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Mimi Zumwalt
Maria Fernandez-del-Valle
Editors

The Active Female

Health Issues throughout the Lifespan

Third Edition

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I am dedicating this book to my husband, Robert Parks McComb, who is always there to support me, no matter what the cost.

Jacalyn J. Robert-McComb, PhD, FACSM

I would like to dedicate this book to all the significant females in my life: my grandmother who helped to raise me but now has passed, my mother who fought to bring me here from Vietnam, and especially my daughter who provides me with more joy than words can express. I dearly love and appreciate them all!

Mimi Zumwalt, MD

I would like to dedicate this book to my beloved family—my dear dad, mom, and sister—who helped me in all things great and small. This is for all of you.

Maria Fernandez-del-Valle, PhD

Preface

It is well known in the sports world that many times, young female athletes do not take in enough calories to meet their energy demands [1, 2]. This deficiency is not always associated with an eating disorder [3]. This is not only true for athletes, but is also true for female recreational players, given society's role in subsidizing body image distortions in the broad realm of social media [4]. An imbalance between caloric intake and energy demand for exercise or sports performance may cause bodily impairments or impaired physiological function that continue to evolve undetected, unless professionals, educators, and family members are trained to recognize the risk factors that contribute to energy deficiency [4–6]. It is not well known why some girls and young women are more vulnerable to this pathology than others. Yet there are some commonalities that can be elucidated or demystified for early detection. Contributing variables to energy restriction or imbalances between energy intake and energy expenditure can be grouped into two broad categories: high training volume and inadequate energy intake [5].

Yet what are the hypothesized factors that contribute to these broad categories? High volume of training may result from: high training demand, poor training program, and/or exercise dependence/addiction [3, 7, 8]. Inadequate energy intake can be impacted by body image dissatisfaction and disordered eating and eating disorders [5, 9, 10].

Also sports in which a lower body weight enhances sports performance or is aesthetically desirable may cause girls and young women to intentionally restrict caloric intake without an underlying pathology such as an eating disorder [8, 11, 12]. Additionally, some athletes, particularly college athletes, significantly underestimate their energy requirements for their sport [13, 14]. Sports which have a high energy demand, such as swimming and ultradistance sports may require athletes to consciously increase food consumption throughout the day even when they are not particularly hungry [15–18].

Slightly outside the arena of sports performance is another possible contributing construct to energy deficiency which is behavioral in nature and that is exercise addiction [19, 20]. These individuals feel constantly pressured to exercise. While not always the intent, this condition is associated with negative energy balance and weight loss. Another behavioral pattern that is not so well known in the sports arena that may contribute to energy deficiency is orthorexia nervosa. Orthorexia is a pathological fixation on healthy eating. This may lead to restrictive eating and malnourishment [21].

It is for these reasons and many others that this book was written, namely, to help alleviate the suffering of girls and women who may be walking down a pathological walkway that has long-term adverse health outcomes without even knowing it. It is up to the professionals and educators who touch the lives of these young girls and women to be knowledgeable about the signs and symptoms suggesting impaired physiological function.

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About the Editors

Jacalyn J. Robert-McComb, PhD, FACSM is a Professor of Exercise Physiology in the Department of Kinesiology at Texas Tech University (TTU). She is a Fellow of the American College of Sports Medicine (ACSM) and is certified by ACSM as a Program Director (PD) in the Rehabilitative Sciences. She is also certified by ACSM as a Clinical Exercise Physiologist (CEP) and Exercise Test Technologist (ETT). As an exercise physiologist, she believes that "Exercise is Medicine." Additionally, she maintains certifications from the American Council of Exercise (ACE) and the Biofeedback Certification International Alliance (BCIA). In order to maintain these certifications, professionals must meet education and training standards progressively to recertify. She is continually studying and learning.

Her area of research for the past 30 years has been examining how psychological stress affects physiological functions. She has been interested in two primary axes: the Gonadotropin-Releasing Hormone (GnRH) axis and the Cortisol-Releasing Hormone (CRH) axis. The GnRH axis affects the female menstrual system through the production of Follicle-Stimulating Hormone (FSH) and Luteinizing Hormone (LH) by the Anterior Pituitary. These two axes are intricately connected. In times of war, or extremely stressful situations, we may see women's menstrual cycles abrupted through the disruption of GnRH by CRH at the level of the hypothalamus. However, in a laboratory setting, it is almost impossible to stimulate a severe enough stress response to elicit menstrual dysfunction in women.

Because of the difficulty in eliciting a strong enough stimulus to disrupt the GnRH axis in a laboratory setting, her studies have evolved into examining exercise programs that alter the stress response positively. The coping programs or behaviors that she examined in her studies include walking, yoga, heart rate variability (HRV) breathing training using biofeedback and meditation. These types of programs help women cope with the daily stressors in their life.

Her future career plans are to begin a web-based consulting program for women and children who suffer from anxiety and disordered eating using exercise and meditation as a coping tool. Exercise changes your physiology and meditation opens your mind to the many gifts that are available in your life. Her plans are to retire to Tucson AZ where she will use her gifts to help others.

