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Testosterone Supplementation Effects on Low BMD in Males Ages 19-62: A Six-Month Intervention

Kara Palmer
University of Southern Mississippi

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The University of Southern Mississippi

TESTOSTERONE SUPPLEMENTATION EFFECTS ON LOW BMD IN MALES
AGES 19-62
A SIX-MONTH INTERVENTION

By

Kara Palmer

A Thesis

Submitted to the Honors College of
The University of Southern Mississippi
in Partial Fulfillment
of the Requirements for the Degree of
Bachelor of Science
in the Department of Human Performance and Recreation

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Approved by

David R. Davies, Dean
Honors College

Abstract

The purpose of this study was to examine the effects of a six-month testosterone supplementation on bone mineral density (BMD) in males ages 19-62. Recruiting potential subject through a local clinic, five subjects were eligible for participation in the study. A pre-supplementation DEXA scan was used to measure BMD of the lumbar spine and hip. A post-supplementation DEXA was done after six months of supplementation; the same sites were scanned. Of the initial five subjects, three subjects completed the study. All subjects showed an increase in serum testosterone levels ($\Delta = +537$ ng/dL). After the supplementation subject one showed an increase in BMD for both hip locations, and his total BMD from all three scans improved. Subject two also showed increases in BMD in both hips and total BMD. Despite overall increase in BMD, subject one and subject two both showed a decrease in BMD in the lumbar spine region. Subject three showed a slight decrease in cumulative BMD; however, subject three lacked an initial scan for the lumbar spine region, which could have contributed to the final changes in BMD. Post supplementation, all three subjects observed augmented energy levels. Overall, testosterone supplementation was shown to help maintain or improve BMD in two out of three subjects. Continued addition of subjects will allow for statistical evaluation of data in the future.

Keywords: testosterone, bone mineral density, supplementation, lumbar spine, hip

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Chapter One

The U.S Department of Health reports state that in 2004 and 2006 ten million Americans were diagnosed with osteoporosis; two million were males (U.S. Department of Health and Human Services, 2004; U.S. Department of Health and Human Services, 2006; Pande et al., 2006). However, this number grossly underestimates the number of Americans living with osteoporosis (U.S. Department of Health and Human Services, 2004); however, this number merely scratches the surface of the millions of Americans currently living with low bone mineral density (BMD). Osteopenia is diagnosed when a person is found to have BMD 1 standard deviation (SD) below that of a normal, healthy adult; osteoporosis is diagnosed when a person is found to have bone mineral density 2.5 SD below the bone mineral density of a normal, healthy adult. Hence, having decreased BMD is not synonymous with having osteoporosis. However, just as with osteoporosis, decreased BMD has associated health concerns. Decreased BMD causes bones to be more susceptible to fractures. Annually, osteoporosis causes 1.5 million bone fractures in America with associated costs between 12- 17 billion dollars (U.S. Department of Health and Human Services, 2004; Farley & Blalock, 2009; Pande et al., 2006). Not only are the economic impacts of low BMD fractures substantial, but the physical repercussions of fractures alarming. People suffer bone fractures from low BMD are associated with increased mortality rates, increased morbidity and decreased quality of life (U.S. Department of Health and Human Services, 2004; Vondracek & Hansen, 2004). For example, three months following an osteoporotic fracture, mortality risks among people who experience fractures increases 2.8 to 4 fold (U.S. Department of Health and Human Services, 2004). Though low BMD is easily diagnosed and can be successfully treated if

caught early, the lack of visible symptoms cause low BMD to often go unnoticed until a patient's BMD has decreased to being classified as osteoporosis.

Within the past several decades substantial advancements have been made in research pertaining to causes, consequences and cures of low BMD, particularly in patients with osteoporosis (Farley & Blalock, 2009). As the body's regulation of bone density becomes better understood, physicians and researchers have been able to introduce multiple methods to stop bone loss and prevent low BMD fractures. Initially, physicians and researchers strongly promote the use of preventative measures for everyone who is at risk for low BMD fractures such as the elderly, sedentary individuals and post menopausal women (U.S. Department of Health and Human Service, 2004; Sweet, Sweet, JerMiah, & Galazaka, 2009). Examples of preventative measures include exercise, proper nutrition and methods of fall prevention such as railings and non-slip surfaces (U.S. Department of Health and Human Service, 2004; Sweet et al., 2009). Research also strongly advocates the benefits calcium and vitamin D provide for general bone health, specifically BMD. Medical treatment options for low BMD in both sexes include hormone replacement therapy, bisphosphonates, and other medications (Farley & Blalock, 2009; Nieschlag et al., 2004). Hormone replacement therapy, which includes supplementation of androgens, such as testosterone and estrogens, has been a long-standing method for osteoporosis treatment in females and has recently become a popular method for treating osteoporosis in males (Nieschlag et al., 2004). However, as new hormone treatment methods develop and new understandings of hormones' varied effects within the body are discovered, hormonal therapy requires continued research.

Osteoporosis has been long identified as a “woman’s disease”; therefore, research pertaining to osteoporosis and even low BMD in males drastically lags behind research on osteoporosis and low BMD in women. Thus, the two million males with osteoporosis are limited in treatment options. Today, testosterone supplementation is a common treatment method for low BMD in males. However, the majority of current research available includes populations of males 70 years of age and above (Anderson, Francis, Peaston, & Wastell, 1997; Nayak, Roberts, & Greenspan, 2009; Spry et al., 2009; Snyder et al., 1999). To date, some studies have seen great benefits in using testosterone supplementation as a treatment for low BMD (Anderson, Francis, & Faulkner, 1996; Behre et al., 1997, Farley & Blalock, 2009; Wang et al. 2006). However, several studies, particularly studies done with a placebo group, challenge these findings (Snyder et al., 1999; Tracz et al. 2006). Therefore, more information is needed to understand the effects of testosterone supplementation in men with low BMD who are younger than 62 years of age. Hence, the purpose of this study is to investigate the effect of testosterone supplementation on males 19-62 with low BMD indicating osteopenia or osteoporosis.

