free weights vs. machines) we cannot make definitive conclusions regarding intensities or volumes of total work performed. In order to carefully compare total volumes of work and intensities, choice of exercise stations should be controlled between groups, while intensities are manipulated.

Only recently have investigators (7,45,54) begun to train older adults with resistance exercises using high intensities $\geq 80\%$ of 1 RM. However, all of these weight training intervention have used machine based seated exercise protocols (7,45,54,). Previous studies involving older adults (7,16,18,45,53,54) have used moderate to high intensities (60 to 80% of 1 RM). Using multijoint free weight exercise we report similar changes in strength as compared to other studies involving older adults. In our study we found average lower extremity strength increases in the female participants ranging from 8 to

103%, whereas, increases in upper extremity strength ranged from 16 to 156%. In the men, upper extremity strength increases ranged from 22 to 156%, while increases in lower extremity strength ranged from 11 to 160%. Charette (7) investigated muscle hypertrophy response to resistance training in very old women (mean age 69 years) Training three times per week for 12 weeks, focusing on leg and hip regions using 60-75% of 1 RM, the investigators reported lower extremity strength increases ranging from 28 to 115% and an increase in type II fiber hypertrophy of 28%. Nelson (45), evaluated the effects of high intensity strength training (80 % of 1 RM) on multiple risk factors for osteoporotic fractures in a 12-month randomized intervention trial of 40 postmenopausal women aged 50 to 70 years. This study used a machine based training protocol (two times/week, three sets of eight reps) of five exercises focusing on the hips, knees, back and abdominal muscle groups. The investigators reported strength increases ranging from 35 to 76% over baseline. after 12 months of training. In each of these reports, isokinetic dynamometry, or an alternative neutral measuring device was used to assess peak force (strength). Rather, strength assessments were performed by the 1 RM (repetition maximum) method using the same exercises as those used during training, thus, each training session was a practice session for the measurement test to be used. More trials would provide greater learning opportunity which would increase coordination, which in turn may significantly increase strength gains in novice lifters for a particular exercise.

In contrast to Pyka (54), we did not observe a plateau in strength gain. They reported a gain in strength after 3 months of training, but this gain plateaued, resulting in little or no change in strength between months 3 and 12 of training. In the current study, both training groups demonstrated significant strength improvements across the six month intervention period. Although the participants in Pykas study (mean age of 68 years) were older than in our study (mean age of 52 years), it is unclear as to why strength

plateaued. A possible explanation could be a lack of some form variation in the exercise program in order to obtain optimal gains in strength and lean mass.

It has been suggested that lower limb power is a major determinant of functional ability in older adults (15,16,19). In younger adults, high intensity resistance training has been reported to produce superior gains in maximal muscular power when assessed by cycle ergometry (lower limb power) (46). Our findings support these data in older adults, as training at moderate to high intensities significantly increased maximal muscular power of the lower limbs. However, our data do not we support the notion that high intensity training produces superior gains in maximal power in older adults. Both training intensities produced similar increases in maximal power. Participants in the high intensity training group made improvements of 30% and 18% for females and males respectively, whereas, women and men in the moderate intensity training group improved their maximal muscular power by 21% and 12% respectively. These differences were not statistically significant, likely due to a type II error.

Studies which have evaluated younger adults using the Wingate 30-second protocols have reported no significant differences between genders after accounting for differences in lean mass (3,36,44). These studies have used the ratio method to normalize data between genders. However, use of the ratio variable could be misleading since the rationale for using the ratio method is to control or eliminate the influence of lean mass. This method has been criticized because it does not take into account the non zero y intercept and therefore, does not appropriately remove the effect of lean mass (22,52,67). As a result, the ratio method may introduce bias which may lead to spurious conclusions when making comparisons between individuals who vary in body composition and size. The results of this study do not support the contention that power differences are a function of body size. Our findings demonstrate that significant differences in maximal power still exist between genders after accounting for differences in lean mass using a

covariance analysis. Thus other factors must also account for differences in maximal power.

Our data supports previous findings of significant gender differences in absolute strength in the muscles of both the upper and lower limbs (27,34,35). Currently, most of the evidence suggests that a women's absolute upper and lower body strength is significantly less than a male's. A large discrepancy exists when comparing absolute strength ranging anywhere from as low as 52% of males to a high of 78% (8,11,15, 40,41,58,73). These varying differences may be due in part to the large number of exercise movements possible for both upper and lower body parts. Also, a variety of assessment methods have been used throughout the literature to test subject strength ranging from 1 RM to isokinetic peak torque/force. As a result, it is difficult to conclude specifically just how much of an absolute strength differences exists between genders. In our study we found that men had 52% upper body and 63% lower body strength greater than women at the conclusion of the intervention study.

Although the primary reason for strength differences between genders is unclear, researchers have suggested that the greater absolute strength found in men is due primarily to their larger muscle fibers (27,39,58) given the high correlation between the cross sectional area of the muscle fiber and muscle strength. In older adults, Fontera (19) while expressing strength per kilogram of muscle mass and fat free mass completely reduced or eliminated any significant gender differences. Wilmore (73) on the other hand reported that when leg strength is expressed relative to lean body mass, women's leg strength was 106% of men. Whereas, Hoffman (28) reported that after controlling for body size in younger adults, lower body strength differences disappeared, however, upper body strength of males was still greater, concluding that differences in strength between genders must be due to something other than body size.

We examined gender related differences in peak force and maximal power using ANCOVA, a regression based approach, which has been demonstrated to be a more appropriate statistical technique to adjust physiological data than the ratio method (22,52,67). At baseline, significant gender upper and lower body strength differences existed for both absolute and relative values. However, after adjusting for differences in LM and initial peak force values using ANCOVA, no differences in peak force were found at the conclusion of the weight training intervention. These results suggest that women (aged 50 -60 years) who participate in a weight training exercise program can eliminate gender strength differences provided LM is controlled for. Our findings support the contention that absolute strength differences between genders are a function of body size. Limited data exist on the relationship between weight training and the GH/IGF-I axis. Pyka (55) has reported that participation in a longitudinal weight training intervention study produced no changes in basal IGF-I and IGFBP3. Given that Pyka (55) used a relatively lower intensity machine based program and found a plateau in strength after 3 months of training, we compared a weight training intervention of high intensity (mostly free weight exercises) to a moderate intensity training (machine based) program. However, our findings are similar to those of Pyka (55) (older adults) and Hakkinen (24,25) who studied young elite power lifters over a period of two years of training and observed that basal levels of growth hormone did not increase as a result of training. These investigators concluded that alterations in resting levels of growth hormone are not a plausible mechanism of chronic adaptations due to intense resistance training even though increases in lean mass and strength were observed. The findings of our study corroborate the findings of Pyka and Hakkinen.

Although Pyka (53) reported that in older adults (72 ± 0.8 yr.) acute changes in IGF-I after weight training did not occur. Kraemer (31,32) has demonstrated that weight training protocols using high total volumes of work (approximately 60,000J) with a rest

period of 1 minute between sets, produced significant increases in GH secretion. Given the findings of Kraemer, it is possible that the participants in the Pyka (53) study were not exposed to a high enough training volume to elicit an acute GH response to the exercise protocol. Also, Pyka only allowed a 30 second rest period between sets, which may not have allowed her participants (72 ± 0.8 yr.) enough recovery time.

It may be likely that the changes in body composition and increases in strength from weight training are the result of acute GH secretion over time. Based on Kraemer's findings it would appear that the acute increase response of GH to weight training may be due to an increase in the metabolic energy needs of the exerciser due to the high volume of weight used and the limited amount of rest (1 min.) between sets and exercises. Thus, it is possible that this type of training which is often referred to the hypertrophied stage brings about an increased secretion in GH/IGF-I leading to an increase in LM and a reduction in body fat levels. Therefore, the increase in circulating levels of GH/IGF-I that occur from an acute bout of weight training may account for changes in body composition associated with weight training overtime. Thus, increases in basal levels of GH and IGF-I may not necessarily be required to produce increases in LM and strength.

There have been recent reports of the expression of IGF-I mRNA in skeletal muscle. Gosteli-Peter (22) showed that stimulation of IGF-I has been shown to be mediated by an increased transcription of the IGF-I gene, resulting in an increase of IGF-I mRNA in rat skeletal muscle. Also, even though serum IGF-I levels decline with age in both humans and rats, Hamilton (26) has demonstrated that these declines are not sufficient enough to decrease the concentration of IGF mRNA in rat skeletal muscle. Taaffe (66) reported that IGF-I mRNA within the skeletal muscle of healthy older men (65-82 yr.) does not increase following 10 weeks of daily GH administration (0.02 mg/kg, s.c.). Welle and Thorton (72) reported similar results in older men and women (64-74 yr.) after injections of GH (0.03 mg.kg, s.c.). Although Taaffe (66) and Welle and Thorton (72) analyzed

total IGF-I mRNA from biopsy samples within 24 hours and 2 and 10 hours of final GH injection respectively, one can not rule out the possibility that increased IGF-I mRNA within the skeletal muscles occurs at earlier or later time points after GH injection or during acute increases in IGF-I due to weight training.