Mimi Zumwalt, MD is a native of Vietnam who was evacuated to America in 1973 at 11 years of age. Ever since childhood, she has always wanted to be a doctor. Shortly afterwards, her late foster father got her started in playing sports. Thus, beginning from her teenage years, she has been extensively involved with athletics even before entering high school, which continued into college where she earned an athletic scholarship to compete in tennis. She enrolled in pre-medical studies and traveled to numerous competitions. Then a repeated ankle injury led her to see the Team Physician for treatment, who sparked her interest and eventual specialization in Sports Medicine (fortunate turn of events).

After her collegiate tennis coach introduced the tennis team to weightlifting to augment physical training/conditioning, Dr. Z sought out various ways to improve her knowledge on fitness/wellness. To be more credible, she went on to obtain her American College of Sports Medicine (ACSM) certification as an Exercise Leader, then became certified as a Strength Trainer as well through another fitness organization, both of which helped fuel her passion to learn more about the human body and staying active. Additionally, stemming from her deep love for athletics, she competed in bodybuilding/powerlifting/fitness/extreme sports for a few decades. As a result of these competitions, injuries sustained along with rehabilitation programs she underwent made her more cognizant of the importance of training for and maintaining physical fitness.

Upon obtaining her Biology/Chemistry bachelor's degrees in 1985, Dr. Z wanted to continue her pursuit in the medical field. She completed her postgraduate studies in 1989 via an Army scholarship to earn her M.D. degree (Doctor of Medicine), served and trained in the military, Orthopaedic Residency from 1992 to 1996, then practiced Orthopaedic Surgery as an Army Surgeon for a few years up to 1999, until attending her civilian Sports Medicine Fellowship in 2000. Shortly afterwards she joined the Texas Tech School of Medicine Faculty as an academic clinician-physician/surgeon, teaching and practicing Orthopaedic Sports Medicine ever since.

As a sports specialist/surgeon by trade, Dr. Z trained in performing definitive procedures to address musculoskeletal injuries/conditions. However, being of Asian descent, she approaches medical treatment in a more holistic/preventative fashion. Treating various athletes and realizing that females (especially teenagers) tend to injure certain body parts more so than males while engaged in sporting activity, she sought out ways to help them train/condition in order to prevent injury. She began researching about sex/gender differences in anatomy/biomechanics, in addition to age/hormone-related changes in the musculoskeletal system/neuromuscular control, amongst other factors specific to different sports which could affect overall injury risk.

Dr. Z's involvement with academics/athletics makes it natural for her to enjoy sharing knowledge, distributing pertinent information, and teaching others how to stay active throughout the years without getting hurt. Being in the sixth decade of life herself and experiencing "aches and pains," she wants to let it be known that modifying how one goes about the daily activities and staying "in shape" will serve everyone well in terms of quality of living.

Besides the lectures/presentations given and articles previously published, she hopes her written chapters in this book will give the reader a useful reference source upon which they can build.

Newton's Law states "an object at rest remains at rest, and an object in **motion** remains in **motion**," so it is incumbent upon an individual to start moving and keep on moving. One may have to modify the manner of which to stay active but the key is not to stop; otherwise, the joints will be stiff and stuck!

Maria Fernandez-del-Valle, PhD is a Researcher in the Department of Functional Biology, School of Medicine at the University of Oviedo (Spain). After obtaining her Licentiate in Physical Activity and Sport Sciences, she earned her PhD and completed her training in Clinical Exercise Physiology at the *Hospital Universitario Infantil Niño Jesús* in Madrid. She is certified as a Level 3 Anthropometrist (since 2010) by the International Society for the Advancement of Kinanthropometry (ISAK) and as a Level 3 National Coach by the Spanish Volleyball Association (since 2012).

Dr. Fernandez joined Dr. Jacalyn J. Robert-McComb's lab as a predoctoral researcher in 2011. In 2012, after earning her doctorate degree, she moved to the United States. While in the United States, she received seed funding at Texas Tech University (2012–2016) and Southern Illinois University Edwardsville (2016–2021) which allowed her to run several randomized control trials involving resistance exercise. These studies, along with other research collaborations, have illuminated the need for a multidisciplinary approach in which resistance training could be a key modulator of specific markers and mechanisms of action involved in disease prognosis.

Because of these studies, Dr. Fernandez was able to secure funds from the National Institutes of Health (NIH) and the American Heart Association (AHA) in collaboration with Jon D. Klingensmith (Associate Professor and Chair at the Department of Electrical and Computing Engineering in Southern Illinois University Edwardsville). In 2021, she returned to Spain and has been awarded two grants in Spain: one funded by "La Caixa" Foundation and Caja Burgos Foundation program at Universidad Isabel I and the Margarita Salas Junior Fellowship program at Universidad de Oviedo. These funds support an emerging line of research focused on understanding biological mechanisms underlying anorexia nervosa and the effects of exercise.

Dr. Fernandez's goal as a scientist is to contribute to disease prevention and treatment through exercise with the purpose of growing a healthier society. Decreasing physical inactivity could prevent ~5 million deaths and save approximately INT$68 billion per year worldwide (excluding mental health and musculoskeletal related costs), which aligns with 2030 World Health Organization's objective of reducing inactivity by 15%. Providing more scientific evidence on the benefits of exercise "dose" adjusted to each condition–given its epigenetic benefits–could ultimately lead to the integration of exercise prescription into healthcare systems and policies.