Chapter Two

Low BMD

In 2004, the Surgeon General released data reporting that ten million Americans are diagnosed with osteoporosis. The Surgeon General also specifies that of these ten million Americans with osteoporosis, two million are males (2004). As discussed above, osteoporosis is defined as bone mineral density (BMD) 2.5 SD below the mean and osteopenia as BMD 1 SD below the mean of the average BMD of healthy adults (Surgeon General, 2004). It is estimated that 2-6% of males in the United States are living with osteoporosis with an additional 28-47% of males living with osteopenia (Khosla, Amin, & Orwoll, 2008). Despite the fact that males only account for one-fifth of diagnosed cases of osteoporosis, one-fourth of all hip fractures and half of all vertebral fractures occur in males (Farley & Blalock, 2009). Fractures caused by low BMD not only cost 12 billion dollars annually but also cause high rates of mortality and morbidity among males who suffer from them (Surgeon General, 2004).

A study done by Pande et al. (2006) followed 200 males for two years: the sample included an experimental group of 100 males with low BMD hip fractures and a control group of 100 males without hip fractures. Researchers found a six to seven fold increase in mortality rate among males greater than 50 years of age who had suffered an osteoporotic hip fracture. In addition to increased mortality rates, researchers also saw an increase in morbidity in males who suffered a hip fracture. Two years following the initial fracture, 70 of the 100 males never returned home. Of those 70 males, 58 males died while the remaining 12 were placed in assisted living homes. In correlation with

these findings a study performed by Trombetti et al. (2002) calculated a decrease of 5.8 years in life expectancy after a man experienced a hip fracture.

Though the consequences of osteoporosis are well known, physiological factors initiating low BMD are not well defined. Currently, the causes of low BMD in males can be divided into two categories: idiopathic causes and secondary causes (Vondracek & Hansen, 2004). Idiopathic causes are primary causes and are diagnosed if low BMD appears without depreciated androgen levels, specifically testosterone levels within normal levels (eugonadal). In such a case, low BMD may occur due to the presence of one or more factors such as: age, genetics, low body mass index and low calcium and vitamin D intake or decreased absorption (Vondracek & Hansen, 2004). Secondary causes are diagnosed when low BMD occurs due to lifestyle changes or changes in hormone levels. Secondary causes include abnormally low levels of testosterone (hypogonadism), alcoholism, sedentary lifestyle, hyperthyroidism and aging (Vondracek & Hansen, 2004).

Androgens and Bone Health

When osteoclast (bone reabsorbers) activity outweighs osteoblast (bone builders) activity, the bone is left porous and brittle (Vanderschueren et al., 2005). Androgens play a role in osteoblast and osteoclast balance through two pathways: decreasing osteoblast apoptosis and decreasing osteoclast reabsorption of bone. Androgens, specifically estrogen, play a role in osteoblast and osteoclast balance through the production of RANKL, a physiological agent known to lift osteoclast off the surface of the bone (Hadley & Levine, 2007). With osteoclast removed from the surface, osteoblasts have

the opportunity to lay down bone without reabsorption leading to an overall increase in bone density. Consequently, the decrease in the production of estrogen, which occurs in postmenopausal females, will lead to a drastic change in BMD. In males, testosterone produced in the testes will be transformed into estrogen by the enzyme aromatase at the target tissue, in this instance the surface of the bone. Therefore, testosterone in males plays a similar physiological role in the conservation of BMD as estrogen plays in females. However, due to the complexity of testosterone's role in BMD maintenance, testosterone supplementation alone in males does not yield the same results as estrogen supplementation in females.

Vanderschueren et al. supplemented castrated mice with androgens and observed that the addition of testosterone and estrogen helped protect the mice from bone loss (2005). Androgen concentrations, such as testosterone and estrogen, decrease over the lifespan. Testosterone and estrogen levels are lower in older adults, and low levels of testosterone and estrogen are related to an increased osteoblast apoptosis and lower BMD. Due to similarities in mice and human skeletons, if a stable or increasing BMD is seen within mice supplemented with androgens after initial low androgen concentrations, supplementing humans with androgens should elicit similar effects (Vanderscheruen et al., 2005). Thus, androgens should play a significant role in maintaining BMD and could be used to treat patients suffering from low BMD.

Hypogonadism. Males suffering from hypogonadism have decreased testosterone production (testosterone levels are measured in ng/dL). Low levels of testosterone can stem from one of two causes; a decrease in testosterone released from the gonads, or a failure of the central nervous system to produce Luteinizing Hormone

(LH) and Follicle Stimulating Hormone (FSH) (Vorvick, 2010). Secreted by the anterior pituitary, LH and FSH signal the gonads to produce androgens, testosterone in the male. Hence, decreased production or released of LH or FSH would lead to a decreased output of testosterone from the gonads. Regardless of its initial cause, hypogonadism can lead to multiple problems in the body such as: decreased libido, loss of hair or whole-body weakness (Vorvick, 2010). Hypogonadism is linked to an increased chance of developing low BMD and osteoporosis due to androgens' effect on bone health.