Recently, Vitiello (70) has reported that in a group of healthy endurance trained males (mean age 66.9 yr.) and females (mean age 67.1 yr.) no relationship existed between age and IGF-I over a 7 month training period. This lack of an age/IGF-I correlation was also observed by us in our study. In fact the basal IGF-I concentrations of our participants (mean age 53.6 yr.) remained quite stable over the 9-month intervention period. Vitiello (70) suggests that although IGF-I levels decline continually across the life span, the anabolic status of healthy older adults, as indexed by IGF-I, remain relatively stable across moderate periods of time (i.e. 9 months).

Estrogen therapy for postmenopausal women is routinely prescribed to prevent the development of osteoporosis. A number of cross-sectional studies have shown a significantly greater decline in bone mass following menopause (47,56). However, very little is known about the effects of estrogen replacement on lean mass and strength in older women. Seely (60) reported no beneficial effects associated with estrogen use on muscular strength in elderly women. While, others (6) have reported that postmenopausal women taking estrogen replacement therapy have greater hand grip strength than those not taking estrogen. Whereas, Phillips (49) findings suggest that estrogen therapy in elderly women may help preserve muscle strength. As a result we can not overlook the effects estrogen may have on muscle strength or in our case the lack of estrogen in our estrogen depleted postmenopausal subjects.

We have shown that resistance training provides an efficacious, safe method of increasing strength, power, and lean mass in healthy older adults. Both free weight and machine weight training programs of moderate to high intensities were effective in

promoting muscular adaptations. Further, it is clear that older adults can tolerate regular participation in a resistance training program which uses high intensities without incurring injury. These patterns of adaptation may have important implications for individuals in this age group. As long as older adults continue to exercise on a regular basis, consistent physical activity may help offset many of the declines often associated with aging and allow them to continue to take part in strenuous activities often associated with daily living well into their senior years.

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Chapter IV

CONCLUSIONS

Progressive declines in muscular strength are one of the most predictable consequences of growing old. However, still puzzling to scientists regarding this phenomenon are the contributions of biological aging, cumulative diseases, poor nutrition and inactivity towards this inevitable decline. Presently, there is a limited amount of research available which focuses on long term strength development in older adult populations.

The present study was designed to compare the effects of two different weight training protocols over a 6-month weight training intervention period on bone mineral density, lean mass, strength, anaerobic power and circulating levels of GH and IGF-I in older adults (50-60 years of age). A moderate intensity seated machine weight resistance training program (MIM) was compared to a high intensity training free weight program (HIF) using exercises such as standing back squats and deadlifts. It was hypothesized that the HIF training would result in significantly greater improvements in hip and spine bone mineral density and circulating levels of IGF-I, lean mass, strength and anaerobic power.

Twenty-eight healthy older men (54.58 ± 3.20 yr., mean \pm SD) and twenty-six healthy older women (52.83 ± 3.26 yr., mean \pm SD) were randomized to either a 3d/wk, 6-month moderate intensity (60% of 1 RM) or high intensity (70-90% of 1 RM) resistance training protocol. The HIF exercise program consisted of two 12 week cycles of upper and lower extremity free weight exercises (intensity: 70-90% of 1 RM) while the MIM program used variable resistance machine exercises (intensity: 60% of 1 RM). Before and after training, bone mass and body composition were assessed by dual-energy

x-ray absorptiometry, muscle strength by isokinetic dynamometry, muscular power by modified Wingate Anaerobic Power Test, and IGF-I by fasting blood sampling.

High intensity free weight training resulted in a significant gain in lumbar spine bone mineral density (BMD) in men of (+1.9%) while maintaining whole body BMD (+.18 %) but not in women. Males in the moderate intensity (MIM) group observed no change in lumbar spine BMD, however, a significant decline in whole body BMD (-0.21%) occurred. At the hip, we observed a significant difference in change in bone mineral density between the femoral neck and trochanter for women and men from high intensity training. Femoral neck BMD decreased by -1.76% while trochanter BMD increased by 1.24% in men and by -1.78% and 2% in the women. Also, there was a trend for hip BMD to shift in the same direction among women in the moderate intensity group, suggesting a dose response. Neither the high or moderate intensity training protocols produced any changes in circulating IGF-I or IGFBP3.

We report similar changes in strength as compared to other studies involving older adults. In the present study, lower extremity strength increased in the female participants ranging from 8 to 103%, whereas, increases in upper extremity strength ranged from 16 to 156%. In the men, upper extremity strength increases ranged from 22 to 156%, while increases in lower extremity strength ranged from 11 to 160%.

Improvements in lean mass were statistically significant for both training groups regardless of gender or training protocols. Males and females in the HIF group had a mean increase in lean mass of 2.96 and 3.0 kilograms respectively, whereas, males and females in the MIM groups increased their LM 1.80 and 1.88 kilograms respectively. Although increases in LM were higher for males and females in the HIF group, these differences were not statistically different. In order to achieve a statistically significant difference between groups with a power of 0.80, the number of participants required in each group would have to be 25 males and females in each group. A possible explanation

as to why the HIF group did not produce even greater increases in LM may be a reflection of the amount of time this group spent training with low training volumes during the strength and power cycles. It is assumed that muscle hypertrophy occurs during periods of high volume and moderate intensity (60-70% of 1 RM). Thus, during periods of training involving low volumes of work and high intensities (80-90% of 1 RM), the primary goal is to produce increases in strength and power (stone) and not lean mass. Volume appears to be an important variable regarding the principle of overload. Large training volumes provide greater overloads to the muscular structure, thus leading to greater increases in lean mass (stone). Therefore, it is possible that during the strength and power cycles, the volume of work was not sufficient enough to stimulate muscle hypertrophy.

Regardless of initial gender differences or training protocols, we report that when strength gains (peak force) were expressed as a percentage of improvement over the training period, both men and women improved equally. This is encouraging, especially since many women use resistance training as their primary mode of exercise. Not only can older women (50-60 years) significantly increase their strength by weight training three days per week, they can also make similar gains in strength as males when expressed as a percentage of improvement.

However, despite these increases in lean mass, muscular strength, anaerobic power and bone mineral density of the lumbar spine (HIF group only), neither weight training program significantly increased circulating levels of IGF-I. Further, the changes in strength, maximal muscular power, and body composition were similar in both the high intensity (HIF) and moderate intensity (MIM) groups.

Results from cross-sectional research are helpful in identifying possible connections between factors in which subsequent longitudinal evaluation may establish a causal relationship. Presently, several cross-sectional studies have shown that strength

positively correlates with a high bone mineral density (BMD). While resistance training may provide one possible method of decreasing the risk of fracture resulting from falls by increasing BMD, it may also play an important role in maintaining postural control and therefore, reducing the incidence of falling in older adults. Most of the weight training studies reviewed have produced modest gains in BMD (primarily at the lumbar spine), however, all of the studies have resulted in large and significant increases in muscular strength

Recent studies have selectively compared athletes of different types of sports to less active or inactive controls in order to determine the sport-specific effect of exercise on bone mass. When attempting to interpret the findings of studies which involve highly trained athletes, the reader must take into consideration a number of confounding factors. Pocock et al., (1987) suggests that genetics can play an important role in determining if one is to become a world class power athlete. In fact, genetics can account for up to 80% of the variability in bone mineral density (Pocock et al., 1987). Elite power athletes may be drawn to a power sport because of a favorable genetic disposition. This type of athlete also has a significantly greater amount of fat free mass than endurance trained athletes and untrained individuals. Findings reported by Lindsay et al., (1992) and Smith and Rutherford, (1993) support the notion that heavier individuals tend to have greater bone mineral density, making it difficult to compare this population to an age matched sedentary population. Other confounding factors to consider include the use of ergogenic aids by this population.

The interpretation of these results from cross-sectional studies must take into consideration what effects the use of anabolic steroids, training volumes and body weight may have on bone development in conjunction with intense heavy resistance training.

Chapter V

RECOMMENDATIONS FOR FURTHER STUDY

1. Replication of the current study is warranted utilizing a larger sample size involving only one gender. Also, greater attention should focus on the shift in bone mineral density between the femoral neck and trochanter.
2. It is recommended that a control group be used in order to perform comparisons between the intervention group and a non exercising control group.
3. It would be of interest to have two training groups doing the same exercises but training with significantly different intensity levels, while focusing only on the back squat and deadlift exercises to determine their effects on BMD.
4. It would be of benefit to add a group which combines squats and deadlifts with high-impact training (e.g., jumping with weighted vests) in order to determine the effects of this combination on hip BMD.
5. If a replication study were to be performed, when assessing peak force by isokinetic dynamometry, it would be advisable to ensure that the training velocities match the testing velocity employed.
6. Use multiple baseline measures of BMD (e.g., example 3 months apart) to allow the researcher to account for remodeling drifts which may confound the baseline measure if only taken once.