Role and Scope Statement

The times certainly are changing as present-day society demands more equality in gender and race. This third edition of our Active Female textbook serves as a second update of information originally written in 2008, with the first revision published in 2014. We have retained the majority of previous authors and added others (including international authors), increased the number of chapters/expanded topics to include more current literature, and exchanged one of the three editors. We hope that by sharing our combined fund of knowledge backed up by collecting research studies/evidence, the reader can utilize specific scientific findings to educate themselves or to teach and/or share with others. Recognizing that our book is not completely inclusive, depending on the level of curiosity, we encourage further individual searching or exploring referenced articles for more details on the desired topic(s) of choice.

As editors, we have tried to preserve uniformity/similarity in structure/form of our new book. However, each author possesses his/her own unique writing style, thus certain differences may exist. We also aimed to address most health aspects of being an active female, stages of life she experiences, beginning from childhood then progressing through adulthood and beyond. We concentrated on sex/gender/age-related differences along with some variations due to ethnicity. We strived to address several important systems within the human body, starting with basic structure/anatomy, then continuing on to physiology/psychology. Within and in addition to these general domains, we also included musculoskeletal, physiological, neurological, nutritional, cardiovascular, endocrine (hormonal), and immunological related issues along with more specific entities.

Additionally, we outlined recommended guidelines in terms of injury prevention, alternative modalities for pain management, dietary/other supplements, postural considerations; also, how to exercise safely (resistance training/cardiovascular) from both a musculoskeletal and physiological standpoint. Furthermore, we delved into ways to help keep the body energy balanced for pregnant and obese females, concentrating on safety for these special female populations while being/staying physically active.

Although not entirely encompassing, what we have produced is a composite of over 30 chapters to distribute detailed information/impart pertinent knowledge on how to keep the female active and healthy, no matter at what age/stage of life she may be. Our charge is to make meaningful improvements upon previous editions, both online and in printed formats. Realizing that our book is indeed not a novel (primarily factual), we are hopeful that the reading experience is still interesting enough to leave longer than just a mere brief impression. Questions are also provided at the end of each chapter in hopes that those who read it will test themselves upon completion by evaluating their own level of material retention. This book, although quite extensive, is not meant to solely be “THE Bible” for the Active Female. Rather, it should be utilized as a source of reference for all individuals who are interested in female health and wellness. Everyone has family, friends, colleagues, relatives, and possibly knows numerous others who could potentially benefit from learning how to do things to take care of their own bodies, both physically and psychologically for enhancing the quality, if not the quantity of life.

Many thanks for the time and effort toward reading our book. Again, hopefully more insight and confidence about approaching the active female have been gained in doing so. We welcome any feedback or comments the reader may have regarding this published material.

Audience

Appropriate audiences for this book are teachers in health and fitness at all levels of education from junior high or high school to the college and university level since adolescence and young adulthood is a particularly momentous time for bone remodeling and reproductive health issues that may be impacted by energy deficiency.

This book would also be a useful textbook for a women's health issues class in a Women's Studies Program at the university level.

Fitness and wellness coaches, and students who are interested in advancing women's health issues in the field of sports medicine would find this book very insightful and useful in the field of preventative medicine. Others include:

- sports medicine specialists
- family practitioners
- gynecologists
- team physicians
- residents doing fellowships in sports medicine
- athletic trainers
- nurses
- physician assistants
- physical therapists
- sport psychologists
- licensed and certified professionals in the field of sports medicine

Lastly, the educated lay person or woman who may be experiencing these gender-specific problems or have daughters who may be experiencing this triad of disorders would find this book interesting and informative.

This book is by no means all-encompassing in terms of female fitness but provides a foundation upon which more information can be added, and innovative ideas built upon. It serves as a guide for any reader who is seeking further knowledge of girls and women who choose to stay physically active or want to become physically active from birth till death.

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Jacalyn J. Robert-McComb PhD, FACSM

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Mimi Zumwalt, MD

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Maria Fernandez-del-Valle, PhD

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Part I

Unique Gender and Sex Related Physical, Psychological and Physiological Characteristics of Females

1 Considerations of Sex Differences in Musculoskeletal Anatomy Between Males and Females

Kyla A. Petrie, Kimberly Burbank, Phillip S. Sizer, C. Roger James, and Mimi Zumwalt

Learning Objectives
After completing this chapter, you should understand

- sexual dimorphism and how it applies to humans
- sex differences in general morphology
- sex differences in skeletal geometry
- sex differences in collagenous, cartilage, and bone tissue
- sex differences in the upper extremity anatomy and mechanics
- sex differences in the lower extremity anatomy and mechanics
- sex differences in the spine anatomy and mechanics