Due to the physiological diversity among humans, each body needs and produces an individualized amount of testosterone. Testing for testosterone levels requires a simple blood test. On average, a male's testosterone levels will be between 300-1000 ng/dL. A male suffering from hypogonadism will have a testosterone concentration below 220-250 ng/dL (Fairman, 2000) or below the adjusted value for males their same age and current fitness level. Often, physicians use his/her own discrepancy when diagnosing a man with hypogonadism.

Treatment of low BMD

To date, there are four main medical treatments for low BMD in both males and females: calcitonin, raloxifene, hormone therapy, and bisphosphonate (Farley & Blalock, 2009). Bisphosphonates are considered to be the first-line treatment, followed secondly by calcitonin and raloxifene and lastly by hormone therapy. Though the study done by Farley and Blalock encourages medical treatment of low BMD, specifically osteoporosis, with bisphosphonates, it is important to note that the study included a male and female population. Due to differences in the roles hormones play in the female body and

hormonal changes that occur as the female ages, males and females respond to hormonal therapy differently. Farley and Blalock addressed the benefits associated with all treatment types; specifically how hormonal replacement therapy has shown great success in treatment of males with low BMD due to hypogonadism (2009).

Effects of Testosterone Supplementation. As discussed above, decreased testosterone levels are not only associated with aging, but also can occur as a result of secondary causes such as hypogonadism, hypothyroidism, alcoholism, or sedentary lifestyle (Francis, 1999). Regardless of initial causes of low testosterone, low levels in males may lead to erectile dysfunction, altered mood, decreased erythrocytosis, decreased fertility or low BMD (Rhoden & Morgentaler, 2004). Low testosterone levels can be reversed with testosterone supplementation. Side effects of testosterone supplementation include: potential improvements on cardiovascular disease risks, increased erythrocytosis, sleep apnea, infertility and gynecomastia (Rhoden & Morgentaler, 2004).

Anderson, Francis, & Faulkner (1996) examined the effects of testosterone on BMD as well as cardiovascular risk factors such as cholesterol levels, triglyceride levels, diastolic blood pressure, hematocrit composition and plasma viscosity. Twenty-three eugonadal males with osteoporosis were followed for a six-month period during which time they received intramuscular injections every other week. Cardiovascular disease risk factors were examined every three months of the intervention. BMD was measured pre and post treatment. Subjects saw a significant increase in lumbar spine BMD from the initial measure of $0.799 \pm 0.019 \text{ g/cm}^3$ to the final measure of $0.839 \pm 0.018 \text{ g/cm}^3$, no significant ($p=0.05$) changes were found in the neck, femoral trochanter, or hip. The effect of testosterone on cardiovascular risk factors include the following: decrease in

total cholesterol by 0.3 mmol/L, decrease in triglyceride levels by 15-20%, decrease in blood pressure by 5 mmHg in both systolic and diastolic measures, increase in hematocrit due to an anticipated erythrocytosis and an increase in plasma viscosity due to increased levels of hematocrit. No adverse effects on cardiovascular disease were seen from the supplementation of testosterone (Anderson, Francis, & Faulkner, 1996).

Testosterone Supplementation and BMD

Studies with Hypogonadal Males. BMD in hypogonadal males can be improved through the use of testosterone supplementation (Wang et al., 2004; Farley & Blalock, 2009; Behre et al., 1997). A two-year study by Wang et al., (2004), followed BMD of 163 hypogonadal males ages 19-64. The men took daily testosterone supplements via T-gel applied daily at multiple sites on the body. The only side effect reported was mild skin irritation at application site. At the end of the initial six-months, there was an average 2% increase in lumbar spine BMD accompanied by an increase in testosterone from hypogonadal to normal levels. At the end of the two-year intervention both hip and spine showed improvements in BMD. In addition subjects reported an increased sexual function, elevated mood, improved body composition and restoration of testosterone levels (Wang et al., 2004).

Behre et al., (1997) completed a longitudinal study examining the long-term effects testosterone supplementation has on 72 males ages 19-74 suffering from both idiopathic and secondary causes of osteoporosis. Mean age of subjects was 35 years. The study lasted up to 16 years. Subjects were treated with intramuscular injections (n=52), transdermal patches (n=11) and testosterone pellets (n=2). In all three methods,

the greatest increase in testosterone levels occurred in the first year of supplementation. Subjects all reached normal testosterone levels within three years of supplementation. Researchers concluded that after restoring testosterone levels, BMD remained within normal range as related to age regardless of supplement method used. No serious side effects or reasons to quit treatment were observed (Beher et al., 1997).

Placebo Studies. A study by Snyder et al. (1999) looked at the differences between males supplemented with testosterone versus males supplemented with a placebo pill. The study involved 108 hypogonadal males over the age of 65. Prior to treatment each group had a mean age of 73. Researchers randomly divided 108 males into placebo or testosterone groups, so that no significant differences in age or physiology existed between the two groups. Testosterone supplementation or administration of a placebo was done through orally ingested pills taken daily for a total of 36 months. Of the 108 males that began the study 96 males completed the study. The study showed the placebo group had an initial serum testosterone level of 369 ± 75 ng/dL and a BMD in L1 and L2 of 1.214 ± 0.132 g/cm³, and the testosterone group had an initial serum testosterone level of 367 ± 79 ng/dL and a BMD in L1 and L2 of 1.184 ± 0.142 g/cm³. After the six-months of supplementation, the testosterone group's serum and free testosterone levels rose to 625 ± 249 ng/dL. The group's testosterone levels remained stable throughout the rest of the trial. No change in serum and free testosterone was seen in the placebo group. BMD increased within both groups: a 0.6% increase of BMD in placebo group and a 0.8% BMD increase in testosterone group. Post three years of supplementation no significant differences in BMD were found between the two groups. However, there was a significant increase in BMD between the placebo and testosterone

groups as related to the initial serum testosterone (IST) levels: 0.9% increase seen in IST of 400 ng/dL; 3.4% increase seen in IST of 300 ng/dL, and 5.9% increase seen in IST of 200 ng/dL (Synder et al., 1999).