7. Include a detraining phase, allowing researchers to determine if significant increases in bone are permanent or transitory, when the osteogenic training stimulus is removed. The extent of a detraining response in individuals with normal or below normal bone mass has not been examined.

8. Calculate and report all training volumes, given that large training volumes provide greater overloads to the muscular structure. Few researchers equate volume for their training protocols, as a result, it is not clear which weight training programs are superior. Often it is not clear if the differences reported among studies are due to the increased volume, intensity, or structure of the model used.

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APPENDICES

APPENDIX A

IRB PROPOSAL, CONSENT FORMS AND PHYSICIAN CLEARANCE FORM

Application For Approval Of The OSU Human Subjects Board

Significance of the Project

The insulin-like growth factors (IGF-I, IGF-II) are anabolic peptides produced in response to growth hormone (GH). The IGF's play an important regulatory role in numerous processes, including cell proliferation, glucose transport, protein and lipid synthesis. The IGF's also mediate the effects of GH on bone, cartilage, skeletal muscle. Circulating IGF-I is derived from local synthesis of GH from liver, bone, and muscle on other sites. The function of circulating IGF-I is not yet certain, although environmental factors such as exercise and nutrition may affect the levels of IGF-I, and therefore, may play an important role in determining body composition and bone mass. IGF-I is transported to and from target tissues by insulin-like growth factor binding proteins (IGFBP's), six of which can be found in human serum. The IGFBP's also act to enhance or inhibit the biological action of IGF-I. Growth Hormone (GH), has been shown to be responsible for skeletal elongation and somatic growth primarily by inducing hepatic synthesis of somatomedin of IGF-I and II, which act directly on tissues to stimulate a variety of growth-promoting and metabolic effects via an interaction with type I IGF receptors. It is still unclear whether the decline in IGF-I associated with aging is a result of the effects of aging or a reflection of the sedentary life style often associated with aging populations.

The primary hormonal regulator of IGF-I is GH; therefore, serum IGF-I levels reflect GH status. A reduction in the secretion of growth hormone (GH) and a significant decline in plasma IGF-I with advancing age has been linked to many of the physiological declines associated with aging. Some of these factors include, an increase in body fat, a decrease in muscle mass (lean body mass), a decrease in muscular strength and osteopenia in older populations. In this study, the role of resistance training exercise (intensity, volume and duration) on the control of serum IGF-I, II and IGFBP-3 will be investigated. The regulation of the IGF's could help explain changes in body composition seen with various exercise regimens. Also, through data on the IGF regulatory system, insight may be gained as to physiologic role of GH during exercise. This might prove important when designing preventative measures to enhance body composition and/or bone mass in this population (e.g., middle aged adults). Understanding of the IGF regulatory system may prove useful in defining the effects of long-term exercise in middle aged adults.

Methods

Experimental Protocol

Subjects

The subjects participating in this study will be volunteers from Benton County Oregon. Forty previously untrained middle aged males and females (50-60 years) will be recruited to participate in a 36 week resistance training study. In order to be accepted as a subject for this study participants must either be sedentary or moderately active and not have participated in a resistance training program during the past year. All subjects will be subjected to a screening process which will include: a). completion of a health questionnaire and b). written permission from their family physician allowing them to

participate in the training study. Following the screening process, all subjects' will participate as controls for a 12 week period. Immediately following this period, subjects will be randomly assigned to either the periodization group or the circuit training group. All subjects agreeing to participate will have the study verbally explained to them. Following the explanation each subject will sign the informed consent form.

Methods

Strength Testing

Muscle strength will be tested at baseline and weeks 12, 24 and 36 of the training study, using the Kin-Com 500H isokinetic machine (Chattecx, Corp.). Peak contraction force, using gravity correction, will be measured in the following muscle groups: trunk, hip, adductors and abductors, knee extensors, and elbow flexors. Isokinetic testing means that the speed of the movement is constant (either 150/sec, trunk, or 300/sec, all other exercises) throughout the range of movement. As a result, force produced by the muscles while performing a given movement is used as a measure of strength, rather than the amount of weight lifted. Previous studies at this institution using the Kin-Com have shown intraclass correlation's for these measures to range from .92 to .98, in populations of 18 to 75 year old men and women.

Basal Metabolic Rate

All subjects will report to the OSU laboratory after a minimum 8 hour fast. After resting quietly in the lab for 90 minutes, oxygen consumption (VO_2) and carbon dioxide production (VCO_2) will be measured using a Sensor Medics Metabolic Cart. The instrument will be calibrated against standardized gases. Three measurements will be made during a 90 minute period, each taking approximately 12 minutes. After two minutes of equilibration, respiratory gases and ventilation will be analyzed continuously and averaged over three minute intervals. Basal metabolic rate will be calculated using the following equation: $\text{BMR (in kcal/day)} = 1.44 (3.796 \text{ VO}_2 [\text{in ml/min.}] + 1.214 \text{ VCO}_2 [\text{in ml/min.}])$

Bone Mineral and Body Composition

Bone mineral will be measured on all subjects at baseline, weeks 12, 24 and 36 of the training study. A Hologic QDR 1000/W dual-energy x-ray absorptiometer will be used to measure bone area (in cm^2), bone mineral content (BMC, in g/cm^2) of the lumbar spine (L2-L4), proximal femur (especially the femoral neck), and the whole body. Bone-free lean mass and percent body fat will be assessed at baseline and weeks 12, 24 and 36 of the training study from the whole body scan. The Hologic QDR 1000/W uses quantitative digital radiography to accurately quantify BMD, in terms of the amount of calcium hydroxypatite relative to bone area (the major component of bone mineral). The resulting image is digitized and displayed on the counter top terminal. The x-ray absorption of the bone is calculated via constant comparison against a known reference or calibration wheel. Radiation doses to the subject are very low: 2.0mR to 5.0 mR for the regional scans less than 1.5 mR per whole body scan. The Hologic Densitometer in the Bone Research Laboratory at Oregon State University has been approved for radiation safety, and x-ray scatter is minimal, undetectable at greater than one meter from the scanning arm. Scans take 13 to 15 minutes for the whole body and 6 to 8 minutes for each regional scan. The measurement precision error for all scans is less than 1.0%.

Subjects and Experimental Protocol

Blood Sampling and IGF-I, IGF-II and IGFBP-3.

All subjects will undergo a fasting blood draw of approximately 10 to 15 ml (2 Tablespoons) at baseline and weeks 12, 24 and 36 of the study. The blood will be drawn by trained personnel, taking all the necessary precautions when dealing with blood. The blood draw will take place in the early morning after a minimum 8 hour fast. The blood sample will sit at room temperature for 30 minutes, and then will be centrifuged for 10 minutes at a speed of 1200 x gravity in order to separate the serum. The serum sample will then be frozen at -20°C (and stored at -70°C) until it can be shipped to Dr. Clifford Rosen at the Maine Center for Osteoporosis Research and Education for analysis. The serum concentrations samples will be analyzed for IGF-I and II and IGFBP-3 levels. Ratios of IGF-I and IGF-II to IGFBP-3 will be constructed as a potential marker of bioavailability.

Control Group

All subjects recruited for this study ($n=40$) will serve as their own controls during the first 12 weeks of the study. Subjects will be asked not to participate in any type of resistance training or fitness related activities. Following this 12 week control period, subjects will be randomly assigned to either the periodization group ($n=20$) or the circuit training group ($n=20$).

Resistance Training Protocols

All subjects participating in this study will follow a training program consisting of 13 different resistance exercises involving all major muscle groups. The exercises will be done using Hammer Strength training equipment. All training sessions will be conducted under close supervision to ensure proper technique, provide positive motivation and decrease the risk of injury. Training sessions will be conducted three times per week and each workout session will last approximately 75 minutes. All exercise sessions will include with a 10 minute warm-up and cool down period consisting of Stair Master and Stretching.

Circuit Resistance Training Group

Subjects assigned to this group ($n=20$) will perform an training protocol consisting of 3 sets of 12-15 repetitions for 13 exercises (40-60% of 1 RM; 30-60 second rest between stations) for 24 weeks. Subjects will be asked to execute the concentric phase of each exercise over 2 seconds and the eccentric phase over 3 seconds. For each workout, subjects will record the number of sets, repetitions, weight lifted and any difficulties they experienced. Training loads will be adjusted after each 1 RM is determined. Exercise intensities will initially be set at 40% of individual 1RM for the first 3 weeks. After retesting and establishing new individual 1 RM, training loads will be adjusted to 50 % of their new 1 RM for 6 weeks. For the remaining 15 weeks, subjects will exercise at 60% of their 1 RM values, with retesting and load adjustments every 3 weeks.