1.1 Introduction

The musculoskeletal anatomy of women and men is grossly similar yet individually distinctive. Structural differences exist between the sexes, and these differences are due to both environmental and genetic factors. Sex differences in musculoskeletal anatomy can be described in terms of sexual dimorphism, which refers to physical differences in secondary sexual characteristics, such as size or color, between male and female individuals of the same species [1, 2]. Sexual dimorphism is present in many species of birds, spiders, insects, reptiles, fish, and mammals. For example, male pheasants are larger and more brightly colored than female pheasants, female spiders are usually larger than their male counterparts, male deer grow antlers, and males are larger than females in most species of mammals [2]. However, with a few well-recognized exceptions, such as body hair, muscle mass, and breast differentiation, sexual dimorphism in humans is more subtle compared to other species [2]. Yet, most people recognize that men and women exhibit different physical characteristics, including differences in body height, weight, shape, size, constituents, and alignment of the extremities (e.g., pelvic width, body mass distribution, and ligament/tendon laxity) [2–4]. Some of these differences in body structure are widely recognized and ingrained in cultural beliefs and stereotypes. For example, an artist's rendition of a typical man and woman was used to depict the sexes of the human species on the plaque of the Pioneer 10 spacecraft (Fig. 1.1) where the differences in gross structure are evident.

The typical differences in physical characteristics of the sexes are further exemplified by population data. Data from standard growth charts [6] demonstrate typical sexual dimorphic differences, but the division between men and women is usually less than one standard deviation and is age dependent [7]. For example, according to the clinical growth charts provided by the Centers for Disease Control (CDC), girls and boys at the 50th percentile are approximately the same height (usually within 1–2 cm) until puberty. However, beginning at about 14 years, the heights of girls and boys diverge at an increasing rate until the late teen years when growth slows down in both sexes. At 20 years, men are an average of approximately 14 cm taller than women. Similar relationships are documented for body weight, with a relatively small sex difference observed before the age of 14 years and an approximately 12.5 kg difference (men greater than women) at the age of 20 years (Fig. 1.2) [6].

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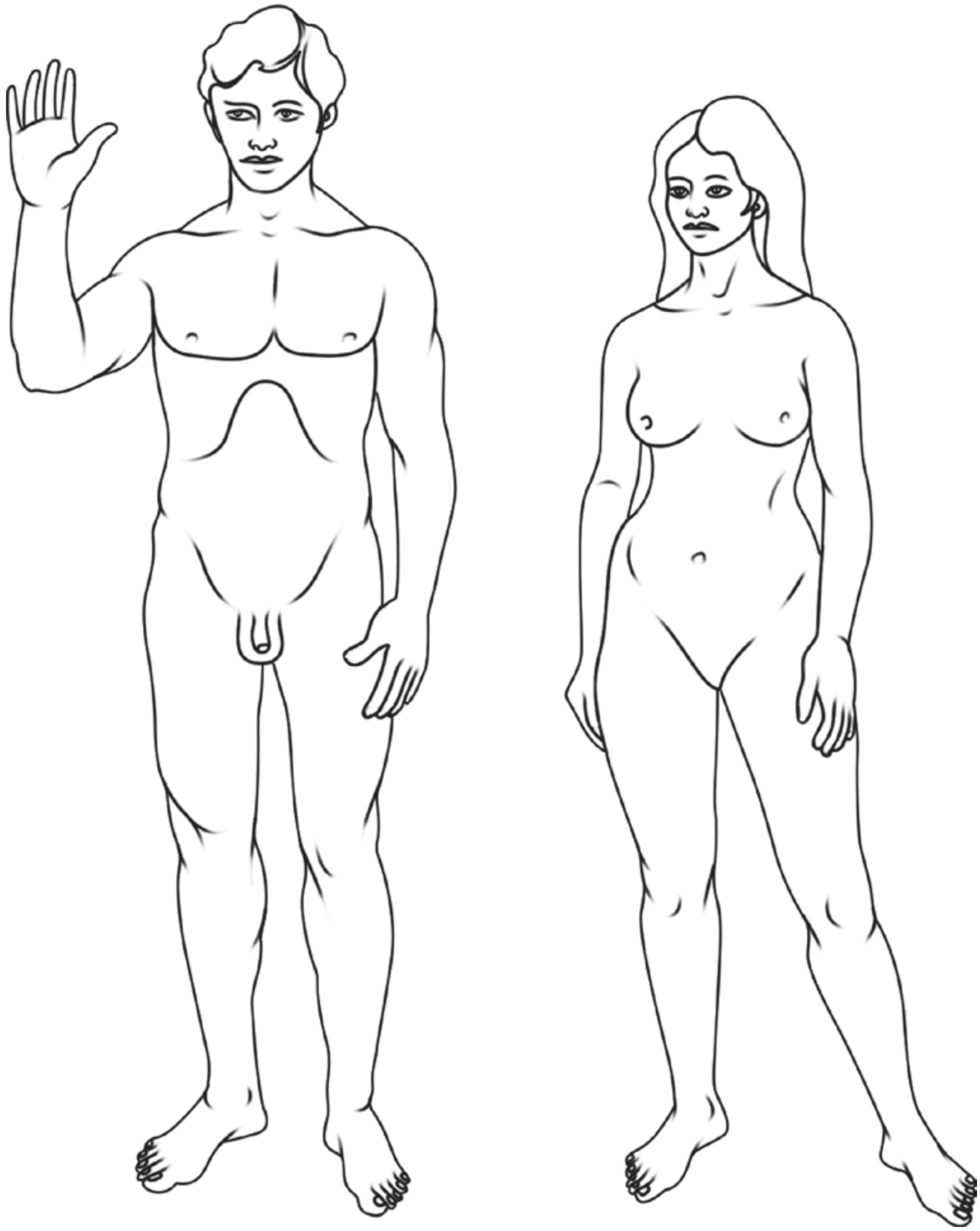