Tracz et al. (2006) compiled a meta-analysis of eight studies on testosterone supplements versus placebo supplements. Variation between studies included: mean subjects ages ranging from 42 to 73 years, initial serum testosterone levels ranging from 291ng/dL to 457 ng/dL, sample from 16 subjects to 108 subjects, and intervention durations from three to thirty-six months of treatment. Analysis of studies revealed a 4% increase in lumbar spine BMD using intramuscular testosterone injections but no significant improvement in neck or femoral densities. No significant increases in BMD were reported at any region for placebo and transdermal testosterone groups (Tracz et al., 2006).

Studies with Eugonadal Males. The question remains, can low BMD in eugonadal males be improved through the use of testosterone therapy? A study conducted by Anderson, Francis, Peaston, & Wastell (1997) tested the effects of testosterone intramuscular injections on eugonadal males suffering from osteoporosis. Subjects did not supplement with calcium or vitamin D (Anderson et al., 1997). A sample of 21 males ages 23-73 completed the study with injections of testosterone every other week. At the end of six months, subjects had an average 5% increase in lumbar spine BMD with no significant changes in BMD of the neck, trochanter of femur, or hip (Anderson et al., 1997). Two men failed to complete the study due to non-related health complications (Anderson et al., 1997). Complaints from the remaining males consisted

of stiffness and soreness at the injection site, but no other adverse side effects were reported (Anderson et al., 1997)

Conclusion

Some studies show that testosterone supplementation has beneficial effects on the treatment of low BMD in hypogonadal and eugonadal males (Anderson, Francis, & Faulkner, 1996; Behre et al., 1997, Farley & Black, 2009; Wang et al.2006). However, some literature suggests that testosterone supplementation has no significant effect on BMD (Synder et al., 1999; Tracz et al., 2006). Thus, this study will investigate the effects of a six-month testosterone supplementation regiment on BMD in osteopenic and osteoporotic males ages 19-62.

Chapter 3

Purpose

The purpose of this study is to investigate the effect of six-months of testosterone supplementation on younger men ages 19-62 with low BMD indicating osteopenia or osteoporosis.

Sample

All subjects included in the study were males ages 19-62. To qualify, all subjects had a BMD T-score measure of -0.9 or less (diagnosis for osteopenia) in at least one site measured. Measurements were taken from both the lumbar spine and dual femur regions via DEXA scan (GE Lunar Prodigy, Diegem Belgium). Subjects were referred to the study through a local health clinic, Forward Health Solutions. Dr. Rebecca Boyd, D.O. recommended the study to all males with low testosterone levels. Males were not receiving testosterone supplementation for more than three weeks prior to initial DEXA scan.

Procedures

Before consenting to participate, subjects were reminded of the beneficial and adverse effects of testosterone supplementation before the initial DEXA scan. Beneficial and adverse effects of supplementation were also thoroughly discussed with subjects by Dr. Rebecca Boyd prior to referral to the study. Prior to inclusion in the study, all subjects completed a health history questionnaire (HHQ) and a full physical examination. Eligible subjects were then provided with a written consent form outlining the purpose,

benefits and risks. All consent forms were completed prior to initial DEXA scan. Researchers also gave a verbal explanation of the study prior to initial DEXA scan. The adverse side effects of testosterone that were discussed with subjects included: erythrocytosis, gynecomastia, decreased fertility and fluid retention. Dr. Rebecca Boyd supervised and managed all testosterone administration and adjusted testosterone supplementation as needed.

Subjects contacted Kara Palmer to schedule initial DEXA scans. The DEXA scan measured BMD in the lumbar spine and femoral trochanter. After the initial DEXA scan, subjects with a BMD below -0.9 SD below the mean at one or more sites were asked to participate in the study. Subjects who consented to participate in the study were given a verbal reminder of participant expectations, benefits and possible adverse effects. Serum testosterone levels were obtained from Dr. Rebecca Boyd upon subject entrance into the study.

Subjects with health complications or a health history deemed unsuitable for participation in the study were excluded. Exclusion criteria included failure to complete the full six-month supplementation regimen or a subject choosing not to continue participation. The University of Southern Mississippi IRB Board approved all procedures.

Variables

Dependent Variables. In this study, the dependent variable measured was the BMD of both the lumbar spine and femoral trochanter. All BMD measurements were operationalized via DEXA scan. DEXA scans are non-invasive, include minimal

radiation exposure and are frequently performed at the Laboratory of Applied Physiology. Completion of a DEXA scan takes an approximated 6 minutes. Subjects were asked to complete two DEXA scans, one at the beginning of the study and one after six-months of supplementation

Subjects were given results of DEXA scan, a \$350 value each, at no cost. The study then compared the initial and final DEXA scans and determined the changes in BMD in the spine and femoral trochanter. The overall BMD change was then used to determine the impact of testosterone supplementation on BMD at each site measured and overall BMD.

Independent Variables. In this study the independent variable was testosterone supplementation. Testosterone supplementation may be administered one of three ways: crème, injections, or pellets. Supplementation methods were individualized to each subject and tailored to each subject's personal needs.

Control Variables. Since evidence links environmental factors to the development of low BMD, control variables include weekly physical activity, calcium intake, vitamin D supplementation, weight lifting activities, age, occupation, and diet with special interest in dairy intake (Sweet et al., 2009). All control variables will be accounted for through a brief questionnaire the subject will complete prior to initial DEXA scan. However, until sample size increases to where statistical analysis is possible, control variables were not represented here.