Periodization (high intensity) Resistance Training Group

Subjects assigned to this group (n=20) will be involved in a modified periodization training program. The overall training period (referred to as the macrocycle) will consist of 25 weeks. The 25 week training cycle will be divided into three phases: 1). preparatory (12 weeks), 2). transition (1 week) and 3). preparatory (12 weeks). Stone and O'Bryant (1987) divide the preparatory period into three phases that differ in the intensity and volume of training. Phase 1 (hypertrophy) will consist of 1 warm-up set of 10-12 repetitions and 3 working sets of 10-12 repetitions (intensity: 70 % of 1 RM) for each exercise, with 1-minute rest between sets and exercises. Phase 11 (Strength) will consist of 1 warm-up set of 10-12 repetitions and 3 working sets of 5-6 repetitions (intensity: 80 % of 1 RM) for each exercise, with 3-minute rests between sets. Phase 111 (power) will consist of 1 warm-up set of 10-12 Repetitions and 3 working sets of 2-4 repetitions (intensity: 90+ % of 1 RM) for each exercise, with 3-minute rests between sets. During the power phase, repetitions of 2-4 will only be done for the large muscle groups: legs, chest, back and shoulders. Smaller muscle groups, biceps, triceps and calves will perform reps of 10-12 at 70% of 1 RM. Subjects will be asked to execute the concentric phase of each exercise over 2 seconds and the eccentric phase over 3 seconds. For each workout, subjects will record the number of sets, repetitions, weight lifted and any difficulties they experienced. Training loads will be adjusted after each phase is completed. The transition phase (1 week) will consist of non resistance training fitness activities. Following the transition phase, subjects will repeat preparatory phases 1, 11 and 111 previously described. Retesting of each individual's 1 RM and load adjustments will be done every 3 weeks.

Benefits and/or Risks to Subjects

As with any blood draw, there is the possibility of risk of infection. All necessary precautions will be taken to keep the laboratory environment as sterile as possible. Individuals who have ever had hepatitis B or C, who have tested positive for HIV or any AIDS virus, or individuals who have AIDS should not donate body fluids or tissues. Individuals at risk for getting and spreading any AIDS virus also should not donate body fluids or tissue and should not participate in this investigation. This includes males who has had sex with another man since 1977, even one time, individuals who have shared a needle, to inject drugs or medication, individuals who have taken clotting factor concentrates for a bleeding disorder such as hemophilia, individuals who have ever had a positive test for any AIDS virus or hepatitis B or C or any AIDS antibody, individuals who have had sex with any individual described above and individuals who have had sex with a male or female prostitute since 1977.

The technique used to assess bone mineral content gives an accurate measure of bone density with a very low exposure to radiation. This radiation dose is considered safe to administer on several occasions to men and women in my age group provided that the women are not pregnant. The external beam is the only ionizing radiation to which the subject will be exposed. No injections are given and there are no known hazards from radiation at such a low level. The calculated radiation exposure with this procedure per scan is approximately one-tenth of a standard chest X-ray or the equivalent of the background radiation one would receive flying across the country. Therefore, risk from participation in this study is negligible.

Risk from participating in either the circuit training program or Periodization exercise program consisting of 13 different resistance exercises involving all major muscle groups is minimal and will be under the guidance and supervision of highly trained personal. All training sessions will be conducted under close supervision to ensure proper technique, provide positive motivation and decrease the risk of injury. Training sessions will be conducted three times per week and each workout session will last approximately 75 minutes. All exercise sessions will begin and end with a 10 minute warm-up and cool down period consisting of Stair Master or stationary bike or treadmill and Stretching.

Risk associated with the calculation of Basal metabolic rate are minimal. Oxygen consumption (VO_2) and carbon dioxide production (VCO_2) will be measured using a Sensor Medics Metabolic Cart. Three measurements will be made during a 90 minute period, each taking approximately 12 minutes. This procedure involves the subject breathing into the Sensor Medics Metabolic Cart through a mouth piece at rest. All necessary precautions will be taken to keep the laboratory environment and equipment as sterile as possible.

Benefits

The average cost of bone density assessment is \$250-\$300 and a body composition analysis is \$30. I have been informed that this evaluation is not diagnostic and that any questions regarding my bone mineral density report should be directed to my physician. The benefits of my participation include contributing to the scientific study of some of the factors affecting bone mineral density. A six month membership at the fitness center to be used for this study normally cost \$150.00 and that personal trainer's generally charge \$25.00 per workout session.

Each subject will also experience the benefits of increased muscular strength and endurance, increases flexibility, a decrease in body fat, an increase in lean body mass, better overall health and a better understanding of how his or body works.

Informed Consent

Attached is a copy of the subject's informed consent for this research proposal. All subjects will receive an oral explanation of the significance and procedures of this research study prior to signing the consent form. Confidentiality and subject anonymity will be maintained at all times. At no time will the subjects name appear on record forms or in computer files in reference to the study. A code number will be used to identify each subjects data and all records shall be kept using the code number. Only the researchers will have knowledge of the subjects name. Blood samples will be identified only with a code number, and no one in the laboratory performing the analyses will have knowledge of the subjects name. The results of this study will be published in scientific literature and that any data that may be published in such a journal will not reveal the subjects identity. The code number will be destroyed once the study is over and the investigators are finished with the data, so that the subjects anonymity is assured.

OREGON STATE UNIVERSITY BONE RESEARCH LABORATORY

Informed Consent

It has been explained to me that the purpose of this research training study which will last 36 weeks is to measure my blood serum levels of insulin-like growth factors (e.g., IGF-I & II) and insulin-like growth factor binding proteins (IGFBP-3). IGF-I and II and the IGFBP-3 are involved in the regulation of growth hormone, which affects many tissue, including bone and skeletal muscle. Exercise and nutritional habits are two factors which may affect the levels of IGF and hence, influence my body composition and bone mass. Results of the findings may prove useful in understanding the IGF regulatory system, and how it interacts with long-term resistance training exercise in middle aged males and females to affect the skeletal system.

I understand that I will be asked to give one small blood sample on four different occasions, baseline, weeks 12, 24 and 36 of the training study. I will arrive in the laboratory in a fasted state (i.e., not having eaten in at least 8 hours). Trained and qualified personnel will draw a fasting blood draw of approximately 10 to 15 ml (2 Tablespoons) sample from my forearm vein. Discomfort from the needle stick will be minimal. The blood will be spun and the separated serum will be immediately frozen until it is sent to the laboratory for analysis.

It has been explained to me that the risk of infection from this blood draw is minimal. Individuals who have ever had hepatitis B or C, who have tested positive for HIV or any AIDS virus, or individuals who have AIDS should not donate body fluids or tissues. Individuals at risk for getting and spreading any AIDS virus also should not donate body fluids or tissue and should not participate in this investigation. You are at risk if:

- you are a man who has had sex with another man since 1977, even one time
- you have shared a needle, even one time, to inject drugs or medication
- you have taken clotting factor concentrates for a bleeding disorder such as hemophilia
- you have ever had a positive test for any AIDS virus or hepatitis B or C or any AIDS antibody
- you have had sex with any individual described above
- you have had sex with a male or female prostitute since 1977.

I understand that I will be tested for bone mineral content on three different occasions. I have been informed that the scan requires that I lie quietly on a table for 8 minutes for the spine and hip evaluations and 15 minutes for whole body mineral determination.

This technique used to assess bone mineral content gives an accurate measure of bone density with a very low exposure to radiation. It has been explained that this radiation dose is considered safe to administer on several occasions to men and women in my age group provided that the women are not pregnant. The external beam is the only ionizing radiation to which I will be exposed. No injections are given and there are no known hazards from radiation at such a low level. The calculated radiation exposure with this procedure per scan is approximately one-tenth of a standard chest X-ray or the equivalent of the background radiation one would receive flying across the country. Therefore, risk from participation in this study is negligible. I further understand that I will experience no discomfort from the procedures.

I understand that I will be muscle strength tested on four different occasions, baseline, weeks 12, 24 and 36 of the training study. An isokinetic machine will measure the strength in my back, hips, legs and arms. This testing will require that I push against a lever arm, designed to move at a constant speed throughout the exercise, with my legs, arms or back, with as much force as I can. The effort that I make to move the equipment will reflect the strength of the muscles that are being tested. I understand that I will receive a thorough warm up period before each muscle group is tested, including stretches recommended by the investigator. Each exercise will consist of 5 trials of maximal effort, with 30 seconds rest in between trials. Each exercise will be followed by a 5 minute rest period.