Fig. 1.1 Symbolic representation of men and women as depicted on the plaque of the Pioneer 10 spacecraft in 1972. Source: NASA (https://www.nasa.gov/centers/ames/images/content/72419main_plaquem.jpg) [5]

While sexual dimorphism is apparent in general body characteristics, other sexual dimorphic traits are less obvious. Reports of sex differences in skeletal and soft-tissue components are prevalent in the literature, which not only explain the differences in general appearance but also may influence movement patterns, injury risk, plus the development, and progression of musculoskeletal pathology. Consideration of the sex differences in musculoskeletal anatomy is important for both the general public and health care professionals in order to provide a basis for understanding of normal versus abnormal conditions that may exist. Moreover, a thorough appreciation that men and women have differences in musculoskeletal anatomy may indicate that they have distinctive health care needs. Therefore, the purposes of this chapter are to (1) examine sex differences in the anatomy of selected musculoskeletal components and (2) explore selected regional considerations in female functional patho-anatomy that are pertinent to women's health issues.

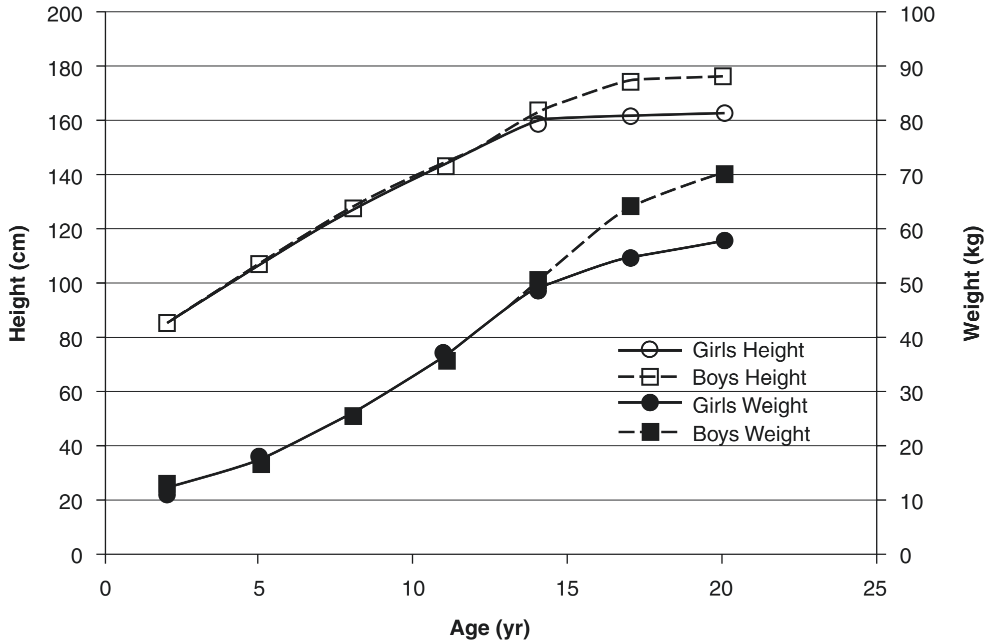

Fig. 1.2 50th-percentile height and weight of girls and boys from 2 to 20 years. Sexual dimorphic differences in height and weight begin to emerge at about the age of 14 years. Values are rounded to the nearest 0.5 cm and 0.5 kg. Adapted from Centers for Disease Control and Prevention, National Center for Health Statistics. CDC growth charts: United States. http://www.cdc.gov/growthcharts/. May 30, 2000 [6]

1.2 Research Findings

1.2.1 Sex Differences in the Anatomy of Selected Musculoskeletal Components

1.2.1.1 Sex Differences in Skeletal Geometry

There are several differences in skeletal geometry between men and women. In sports medicine literature, sex differences in musculoskeletal anatomy, including skeletal geometry, have been reported in context of common injuries that occur in active women and have mostly focused on lower extremity characteristics. For example, differences in size, shape, structure, or alignment of the pelvis, femur, tibia, tarsals, and toes all have been reported [3, 8–12]. Sex differences in the pelvis include a larger inlet and outlet [3], greater interacetabular distance [9], and a greater hip width normalized to femur length [4, 8] in women compared to men. Sex differences in the femur include increased femoral anteversion [4], and some researchers have reported a narrower femoral intercondylar notch width [10, 13] in women. However, other authors have reported no differences in notch width between the sexes [14, 15]. Greater genu recurvatum [3, 12], more lateral patellar alignment [3], increased internal tibial torsion [12], greater slopes of the medial and lateral tibial plateaus [16], plus more bunions and deformities of the lesser toes [3] in women have been reported, as well. Because of the mechanical linkage and interaction among structures of the lower extremity, skeletal differences in one or more interacting structures may result in differences in overall lower extremity alignment. For example, quadriceps angle (Q-angle) is the angle formed by the intersection of a line connecting the anterior–superior iliac spine and the midpoint of the patella with a line connecting the midpoint of the patella and the tibial tuberosity. In the literature, the Q-angle is generally reported to be greater in women than in men [8, 11] and is a function of the structural and alignment characteristics of the involved bones (e.g., pelvic width, patella position, and tibial torsion). Additionally, large deviations in Q-angle have been suggested to contribute to selected knee and foot pathologies [3, 17], although reports are equivocal.