Final Disposition of Data

Throughout the duration of the study, all data collected was assembled and filed in the office of Dr. Joseph Boyd at the University of Southern Mississippi. All data is to be kept confidential and findings are reported in such a way that protects the subjects' identity. For publication purposes, all participants are referred to by a pseudonym. All data will remain on file for three years following completion of study.

Chapter 4

Of the original five subjects that began the study, three completed the final six-month scan. Of the two that were excluded from the study, one discontinued use of testosterone supplementation and the other failed to comply with the regulations of the study. Demographic information about the three subjects that completed the study is provided below (see Table 1).

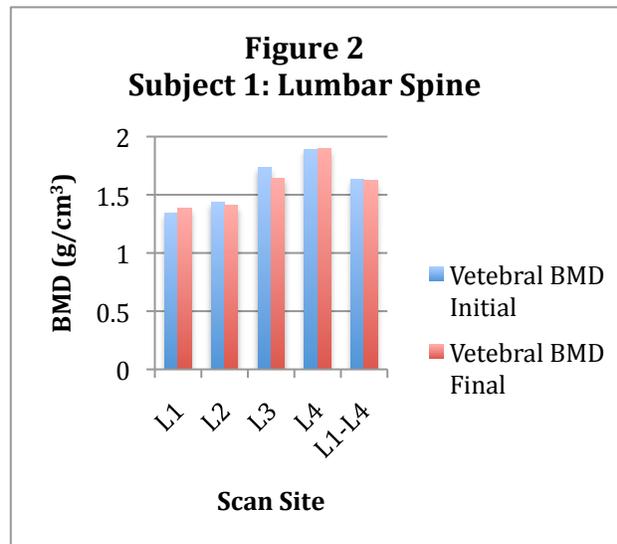
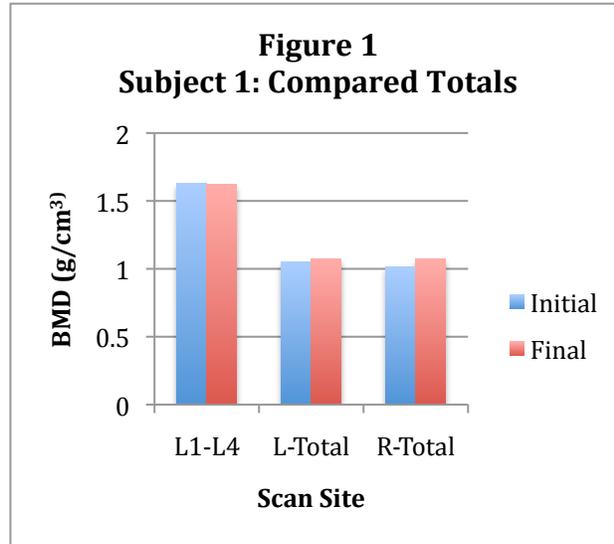
Table 1 <i>Demographic Analysis</i>	
Age (yrs)	48 ± 3.5
Height (in)	71 ± 2
Weight (lb)	196 ± 30
Race	
Caucasian	2
African American	1
T Levels (ng/dL)	
Initial	322 ± 175
Final	855 ± 238
Δ	537

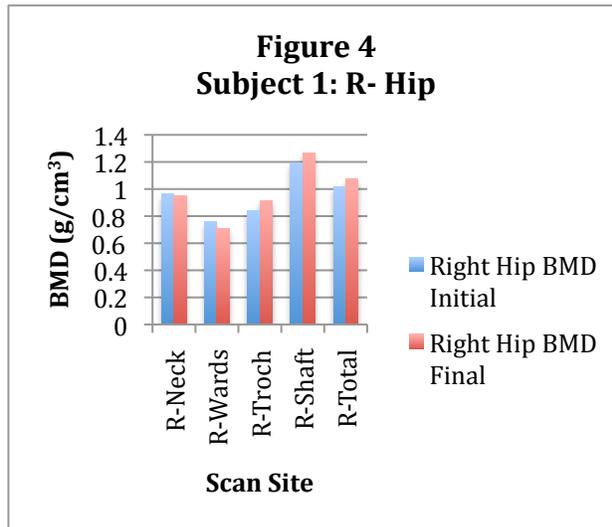
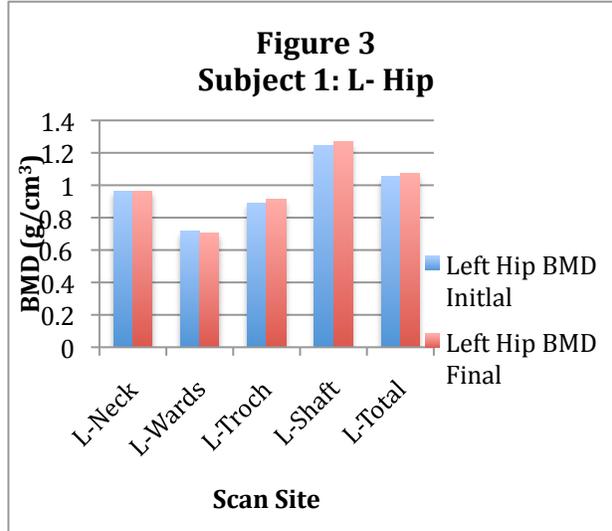
Due to a sample of three ($n=3$), statistical evaluation of data is not feasible at this time. In this presentation of data, the results are presented as individual case studies specific to each subject. The difference in BMD in all three locations scanned and the overall change in BMD will be featured. As researchers continue to gather data, a desired population size of $n=8$ should be accomplished in the future and the current data revisited for statistical evaluation.