I understand that I will participate in either a circuit training program or periodization exercise program consisting of 13 different resistance exercises involving all major muscle groups. All exercises will be done on Hammer Strength gym equipment. All training sessions will be conducted under close supervision to ensure proper technique, provide positive motivation and decrease the risk of injury. Training sessions will be conducted three times per week and each workout session will last approximately 75 minutes. All exercise sessions will begin and end with a 10 minute warm-up and cool down period consisting of Stair Master and Stretching. I further understand that I may experience some discomfort as a result of participating in either of the resistance training exercise programs. I also understand that as my body begins to adapt to these exercise prescriptions, the discomforts I will experience will gradually diminish.

I understand that I will serve as part of the control group. During the first 12 weeks of this study, I will be asked not to participate in any type of resistance training or fitness related activities. I understand that this is so that the data collected from me during the 24 week training portion of the study can be compared to my control period (weeks 1-12).

I understand that muscular power will be assessed by the Wingate Anaerobic Power Test (WAPT) for Older Adults (Bar-Or, 1992). Muscular power will be measured at baseline, weeks 12, 24 and 36 of the training study. The WAPT will be performed on a bicycle ergometer and is designed to assess power of the lower extremities. A Monark 814E cycle ergometer equipped with pedals with plastic toe straps, an adjustable seat, handle bars and a weight basket will be used for this study. Weights of one kilogram, one-half kilogram and one-tenth kilogram will be placed in the weight basket to apply a breaking force to the fly wheel. The weight will apply force to the fly wheel (1.615 meters, distance) during the test. I understand that I will be asked to pedal at a prescribed intensity at maximal effort for approximately 15 seconds. I will be asked to perform a warm up session prior to the test.

The Benefits of my participation in this research study include contributing to the scientific study of how various exercise regimens alter body composition and bone mass through the regulatory influence of the insulin-like growth factor system. Understanding these mechanisms and interrelationships may prove useful in defining exercise effects (acute and chronic) on many different middle aged male and female physiological system, throughout the life-span. I understand that these measures of bone mineral density will give me an accurate indication of my bone density and body composition. This information will be valuable to me, to my doctor, to John Maddalozzo and to Dr. Snow-Harter for the determination of bone mineral density in middle aged males and females as a result of participating in a resistance training exercise program. Further, this evaluation is offered at no charge. The average cost of bone density assessment is \$250-\$300 and a

body composition analysis is \$30. I have been informed that this evaluation is not diagnostic and that any questions regarding my bone mineral density report should be directed to my physician. The benefits of my participation include contributing to the scientific study of some of the factors affecting bone mineral density.

I also understand that the use of a fitness center for six months normally cost \$150.00 and that personal trainer's generally charge \$25.00 per workout session.

I understand that I will be required to keep records of every workout I participate in. I must keep accurate records of my repetitions, sets and weight lifted during each workout.

I understand that my confidentiality will be maintained at all times. At no time will my name appear on record forms or in computer files in reference to the study. A code number will be used to identify my data and all records shall be kept using the code number. Only the researchers will have knowledge of my name. My blood samples will be identified only with my code number, and no one in the laboratory performing the analyses will have knowledge of my name. I have been informed that the results of this study may be published in scientific literature and that any data that may be published in such a journal will not reveal my identity. The code number will be destroyed once the study is over and the investigators are finished with my data, so that my anonymity is assured.

I understand that in order to receive the benefits of exercising at the fitness center and the benefits that go along with my membership, I must commit to the training protocol and attend all of my training sessions on a regular basis.

I have been completely informed and understand the nature and purpose of this research. I understand that Oregon State University does not provide a research subject with compensation or medical treatment in the event a subject is injured or becomes sick as a result of participation in the research project. I understand that my participation in this study is completely voluntary and I may withdraw from the study at any time, or decide not to partake in the blood draw, without prejudice or loss of the benefits to which my participation entitles me. If I have any questions about the research or my rights, I understand that Dr. Christine Snow-Harter (Principal Investigator) at 737-6788 and/or John Maddalozzo (Student Investigator) at 737-6802 will be happy to answer them.

I have read the foregoing and agree to participate.

Subjects

Signature _____ Date _____

Address _____

Phone Number _____

Investigator's:

Signature _____ Date _____

PERSONAL PHYSICIAN CLEARANCE

My patient _____ has notified me about his/her interest in participating in the study titled Effects of Resistance Training on IGF-I and II in Older Adults. I have read the consent form which outlines the test procedures and training program. I understand that only healthy men and women, with no known cardiovascular, respiratory or metabolic disease will be recruited for this study. To the best of my knowledge, the aforementioned patient is a good candidate for this research study. I understand that if I have any questions about the testing or training procedures, I may contact Dr. Christine Snow at 737 - 6788 or Gianni Maddalozzo at 737-6802.

Physician Signature

Date

Address

Phone

APPENDIX B
HEALTH HISTORY FORM

OREGON STATE UNIVERSITY BONE RESEARCH LABORATORY

Heath and Physical Activity History

Last name	First	Middle	Date of birth
Address, Street			Home phone
City	State		Occupation and/or sports team
_____pounds Weight	_____ft _____ inches Height		Male Female (circle one)

Please list your present medications and dosages here (incl. birth control pills, vitamins):

**

PAST HISTORY (Check if yes)

Has you ever had:

High cholesterol	_____
Heart murmur	_____
Heart trouble	_____
Lung disease	_____
Epilepsy	_____
Back injury	_____
High Blood Pressure	_____
Operations	_____
Other musculoskeletal injury	_____
Rheumatic fever	_____
Disease of the arteries	_____
Varicose Veins	_____

FAMILY HISTORY (Check if yes)

Have your grandparents, parents or siblings ever had:

Diabetes	_____
Heart attacks	_____
High blood pressure	_____
High cholesterol	_____
Congenital heart disease	_____
Heart operations	_____
Other	_____

Date of last medical exam _____

Physician: _____

If yes to any of the above, please explain:

**

PRESENT SYMPTOMS REVIEW (Check if yes)

Have you recently had:

Chest pain	Other _____
Shortness of breath	_____
Heart palpitations	_____
Cough on exertion	_____

Coughing up blood _____
 Back pain _____
 Painful, stiff or swollen joints _____

HEALTH HABITS

<u>Smoking</u>	YES	NO	
Do you smoke	_____	_____	
Cigarettes	_____		How many/day? _____ How many
years? _____			
Cigar	_____		How many/day? _____ How many
years? _____			
Pipe	_____		Times/day? _____ How many
years? _____			

If you have quit smoking, when did you quit? _____ How many years did you smoke? _____

Alcohol Consumption

Do you drink alcohol daily? Y N (circle one) If yes, how many drinks/week? _____

Consumption of calcium-rich daily products

How many 8 oz glasses of milk do you drink per day? _____ per week? _____
 How many servings of cheese (1 oz) do you eat per day? _____ per week? _____
 How many servings of yogurt (1 cup) do you eat per week? _____

Body Weight

What was your weight 1 month ago? _____ 2 months ago? _____

Cola Beverages

How many cola beverages do you drink daily? _____
 How many years have you been drinking cola beverages on a regular basis? _____

PHYSICAL ACTIVITY

List all sports or activities in which you have participated during the past year: (Examples include aerobics, tennis, golf, softball, dance, football, hiking, swimming, biking, weight training, etc.)

<u>ACTIVITY</u>	<u>AVG # HRS/WK</u>	<u>AVG # MO/YR</u>
------------------------	----------------------------	---------------------------

List your involvement in sports activities for the past 2 years prior to above:

ACTIVITY	# HRS/WK	# MO/YR.	#YRS
----------	----------	----------	------

OSTEOPOROSIS RISK FACTORS

Please circle true or false for the following. If you think a statement may apply to you but are not sure, place a question mark (?) by that statement.