Further evidence supporting the existence of sex differences in skeletal geometry comes from the areas of forensic anthropology and archeology. Scientists from these areas have used knowledge of skeletal sexual dimorphism to determine the sex of deceased individuals from their skeletal remains. A large amount of literature exists, which discusses the skeletal geometric characteristics commonly used and the ability of these characteristics to predict sex. The humerus [18], pelvis [19, 20], femur [18, 21–26], tibia [27–29], talus [30], and calcaneus [30–32] all have been used for this purpose. The ability to discriminate sex based on one or more skeletal geometric characteristics varies somewhat by which bone, as indicated by the percentage of individuals accurately categorized as male or female in the respective studies cited: tibia (96%) [28], femur (95%) [22], calcaneus (92%) [31], pelvis (88%) [20], and talus (81%) [30]. Furthermore, different parameters from the same bone appear to be better discriminators than other parameters [19, 20, 22, 25–27, 32]. For example, some scientists reported that a differing percentage of individuals could be grouped correctly using a discriminant analysis when evaluating different characteristics of the femur. In this study, the femoral head transverse diameter (89.6% of cases correctly categorized) was the best discriminator, followed by the head circumference (87.7%), vertical head diameter (86.8%), condylar width (81.4%), maximum midshaft diameter (72.4%), and maximum length (67.7%). Using a combination of variables (midshaft diameter and head circumference), 91.7% of the cases were classified correctly [25].

The presence and magnitude of sex differences in skeletal geometry appear to be dependent on a number of factors including skeletal maturity [19, 33], environmental stresses (i.e., loading) [18, 22, 24, 29], and genetics (i.e., race) [20–24, 26, 34]. Consideration of these factors is important in establishing sexually dimorphic traits in skeletal geometry. Nevertheless, ample evidence exists to support the presence of sex differences in skeletal geometry.

1.2.1.2 Sex Differences in Musculoskeletal Tissues

In addition to sex differences in skeletal geometry, there are several reported sex differences in musculoskeletal constituents, including collagenous components (e.g., tendon, ligament, skin), cartilage, and bone tissues [35–38]. Collagen is a primary protein of connective tissues in mammals and constitutes more than 30% of the protein in the human body [39]. It provides much of the strength of tendon, ligament, skin, and cartilage [39, 40]. Additionally, it is the main protein component of bone [39, 40].

In collagenous tissues, the collagen molecules align based on stress patterns and provide strength against tensile loads [39, 40]. Some of the reported sex differences in collagen include differences in thickness [35], orientation [35], content [41], diameter [36], volume [37], and metabolism [38] for the specific tissues examined. Some of these sex differences are associated with fiber strength. Moreover, sex differences in collagen degradation have been observed in subjects as young as 2 years of age [38], while other sex differences may not appear until after several decades of life [37]. Many disorders of collagenous tissues (e.g., lupus erythematosus, scleroderma, rheumatoid arthritis, dermatomyositis, and Sjögren's syndrome) have been associated with sex differences. Etiological factors associated with collagenous tissue diseases are thought to exist at many levels (e.g., genetic, cellular, organ, age, behavioral, environmental), but sex hormones are thought to influence the onset and course of these disorders [42].

Sex differences in articular cartilage are reported in the literature [43–46] and have been associated with differences between men and women upon the onset of osteoarthritis [44, 46, 47]. Epidemiological evidence suggests that women are more likely (1.5–4 times at greater risk) to develop osteoarthritis than men [44]. Sex differences in articular cartilage morphology have been reported in children (age 9–18 years), which persist throughout adulthood, and increase during the postmenopausal years [43–45, 48]. Reported sex differences in articular cartilage morphology include greater cartilage volume, thickness, and surface area in male compared to female subjects [43–46]. These differences appear to be partially related to other characteristics such as age, body mass index, bone region, physical activity, and the specific articulation involved [44, 48]. However, research suggests that sex differences remain at some cartilage sites even after adjustment has been made for these other factors [43, 44]. Furthermore, the sex differences in cartilage morphology have been associated with faster cartilage tissue accrual rate in boys compared to girls (i.e., more cartilage tissue early in life) [44] and greater cartilage tissue degradation in older women compared to older men (i.e., greater loss of cartilage later in life) [49].