Subject 1:

As shown in Table 2, subject one increased serum testosterone levels by +695 ng/dL reaching a total of 862 ng/dL from the original 167 ng/dL (see table 2). Along with an increase in serum testosterone levels, the subject's final DEXA scan showed an increase in total BMD in both the left and right hip ($\Delta = +0.022 \text{ g/cm}^3$, $\Delta = +0.059 \text{ g/cm}^3$) but a decrease in BMD in the lumbar spine ($\Delta = -0.012 \text{ g/cm}^3$) (see Table 3). In the lumbar spine, greatest increase was seen at L1 ($\Delta = +0.042 \text{ g/cm}^3$) and the greatest decrease at L3 ($\Delta = -0.094 \text{ g/cm}^3$) (see Figure 2). In the left hip, the greatest increase in BMD was seen in the shaft ($\Delta = +0.024 \text{ g/cm}^3$) and greatest decrease in the wards ($\Delta = -0.01 \text{ g/cm}^3$) (Figure 3). In the right hip, the most substantial increase was seen in the shaft ($\Delta = +0.074 \text{ g/cm}^3$) and the greatest decrease in the ward ($\Delta = -0.052 \text{ g/cm}^3$) (see Figure 4). Overall, subject one had the greatest BMD decrease in L3 and the greatest BMD increase in shaft of the right hip. Total initial BMD was 3.669 g/cm^3 and final BMD was 3.768 g/cm^3 . Therefore, after a 6-month supplementation with testosterone, subject 1 saw an overall positive BMD difference of 0.069 g/cm^3 (see Table 3).

Age	51 yrs
Height	73 in
Weight	230 lbs
Ethnicity	African American
Days b/t scan	181 days
Initial T Level	167 ng/dl
Final T Level	862 ng/dl
Supp. Method	Injections
Dosage	200 mg day
Ethnicity	African American



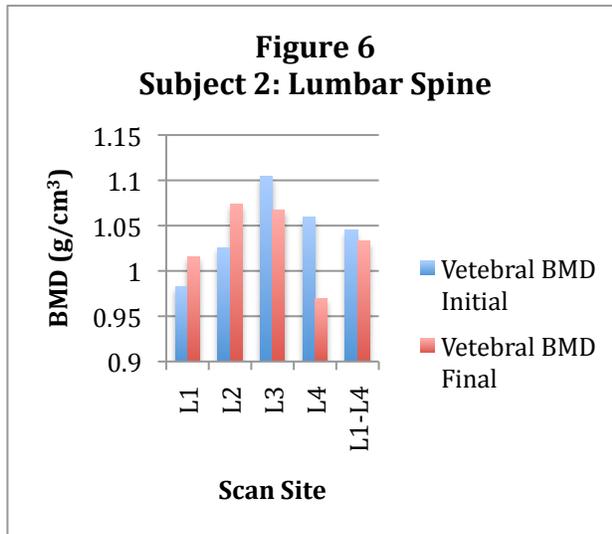
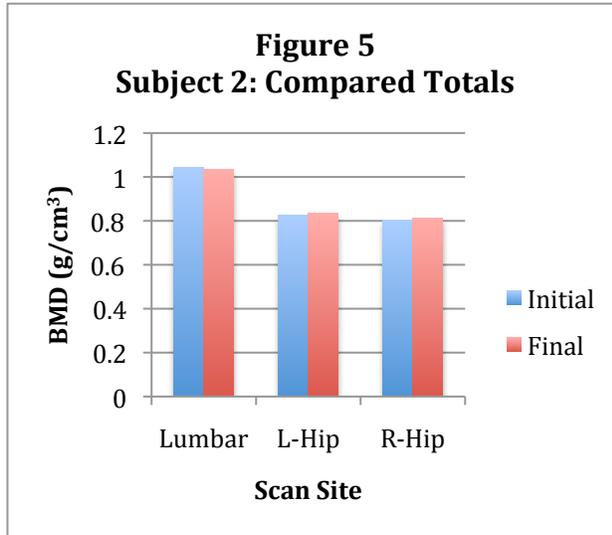


	Initial		Final		Δ	
	(g/cm ³)	T score	(g/cm ³)	T score	(g/cm ³)	T score
L1-L4	1.632	3.4	1.62	3.3	-0.012	-0.1
L-Hip	1.052	-0.3	1.074	-0.2	+0.022	+0.1
R-Hip	1.015	-0.6	1.074	-0.4	+0.059	+0.2
Totals	3.699		3.768		+0.069	

Subject 2:

Over the course of the six-month testosterone supplementation, subject two saw an increase in serum testosterone levels increased from 497 ng/dL to 1093 ng/dL. ($\Delta = +596$ ng/dL) (see Table 4). In addition to increases in testosterone levels, the final scan revealed an increase in both the left and right hip ($\Delta = +0.009$ g/cm³, $\Delta = 0.012$ g/cm³) (see Table 5). However, the BMD in the lumbar spine decreased ($\Delta = -0.012$ g/cm³) after six-months of supplementation (see Table 5). Within the lumbar region, the greatest increase in BMD occurred in L2 ($\Delta = +0.048$ g/cm³) and the largest decrease in BMD occurred in L4 ($\Delta = -0.089$ g/cm³) (see Figure 6). In the left hip the largest increase in BMD occurred in the L-Troch ($\Delta = +0.014$ g/cm³) and the only decrease in the L-Wards ($\Delta = -0.005$ g/cm³) (see Figure 7). Unique to the right hip, only increases in BMD were seen (see Figure 8). In the right hip the largest increase was in the R-neck ($\Delta = +0.015$ g/cm³) (see Figure 8). Therefore, after six-months of testosterone supplementation, subject two saw an increase in total BMD of $+0.009$ g/cm³ (see Table 5).