- | | | | |
|-----|------|-------|--|
| 1. | true | false | I have been treated with cortisone or similar drugs. |
| 2. | true | false | I have a history of the blood tumor, leukemia. |
| 3. | true | false | I have lactase deficiency (inability to digest milk). |
| 4. | true | false | I take anabolic steroids now or have in the past. |
| 5. | true | false | I avoid milk and other dairy products. |
| 6. | true | false | I usually eat meat at least twice a day. |
| 7. | true | false | On average, I usually drink 2 or more soft drinks daily. |
| 8. | true | false | I am physically inactive most of the time. |
| 9. | true | false | I have been treated with chemotherapy for cancer. |
| 10. | true | false | I have received an organ transplant (kidney, etc.). |
| 11. | true | false | I have had trouble with anorexia nervosa or bulimia. |
| 12. | true | false | I have a history of rheumatoid arthritis. |
| 13. | true | false | I have a close relative with osteoporosis. |
| 14. | true | false | I have a history of an overactive thyroid gland. |
| 15. | true | false | I have a history of an overactive parathyroid gland. |
| 16. | true | false | I have a history of alcoholism. |
| 17. | true | false | I have a history of chronic liver disease. |
| 18. | true | false | I have a history of multiple myeloma. |
| 19. | true | false | I have a history of stomach ulcers. |
| 20. | true | false | I have about 3 or more alcoholic beverages daily. |
| 21. | true | false | Some of my stomach has been surgically removed. |
| 22. | true | false | I drink more than 2 cups of coffee or tea daily. |
| 23. | true | false | I follow a vegetarian diet and have so for years. |
| 24. | true | false | I am of Caucasian (white race) ancestry. |
| 25. | true | false | I am of Asian (Oriental race) ancestry. |
| 26. | true | false | I am of Mexican-American or Hispanic ancestry. |
| 27. | true | false | I am of African-American (black) ancestry. |
| 28. | true | false | I have lost more than 1 inch in height. |
| 29. | true | false | I have taken thyroid hormone pills. |
| 30. | true | false | I took phenobarbitol or dilantin for over one year. |
| 31. | true | false | I use Maalox or Mylanta antacids frequently. |
| 32. | true | false | I have taken furosamide (Lasix) for over one year. |
| 33. | true | false | I have been treated with lithium for over one year. |
| 34. | true | false | I take or have taken cyclosporin A (Sandimmune). |

(WOMEN ONLY)

- | | | | |
|-----|------|-------|--|
| 35. | true | false | I lost my period for a year or more before it came back. |
|-----|------|-------|--|

36. true false I have had irregular menstrual periods.
37. true false My menstrual period did not begin until after age 16.
38. true false I have a medical history of endometriosis.
39. true false I lost my periods when I was exercising heavily.
40. true false I have had both ovaries surgically removed.
41. true false I have breast fed a baby for one month or more.
42. true false I take tamoxifen as treatment for breast cancer.
43. true false I went through menopause before age 50.
44. true false I have gone through menopause (change of life).
45. true false I have received estrogen treatment after menopause.

If you take estrogen, for how many years? _____

How many children have you given birth to? _____

What was the date of your last menstrual period? _____

Signature

Date

APPENDIX C
REVIEW OF LITERATURE

The process of aging is often associated with a decrease in lean body mass and an increase in adipose tissue (Cohn et al., 1976). Age related declines in muscle mass may be related to changes in glucose metabolism, and may lead to an increased risk of diabetes and coronary heart disease. It is also related to reductions in basal metabolic rate, which can lead to obesity. The rate at which skeletal muscle can adapt to vigorous and chronic exercise decreases with age. However, adaptations such as increases in muscular strength and skeletal muscle hypertrophy are still attainable. In general, as one ages one can expect declines in muscular strength varying from 20% in early adulthood to 40% by age 70 (Steen, 1988) and a 40% reduction in muscle area from age 20 - 70 years (Rodgers and Evens, 1993).

Progressive declines in muscular strength are one of the most predictable consequences of growing old. However, still puzzling to scientists regarding this phenomenon are the contributions of biological aging, cumulative diseases, poor nutrition and inactivity towards this inevitable decline. It is well documented that inactivity leads to declines in maximal and dynamic strength as well as maximal speed and power. These declines are well documented in elderly populations (Rodgers and Evans, 1993). Declines in strength associated with aging and inactivity are primarily related to a loss of muscle mass with aging. Loss of muscle mass is due to significant declines in type I and II fibers (type II showing preferential atrophy), decreases in the size of the muscle cells, decreases in muscle oxidative enzyme activity and muscle capillarization by approximately 25% and a decreasing ability to recruit muscle fibers and a loss of muscle fibers as a result of a depressed regenerative capabilities and injury (Rodgers and Evens, 1993).

Recent findings have demonstrated that participation in a regular resistance training program can increase muscular strength in older adults through improved motor recruitment of muscle fiber motor units and fiber hypertrophy. Although the rate at which

skeletal muscle can adapt to vigorous and chronic exercise decreases with age, adaptations such as increases in muscular strength and skeletal muscle hypertrophy are still attainable (Charette et al., 1991; Pyka et al., 1994). Until recently, it was hypothesized that the strength gains made by older adults reflected improvements in neurological factors rather than actual muscle fiber hypertrophy (Moritani and deVries, 1979; Moritani and deVries, 1980). Moritani and de Vries, (1979) have suggested that the strength gains of the elderly are due primarily to better neural recruitment whereas, strength gains in younger adults are due to muscle hypertrophy.

Frontera et al., (1988), measured the isokenetic strength of the elbow and knee flexors and extensors of 200 healthy men and women aged 45 - 78 years. The investigators reported that the strength of all four muscle groups measured were significantly lower in older subjects when compared to younger adults. However, when muscle strength was corrected for muscle mass, significant differences were reduced or eliminated for both men and women. The investigators concluded that loss of muscle mass is a major factor in the age related decline in muscle strength rather than a deterioration in the contractile capacities of the muscle.

One of the most frequently cited studies involving older adults and strength development was conducted by Fiatarone, et al., (1990). In this study, the investigators trained 10 institutionalized men and women in their 90's. The 8 week training protocol involved concentric and eccentric isotonic progressive resistance training on a leg extension machine to measure and train quadriceps strength. The subjects trained three times per week and performed three sets of 8 repetitions with each leg. Subjects trained using 80% of their 1 RM and rested 1 to 2 minutes between sets and exercises. At the conclusion of the 8 week training study, the investigators reported lower extremity strength increases ranging from 61 to 374% over baseline. The investigators concluded

that even very old individuals can safely engage in a resistance training program to improve muscular strength.

Presently, there is a limited amount of research available which focuses on long term strength development in older adult populations. Charette, et al., (1991) investigated muscle hypertrophy response to resistance training in older women . In this study the investigators trained 27 healthy females (mean age 69 years). The 12 week training protocol involved a total of seven exercises focusing on the leg and hip regions. The subjects trained three times per week and performed three sets of eight repetitions for each exercise. Subjects trained using 60, 65 and 75% of their 1 RM resting one to two minutes between sets and exercises. At the conclusion of the 12 week training study, the investigators reported lower extremity strength increases ranging from 28 to 115% over baseline. They also reported an increase in type II fiber hypertrophy of 27.6%. The investigators concluded that a progressive weight training program can increase strength in this population and that skeletal muscle in older women can retain the capacity to undergo hypertrophy. Nelson, et al., (1994), evaluated the effects of high intensity strength training on multiple risk factors for osteoporotic fractures in a randomized intervention trial of 40 postmenopausal women aged 50 to 70 years. This one year training study employed a high intensity strength training protocol utilizing five exercises which focused on the hips, knees, back and abdominal muscle groups. Subjects exercised two times per week (80% of 1 RM) with three sets of eight reps per exercise. At the conclusion of the one year training study, the investigators reported strength increases ranging from 35 to 76% over baseline. The investigators concluded that the increases in functional strength was due to training, since the control group exhibited a decrease in performance.

Pyka et al, (1994) investigated muscle strength and fiber adaptations to a year long resistance training program in elderly men and women. In this study, the investigators

trained eight males and 17 females (mean age 68.2 years) for one year. The training program consisted 12 weight training exercises involving both upper and lower body extremities. Subjects trained three times per week and performed three sets of 8 repetitions for each exercise at an intensity of 75% of their 1 RM. The investigators reported strength increases of 30% to the hip extensors and 97% to the hip flexors. They also reported an increase in type I fiber hypertrophy of 29% after 15 weeks and 58% after 30 weeks. Type II showed no changes at the conclusion of 15 weeks; however, at the conclusion week 30, type II fibers had hypertrophied 67%. Strength gains were reported to have increased rapidly over the first 12 weeks then plateaued for the duration of the study. The investigators concluded that a prolonged moderate to high intensity resistance training program can be carried out by older adults and that significant increases in strength can be achieved and that strength increases are accompanied by hypertrophy of both type I and II fibers.

The potential for a reversal of the declines in strength associated with aging and inactivity remains relatively unexplored. Despite evidence from studies involving younger adult populations indicating that muscle hypertrophy and strength gains will only occur in response to loads greater than 60% of maximum, only recently have investigators begun to apply these principles to training studies involving older adults (Charette et al., 1991; Pyka et al., 1994 and Nelson et al., 1994).

The number of repetitions utilized in training also appears to play a critical role in the development of muscular strength in older adults. Low to moderate intensity in resistance training programs have produced little or no increases in the strength of older adults Aniansson and Gustafsson (1991), Larsson (1982) and Hagberg et al., (1989).