The presence of sex hormone receptors in cartilage tissue is thought to be an indicator that sex hormones influence these accrual and degradation processes [46, 47, 49, 50]. Evidence for the role of sex hormones in cartilage morphology/metabolism has been demonstrated in both animal [46, 50] and human [49] models. In mice, sex hormones have been shown to influence the inflammatory induction of cartilage degradation via modulation of cytokine production and release in granulomatous tissue [50]. Additionally, male rats have demonstrated higher levels of proteoglycan and collagen, less glycosaminoglycan loss, and greater proteoglycan synthesis than female rats in vitro. Furthermore, cartilage from female rats was shown to have greater susceptibility to degradation when implanted into female rats compared to male cartilage implanted in female rats or both male and female cartilage implanted into male rats [46]. In humans, urinary markers of cartilage degradation have provided evidence that cartilage loss is greater in women than in men. Additionally, cartilage degradation was shown to be greater in postmenopausal women compared to age-matched premenopausal women and less in postmenopausal women undergoing hormone replacement therapy compared to postmenopausal women not undergoing hormonal supplementation [49]. Therefore, sex differences in cartilage morphology/metabolism that exist early in life appear to increase with advancing age and may be explained by the difference in sex hormones.

Sex differences in bone tissue are also reported in the literature [51–54] and have been associated with disparities between men and women in terms of fracture risk [55–57]. Sex differences in bone tissue vary by skeletal site [33, 58] but are reflected by variation in both morphological [33, 52, 55, 57–61] and remodeling [51, 53, 54, 58, 61, 62] characteristics, particularly in osteoporotic individuals [40, 58, 63, 64]. Sex differences in bone tissue are present at an early age [33, 51, 52, 59], persist throughout adulthood [40, 53–55, 61, 62], and diverge even more in older age groups [40, 53, 54, 56–58, 60, 62]. Bone mass accrues during childhood through adolescence then peaks at about the age of 30 years in both men and women [40]. A lower amount of peak bone mass has been associated with a greater risk for osteoporosis in later life; [51] therefore, sex differences in the development of bone tissue during youth may partially explain some of the bone tissue differences between adult men and women. Several factors influence bone mass accrual, including nutrition (e.g., calcium, vitamin D), physical activity, lifestyle behaviors (e.g., smoking), genetic factors (race, sex), and hormonal factors (e.g., estrogen) [63, 65].

In children, serum markers of bone turnover have been reported to change significantly with pubescence in both boys and girls. In girls, these markers were shown to peak at mid-puberty and decrease thereafter; in boys, the markers continued to increase through late puberty. Moreover, the serum markers of bone turnover were overall higher in boys than girls even after adjustment for age, body weight, and pubertal stage [51]. These sex differences in bone turnover more than likely influence differences in peak bone mass [51], volumetric bone mineral density [52], selected measures of bone area [33], cortical thickness [33], plus ultimately compressive [52] and bending [59] strength. However, some authors have suggested that sex differences in some of these characteristics can be explained by differences in anthropometric dimensions (e.g., height and total lean body mass) [59].

In adults, there are several reported sex variations in bone tissue. Differences between men and women have been reported in bone mineral density (men greater than women) [60], peak bone mass (men greater than women) [40], cortical thickness (men greater than women) [55], age-dependent hormonal responsiveness of osteoblasts (less responsiveness in older cells from women when compared to older cells from men) [53], bone turnover (men greater than women) [61], and bone strength (men greater than women) [40, 55]. In older adults, sex differences in bone mineral density [56, 58], cross-sectional area [56], cortical thickness [56], bone width [56] and strength [40, 56, 60] remain considerable, with some variance (i.e., bone mineral density and strength) further diverging as compared to younger adult values [40, 56]. Furthermore, many of these sex differences do not disappear after adjusting for anthropometric factors such as height and weight [56].

The role of sex hormones in the loss of bone mass in older women has been explored widely in the literature. It is well known that a decrease in estrogen production following menopause is a primary contributing factor to the accelerated loss of bone mass in older women when compared to older men [63, 64]. However, older men also lose bone mass and are at greater risk for hip and vertebral fractures compared to younger men [54]. Even though men do not experience a physiological event comparable to menopause and, therefore, do not undergo a substantial decline in total serum testosterone or estrogen, some evidence suggests that a reduction in the bioavailable estrogen (non-sex hormone-binding globulin bound) might explain the loss of bone mass in both women and men [54].

1.2.2 Selected Regional Considerations in Female Functional Pathoanatomy

1.2.2.1 Upper Extremity

Shoulder

Sex-based anatomical differences of the shoulder complex are tissue and pathology specific. For example, a group of researchers [66] observed significant differences between men and women in the distribution of the articular branch of the axillary artery, which may influence decisions made during shoulder surgery. Differences have been associated with the incidence of external impingement of the shoulder. While women appear to have less prominent coracoid processes [67], no sex-based differences have been found in the role of the coracoid process in subscapularis impingement [68]. However, differences in the role of the acromion with external impingement have been observed. Historically, Bigliani [69] classified the acromial shape into three types. Type I processes are flat, Type II are curved, and Type III are hooked. This orthopaedic surgeon suggested that these differences could lend to the incidence of impingement and any subsequent rotator cuff tearing. Later, he and his coinvestigators [70] reported that 78% of all full-thickness rotator cuff tears were associated with a Type III acromion. More recent investigations have reported an increased incidence of full-thickness rotator cuff tears in women versus men [71]. Selected investigators have suggested that acromial differences are acquired, resulting from altered tension loads imposed by the coracoacromial ligament and deltoid insertions [72]. Another group of researchers [73] observed that Type III acromion was more common in female patients and discovered that Type II acromion was related to adaptive shortening of the glenohumeral joint posterior capsule.