Table 4 <i>Subject 2: Demographic Analysis</i>	
Age	44 yrs
Height	70 in
Weight	195 lbs
Ethnicity	Caucasian
Days b/t scan	223 days
Initial T Level	497 ng/dL
Final T Level	1093 ng/dL
Supp Method	Topical Gel (200 mg/ml)
Dosage	2 clicks (.5 ml) once daily



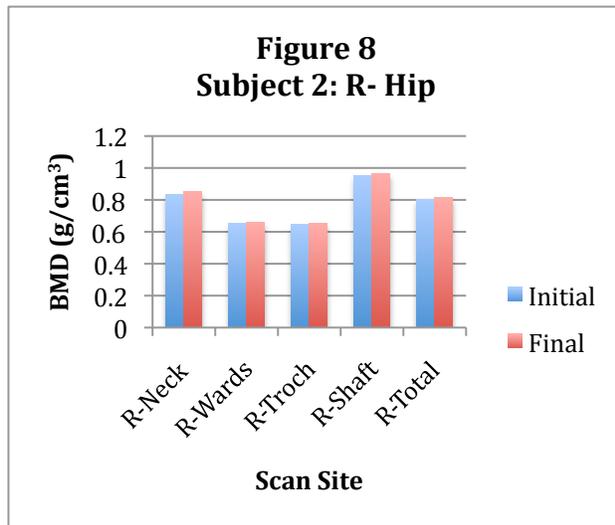
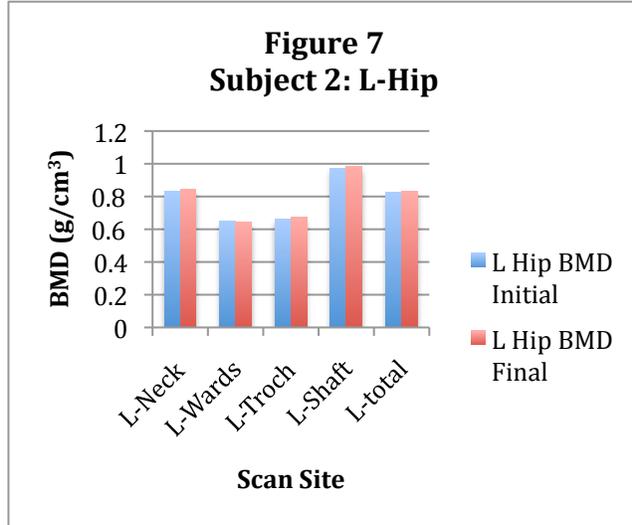
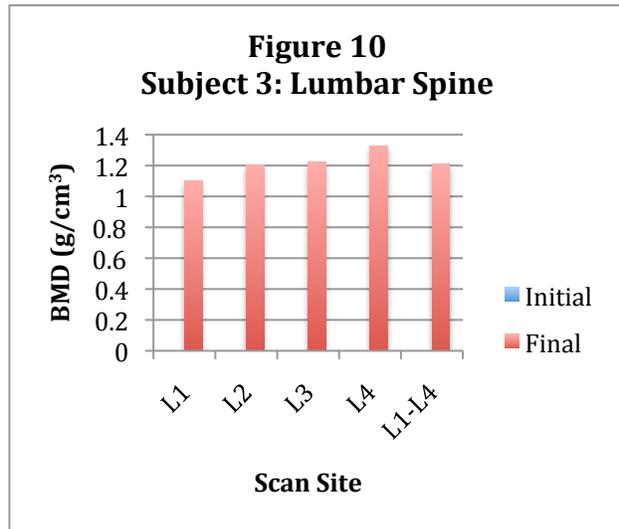
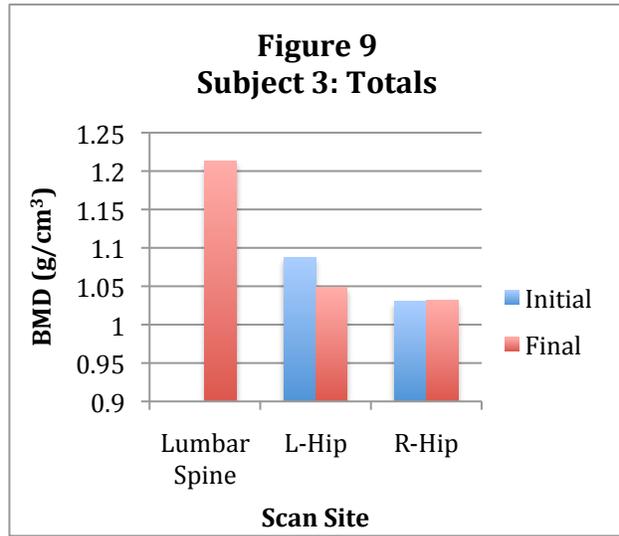