Resistance Training Protocols

Resistance loads utilized in weight training studies have used a variety of protocols. These protocols have ranged from very light (e.g., 15 repetition maximum (RM) or less) to very heavy (e.g., less than 10RM). Heavy resistance training have use loads ranging from 1 to 10RM and are used extensively to increase strength and power. Lighter protocols, which produce increases in strength, are typically used to increase muscle hypertrophy and endurance (Fleck and Kramer, 1987). In more advanced resistance training protocols, periodization techniques are used to vary the loads and volumes (sets x repetitions x loads) of exercises over the course of training (Kramer, 1992). It is believed that these types of training protocols which vary the intensities, loads, rest periods and repetitions will produce significantly greater strength gains than traditional methods of resistance training.

Periodization is a popular training regime among Eastern European weight lifters (Matveyev, 1981). The underlying concept of periodization is based on Hans Selye's general adaptation syndrome (GAS). Selye proposes that there are three phases of the body's adaptation when the human body is confronted with a stress stimulus (in this case resistance training). The three phases consist a). the alarm stage, b). the resistance stage and c). the exhaustion stage. According to Selye's GAS theory, during the alarm stage the body deals with the initial stress stimuli. Symptoms may include a drop in performance due to muscle soreness and stiffness. During the resistance stage, the body begins to make adaptations. These include biochemical (endocrine), structural (skeletal tissue), mechanical (technique) and psychological changes. The goal of periodization is to avoid Selye's final stage, exhaustion. If the total stress is too great, desired adaptations are no longer possible, the body is exhausted due to over training.

Periodization consists of five phases in each training cycle. Periodization is characterized by initial training sessions involving large volumes of exercise using low

intensity levels gradually progressing to a peaking phase utilizing small volumes of exercise with high intensity levels. Stone et al., (1981) compared one cycle of periodization to a traditional training program involving three sets of six repetitions. High school football players were randomly assigned to either a periodization program or a traditional program. The subjects trained three times per weeks for a total of six weeks. The subjects performed the same resistance exercises (squats, leg curls, bench press, behind-neck press and cleans). At the conclusion of the six week training study, the investigators reported that the periodization training method demonstrated significantly greater strength gains than the traditionally trained groups in both squatting ability and squat per kilogram of body weight. Leg power during vertical jumping was significantly greater in the periodization group, however, both groups reported significant increases in vertical jumping ability. Although neither group changed significantly in body weight, only the periodization group exhibited an increase in lean body mass and a significant decrease in percent body fat.

Resistance Training and Bone Mineral Density

Osteoporosis is characterized by a significant loss of both the mineral and collagen matrices of bone. As a result, bones become more susceptible to fractures as we grow older (Riggs et al., 1983). An important consideration is whether or not physical exercise training can enhance bone mineral density and strengthen bone tissue. Existing research has consistently shown that individuals who engage in life long habitual physical activity have greater bone density at certain skeletal sites than less active individuals of the same sex and age (Block et al. 1989). Features of bone strength are developed and maintained by forces applied to bone during daily activity and exercise. Functional loading through exercise appears to exerts a positive influence on bone mass (Block et al., 1989). Bone mass has been shown to continuously increase, within genetic limitations, to a level which

will protect the skeletal tissue from the external stresses which are applied to it (Riegger, 1990). Therefore, the extent of bones ability to adapt may be relevant to the intensity of the stimulus being applied to bone (ACSM Position Statement, 1995). Whalen and Carter, (1988) have proposed a theoretical model which suggests that the magnitude of the load may play a more important role in generating an adaptive response in bone mass than the number of cycles completed.

Recently, osteoporosis in men has been recognized as an important health issue (Orwoll and Klein 1995). No longer is osteoporosis considered a disease which only affects women. The development of adult bone mass is dependent upon changes in both density and size, however, sexual differences are considered to be the primary factors associated with differences in body mass size (Orwoll and Klein 1995).

It is hypothesized that the stimulus for increasing BMD via resistance training is the greater mechanical pull at the attachment sites of muscle to bone resulting from muscular contractions against a fixed load. Presently, several cross-sectional studies have shown that strength positively correlates with a high bone mineral density (BMD). While resistance training may provide one possible method of decreasing the risk of fracture resulting from falls by increasing BMD, it may also play an important role in maintaining postural control and therefore, in reducing the incidence of falling in older adults. Muscle mass and strength are known to decline with aging. Most of the weight training studies reviewed have produced modest gains in BMD (primarily at the lumbar spine), however, all of the studies have resulted in large and significant increases in muscular strength (Nelson et al., 1994, Pruitt et al., 1992, Menkes et al., 1993).

Recently, Snow-Harter et al., (1990) reported that muscle strength is a significant predictor of bone mineral density. However, the few published longitudinal investigations on the effects of strength on BMD have yielded conflicting reports. Gleeson, et al., (1990), reported that participation in a one year weight training program produced a

marginal, but insignificant increase in lumbar spine density in premenopausal women. Although a significant difference in spine mineral was found between weight lifters and controls, the observed increase of 0.8% in bone mass over baseline did not achieve statistical significance. Rockwell et al., (1990) examined the effect of weight training and axial bone loading on bone density in premenopausal women. At the completion of this 9 month training study the authors reported an increase in muscle strength and a decrease in lumbar spine bone mineral density of 2.9% after 4.5 months and 3.9 % after 9 months. Looking closely at these results, it is interesting to note that the greatest decline occurred during the first 4.5 months. Although the authors offer no explanation for the decline in bone mineral density, they do suggest that the initial effects of a training program such as theirs may initially serve to establish a new basal state of bone turn over, and that study over a longer period of time is required to evaluate the ultimate effect on bone mass. Whereas, Snow- Harter et al. (1992) reported a significant increase of 1.2% in lumbar mineral density in young women following participation in a 8 month resistance training program.

Most of the resistance training intervention studies designed to improve BMD have focused their attentions on postmenopausal women, primarily because of the high incidence of osteoporotic fractures associated with this population. Pruitt et al. (1992), reported that early postmenopausal females who participated in a 9-month resistance training program increased their lumbar spine BMD by 1.6% versus a decrease of 3.6% observed in the non exercising control group. The subjects trained three times per week and performed one set of 8-12 repetition for each of exercise. Subjects trained using an intensity of 10 RM. No changes were observed for the proximal femur, distal radius, or serum markers of bone remodeling for either the exercise or control groups.

Nelson, et al., (1994), investigated the effects of high intensity strength training on multiple risk factors for osteoporotic fractures. In this study, the investigators trained 40

postmenopausal white women age 50 to 70 years. This randomized 1 year training study employed a high intensity strength training protocol utilizing 5 exercises which focused on the hips, knees, back and abdominal muscle groups. Subjects exercised on pneumatic resistance machines 2 times per week (80% of 1 RM) with 3 sets of 8 reps per exercise. At the conclusion of the one year training study, the investigators reported that the exercising group increased their BMD at the femoral neck and lumbar spine by an average of 0.9% and 1.0% respectively. This is one of the first training studies to demonstrate an BMD increase at the hip in postmenopausal females not taking exogenous hormone therapy. Physical activity is known to be beneficial to bone in that it provides a mechanical stimulus which enhances bone mass, therefore, increasing bone formation over resorption (ACSM Position Statement, 1995).

Gleeson et al., (1990) examined the effects of a 12 month resistance training program on bone mineral density premenopausal women (23-46 years). The participants in this study were at least 6 months postpartum or postlactation. In this study, the investigators compared a weight lifting group to a nonexercising control group. Their training regimen involved 8 machine resistance training exercises (4 upper body and 4 lower body). Intensity consisted of 2 sets of 20 repetitions at 60% of 1 RM. Although this weight training program did not directly load the spine, exercises were performed which caused contraction in the muscles which directly attached to the spine. This 12 month weight training study did produce a modest, yet significant, increase in lumbar BMD of 0.8% compared to the postmenopausal controls group 0.5%. The investigators concluded that weightlifting may have an influence on BMD due to the influence of the overloads experienced in weight training.

Recent studies have selectively compared athletes of different types of sports to less active or inactive controls in order to determine the sport-specific effect of exercise on bone mass. Nilsson and Westlin (1971), examined the bone density of the lower limb in

different athletic groups including nine international level athletes. Their findings suggest that athletes who participated in power events which required repeated high force movements such as weightlifting and throwing events had higher bone mineral density than distance runners, soccer players and swimmers. Colletti et al., (1989) looked at twelve males (19-50 years) who weight trained for a least one year. They reported that weight training was associated with an increase in bone mineral density (g/cm^2) when compared to age matched controls at the lumbar spine (1.35 Vs 1.22) and trochanter (.99 Vs .96) but not at the mid radius suggesting that resistance training may be associated with increased bone mineral density at weight bearing sites.

Granhed et al., (1987) demonstrated that among elite power lifters, lumbar vertebral bone mineral density was highly correlated ($r=0.82$) with the total poundage lifted over the period of one year. Mathematical modeling has demonstrated that compression forces applied to L3 ranged from 18 to 36.4 kN during the deadlift exercise. Based on these results the researchers concluded that weight training may stimulate bone formation through the direct action of muscle pulling on bone or the increased effect of gravity acting on bone when heavy weights are supported by the skeleton.

Conroy et al. (1993), examined the relationship of bone mineral density to muscular strength in highly trained male athletes. In this study the investigators tested 25 elite junior Olympic weight lifters (mean age 17.4 years). Their training regimen involved very high intensity resistance training programs consisting of multiple sets of multijoint exercises such as squats and power cleans with loads exceeding 85% of 1 RM. The BMD values of the lumbar spine and the proximal femoral neck were found to be significantly greater in elite junior Olympic weight lifters when compared to both an age matched control group and adult reference data (20 - 39 year old men). Both simple and multiple regression analyses demonstrated significant relationships of BMD and strength with strength accounting for 30-65% of the variance. The investigators concluded that in elite junior

Olympic weight lifters, muscle strength, which is highly specific to the sport of weightlifting has a major influence on BMD due to the influence of the chronic overloads experienced in training.

Thus, it would appear that weight training is strongly associated with higher BMD. However, little is known about the possible adaptations of bone to very high intensity resistance training programs consisting of free weight exercises such as squats and dead lifts in untrained older adults using loads exceeding 85% of 1 RM.

Human Growth Hormone

The activity of the growth hormone releasing hormone (GHRH)-growth hormone-insulin-like growth factor (IGF) axis declines with aging, a phenomenon which is referred to as "somatopause" (Hoffman et al. 1993). Growth hormone and insulin-like growth factors are major regulators of cell division and protein synthesis. Decreases in growth hormone (GH) and the insulin-like growth factors are associated with the declines in bone and muscle mass observed with age. Rudman et al. (1985), was the first to call attention to the fact that body composition changes are associated with aging. Some of these changes include an increase in adipose tissue, a decrease in lean muscle mass and strength and a decline in bone mineral density. These declines are also associated with a decline in the secretion of GH. Growth hormone secretion decreases with age, particularly after age 50 Rudman et al. (1985).

It is widely accepted that GH secretion undergoes an age-related decline in both animals and humans (Muller and Nistico, 1989). The primary hormonal regulator of IGF-I is GH; therefore, serum IGF-I levels reflect GH status (Copeland et al. 1990). Decreases in GH and IGF-I circulating levels may account for many of the catabolic changes seen in the normal aging process such as osteopenia, muscle atrophy, increased body fat and a decrease in exercise tolerance (Hoffman et al. 1993). In reference to

muscle atrophy, which is associated with a decrease in circulating GH levels, research suggests that this deficit is accompanied by a significant decrease in muscular strength and endurance (Beivier et al. 1989). Also, it is important to note that Snow-Harter et al. (1992) reported that muscle strength is a significant predictor of bone mineral density. Also, Snow-Harter et al. (1994) reported that IGF-I is related to bone mass and lean muscle mass.

The relative importance of IGF-I as an endocrine or as an autocrine and paracrine factor is not fully understood. It appears that systemic IGF-I activates bone remodeling in humans. Circulating IGF-I is primarily bound to IGFBP-3 but, IGFBP-3 levels do not appear to be dependent on IGF-I, rather they are closely related to GH secretion (Johansson et al. 1992). It is currently believed that IGFBP-3 may be the primary regulator of GH. Johansson et al. (1992), reported a significant relationship between BMD and GH secretion in GH deficient adults. Both IGF-I and IGFBP-3 are regulated by GH; however, IGF-I appears to be more sensitive to change due to GH and nutritional status; therefore, relationships as a result of long term GH dependence may be more easily detected for IGFBP-3 than for IGF-I (Johansson et al. 1992 and 1994). Wuster et al. (1993), reported that patients with osteoporosis have lower levels of IGFBP-3 when compared to healthy controls. This would suggest that GH deficiency may be a possible cause of osteoporosis. Johansson et al. (1992), also reported that IGFBP-3 is closely correlated to BMD in healthy individuals providing support for Wuster's hypothesis.

Pituitary growth hormone is a peptide hormone with profound effects on somatic growth and body composition. Pyka et al. (1992), concluded that circulating concentrations of GH decline with age as well as circulating levels of IGFs. IGFs are the putative mediators of many of the hormone's actions. Rudman et al. (1985), was the first to call attention to the fact that body composition changes are associated with aging. Some of these changes include an increase in adipose tissue, a decrease in lean muscle mass and

strength and a decline in bone mineral density. These declines are also associated with a decline in the secretion of GH. Clemmons and Van Wyk, (1984) investigated IGF-I in a cross-sectional study involving 226 healthy adults. They reported a progressive decline in IGF-I from age 20 to age 60. They noted that the levels of circulating IGF-I which were measured in 70 year old adults was approximately 50% of those of a 20 year old adult.

The skeletal actions of GH within adults is not well defined. Barnard et al. (1991), suggests that GH directly stimulates IGF production in osteoblasts since it has been shown that GH activates cell surface receptors in cultured osteoblast-like cells to increase IGF-I production. Harris et al. (1969), reported that administration of GH to adult dogs increased bone mass. Mann et al. found that recombinant hGH helps maintain bone mass in primates, rendered hypogonadal. These findings may suggest that GH or IGF-I may have the potential to activate osteoblast proliferation and help repair bone mineral deficits of older adults in general, and osteoporosis, in particular. Johansson et al. (1994), investigated the relationship between BMD, IGF-I and IGFBP-3 in the presence of numerous factors which may influence these parameters in healthy men. Some of the factors included age, BMD, strength, Vo2 max, body composition, testosterone, PTH and others. Thirty-eight healthy males 25 to 59 years participated in the investigation. The investigators reported that IGF-I and IGFBP-3 positively related to muscle strength and Vo2 max; however, IGFBP-3 correlated better with BMD than any other study parameter. Based on these findings the investigators concluded that GH is an important regulator of bone mass. These results also suggest that IGFBP-3 reflects GH secretion and has a direct role in the endocrine regulation of bone metabolism.

Insulin-Like Growth Factor-I and Exercise

Insulin-like growth factors-I and II (IGF-I and IGF-II) are small peptides which are structurally similar to insulin and mediate the anabolic growth promoting effects in humans

(Copeland et al. 1990). IGF-I has also been shown to stimulate osteoblasts in vitro and may effect skeletal muscle (Conover and Kiefer 1993).

A number of recent cross-sectional studies have suggested that physical activity may be an independent modulator of plasma levels of IGF-I in healthy adults. Kelly et al. (1990), examined the relationship among circulating GH and IGF-I and physical fitness as determined by predicted maximal oxygen uptake (VO_{2max}) in 134 healthy adult females, 34 of which were postmenopausal. The investigators reported that overall strength correlated with GH levels but not with IGF-I levels. They also reported that a significant relations however, hip existed between plasma IGF-I levels and VO_2^{max} in all women. The investigators also examined the relationship between IGF-I and bone mineral density (BMD) at the femoral neck, lumbar spine and distal radius. Their purpose was to examine if IGF-I played a mediating role on the effects of physical fitness and bone mineral density. They reported a positive relationship between plasma IGF-I levels and BMD at all sites measured. However, they found that this was not independent of the effects of physical fitness. The investigators concluded that based on their findings, decreases in plasma IGF-I concentrations with age may not be due to aging, but may be due to age related declines in physical fitness.

Poehlman et al. (1990), examined the effects of eight weeks of endurance training on changes in IGF-I, IGF-I IGFBP-3 and VO_2^{max} in 18 older adults (mean age 66 years). At the conclusion of the training period, both men and women increased their VO_{2max} by 14%. Significant increases in IGF-I were found in men (19%) but not in women (8%), no significant group changes were reported for IGFBP-3 in response to endurance training. However, they did note a significant relationship between changes in IGF-I and IGFBP-3 in men but not women in response to training. The investigators concluded that their findings support a sexual dimorphism in the response of IGF-I to endurance training, in which older women show a blunted increase in IGF-I when compared to older men.

Since IGFBP-3 is dependent on GH secretion, the researchers suggest that increases in IGF-I may be GH mediated in older men. The findings of this study provides support for the hypothesis that declines in GH with aging may not be due to aging, but may be due to age related declines in physical fitness.

Experimental investigations with weight training intervention remains the only means to test the hypothesis that weight training increases BMD and lean mass. Unfortunately, most studies involving older adults to date are few and varied in the type of exercises and intensities employed. This lack of homogeneity in these studies prevents any strong conclusions from being made regarding which weight training exercises or intensities are best. However, the available data are beginning to lend insight as to which types of exercise are most beneficial to BMD, muscular strength and lean mass. Future studies need to confirm the role of weight training in promoting BMD or more importantly to identify which exercises and training intensities are best for older adults.