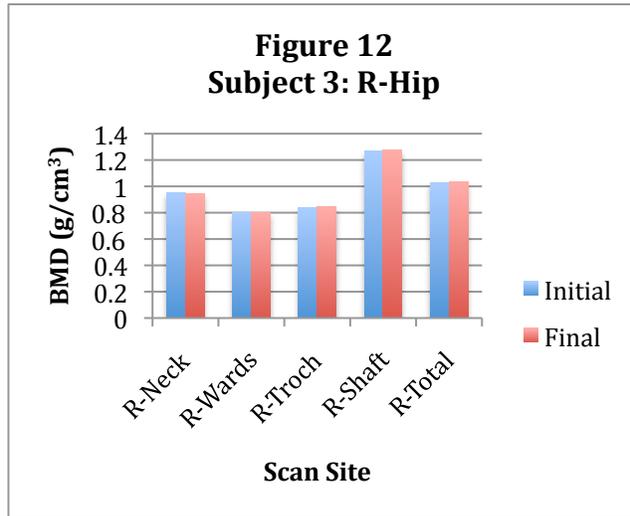
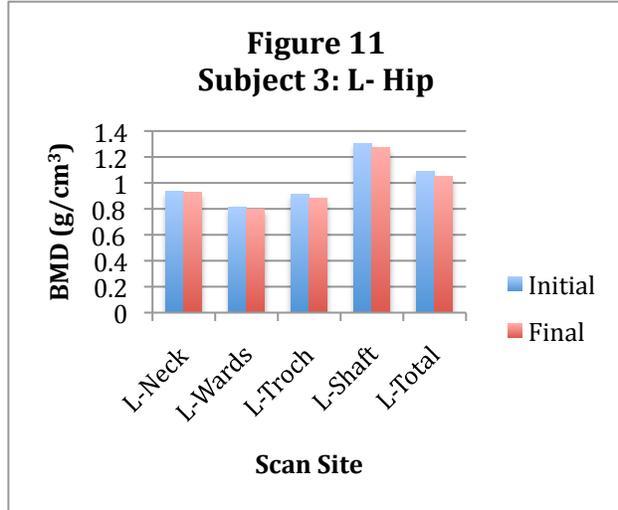
Table 5						
<i>Subject 2: Totals</i>						
	Initial		Final		Δ	
	(g/cm ³)	T score	(g/cm ³)	T score	(g/cm ³)	T score
L1-L4	1.045	-1.5	1.033	-1.6	-0.012	-0.1
L-Hip	0.824	-1.9	0.833	-1.9	0.009	0.0
R-Hip	0.802	-2.1	0.814	-2.0	0.012	+0.1
Totals	2.671		2.68		0.009	

Subject 3:

Subject three saw an increase of serum testosterone from 290 ng/dL to 610 ng/dL ($\Delta = +320$ ng/dL) (see Table 6). This change in testosterone was the smallest increase in testosterone seen among all subjects. Due to a systems failure, the data for the initial lumbar scan for subject three was not usable. Data from the final scan is still presented but not included in the final BMD calculations. After the final scan, subject three's right hip increased in BMD ($\Delta = +0.002$ g/cm³), but his left hip decreased ($\Delta = -0.039$ g/cm³) (see Table 7). In the right hip, the largest increase in BMD ($\Delta = +0.011$ g/cm³) was found at the R-troch (see Figure 12). No change was seen at the R-wards. At the left hip, no increase in BMD was found, but a decrease ($\Delta = -0.039$ g/cm³) was seen at the L-Troch (see Figure 11). Overall, subject three saw the only decrease in total BMD of -0.037 g/cm³ (see Table 7).

Table 6 <i>Subject 3: Demographic Analysis</i>	
Age	49 yrs
Height	71 in
Weight	165 lbs
Ethnicity	Caucasian
Days b/t scan	188 days
Initial T Level	290 ng/dL
Final T Level	610 ng/dL
Supp. Method	Injections every two weeks
Dosage	.75 mL





	Initial		Final		Δ	
	(g/cm ³)	T score	(g/cm ³)	T score	(g/cm ³)	T score
L1-L4	na		1.213	-0.1	1.213	
L-Hip	1.088	-0.1	1.049	-0.4	-0.039	-0.3
R-Hip	1.03	-0.5	1.032	-0.5	0.002	0.0
Totals	2.118		2.081		-0.037	

Chapter 5

The purpose of this study was to examine the effects of a six-month testosterone supplementation on BMD in males 19-62. Addressing this issue and considering the relationship between testosterone and bone density, we hypothesized that an increase in testosterone in males with initially low testosterone concentrations may increase BMD. Sites measured included the lumbar spine region and both hips. Measurements were taken within the first three weeks of testosterone supplementation and after six months of consistent supplementation. Results concluded that a six-month testosterone supplementation increased total BMD in subject one and two. After a six-month intervention subject one and two showed an increase in BMD in both hip regions; however, they also showed a decrease of BMD in the lumbar spine region. In subject three, a decrease in total BMD was shown. This decrease could be attributed to a systems failure resulting in the loss of the lumbar spine, which could have altered final BMD totals.

In addition to just looking at final BMD, researchers should examine the changes in BMD in relation to the difference in serum testosterone levels. Subject one saw the greatest increase in serum testosterone. He also showed the greatest increase in total BMD. Subject three had the smallest increase in testosterone levels; his was the only decrease in total BMD seen. Hence when more data becomes available, researchers need to not only compare supplementation time with improvements, but also compare changes in BMD with changes in serum testosterone levels.

Lastly, during the final DEXA scan researchers asked subjects of any other changes seen throughout the supplementation period. Subjects unanimously reported an

increase in energy levels and decrease in daily fatigue. None of the subjects reported any adverse side effects with supplementation.

Due to demographics of the surrounding area, sample size remained small.

Subjects had to travel to The University of Southern Mississippi campus to receive both scans which proved challenging and often delayed final scans to longer than the desired 180 days. Two participants were discontinued from the program, one due to failure to comply with the terms of the study and one stopped receiving supplementation prior to the six-month scan. Continued research in this study would require a larger population, potentially partnerships with multiple hormonal replacement clinics and more consistent completion of final DEXA scans. Researchers will continue to gather data from new subjects referred to the study.

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