Although external impingement has been associated with sex and age, the relationship between age, sex, and incidence of acromial type is controversial [73–75]. More recently, investigators have suggested that while the changes of the inferior surface of the acromion increased with age, they were not different between sexes [76]. However, investigators have observed limited sex-based differences in the acromiohumeral distance with the shoulder at rest, where women exhibited a narrowed space compared to men [77]. The influence of gender-based differences in scapular position at rest on impingement pathology needs further exploration, where women appear to demonstrate less scapular protraction versus their male counterparts [78].

Although men appear to experience more frequent anterior dislocations of the glenohumeral joint [79], women seem to be more predisposed to glenohumeral instability [80]. This disparity appears to be related to the notion that not all joint instability results in dislocation, where grade I and II instabilities represent increased motion and possible humeral head perching on the anterior labrum, versus frank dislocation of the head from the glenoid cavity in grade III [81]. While glenoid fossa inclination appears to influence instability incidence [82], few sex differences in this architectural feature have been noted [83]. Recently, investigators found that women differ from men because the shape of their glenoid fossa is more oval, more inclined, and exhibits deeper anterior glenoid notches [84]. Although the woman's predisposition appears to be more related to increased anterior capsular laxity and resultant hypermobility along with decreased joint stiffness [80], further research is merited for studying the relationship between these architectural findings and the onset and persistence of glenohumeral pathology.

Finally, women between the ages of 40 and 60 years are more predisposed to developing idiopathic capsulitis [85]. This condition is associated with increased thickening of the anterior–superior joint capsule at the coracohumeral ligament [86], along with a noninflammatory synovial reaction in the proximity of the subscapularis tendon [87]. These changes demonstrate active fibroblastic proliferation accompanied by tissue transformation into a smooth muscle-like contractile tissue phenotype that is similar to Dupuytren's disease [88].

Elbow

Women appear to be at greater risk for developing tennis elbow due to tendinosis that emerges from mesenchymal changes in the collagenous constituents of tendons [89]. Tennis elbow tendinosis is a degenerative condition, typically lasting greater than 12 months in duration, is more likely noninflammatory in nature [90], and affects one of four possible different regions of the tendinous insertions into the lateral elbow. The tendons at risk are specifically located about the lateral epicondyle of the distal humerus. The extensor carpi radialis longus (ECRL) originates on the distal 1/3 of anterior supracondylar ridge, possesses almost no tendon at the origin, and demonstrates an immediate transition into muscle. The extensor carpi radialis brevis (ECRB) starts from a 5 mm by 5 mm square area on the superior surface of the lateral epicondyle (10% of origin) along with collagen/fascial layers of intra-compartmental septa that share fascia with the extensor digitorum communis (EDC) coursing distally to the second and third metacarpals, especially fascia associated with third metacarpal. Thus, resistive wrist plus resisted extension of the second and third metacarpophalangeal joints may be suggestive of tendinopathy at either the EDC or ECRB. The ECRB tendon is juxtaposed between the muscle bellies of ECRL and EDC. This common physical finding merits palpatory discrimination between the two regions for a differential diagnosis. The ECRB can exhibit tendinopathy at its origin, along the tendon between ECRL and EDC, or at its musculotendinous junction more distally. Finally, the EDC can be found at the anterior surface of the lateral epicondyle. If involved in lateral tendinopathy, resistive extension of the second through fifth metacarpophalangeal joints (MCPJ 4 and 5 differentiates this lesion from pathology involving the ECRB. This condition seldom occurs in isolation but is typically discovered in combination with affliction to the ECRB [91].

The woman's predisposition for lateral elbow tendinosis is increased when her estrogen level decreases, especially after premature hysterectomy (at less than 35 years of age) and/or reduced estrogen levels from other causes [89]. While inflammatory tendinitis involves a chemically mediated inflammation due to tendon injury [89], the tendinosis to which women are more predisposed produces a non-chemically mediated degenerative change associated with long-term repetitive tendon stress [92], resulting in a condition that could persist longer than 12–14 months. This process produces tissue necrosis that manifests as a "moth-eaten" appearance within the tendon [93]. As a consequence, the tendon becomes friable, along with possible associated bony exostosis at the lateral epicondyle [89]. This elbow tendinosis, a chronic condition, can be accompanied by an imbalance between vasodilatory or vasoconstrictive variations [93], substance P, and CGRP proliferation in the vicinity of the affected tendon [93], accompanied by a high concentration of glutamate in the surrounding tissues [94].

Women also appear to be more predisposed to ulnar nerve lesions at the medial elbow as well. The medial elbow anatomy affords three different predilection sites for ulnar nerve entrapment. The nerve first courses under the arcade of Struthers just dorsal to the medial intermuscular septum. Distally, the nerve courses through the cubital tunnel, whose boundaries are the medial collateral ligament complex (ceiling), medial epicondyle (medial wall), olecranon process (lateral wall), and cubital tunnel retinaculum (floor). In selected individuals, the retinaculum is dorsally bordered by the anconeus epitrochlearis muscle that is innervated by the radial nerve and is activated simultaneous with the triceps, lending to possible entrapment symptoms during resisted elbow extension. The retinaculum that courses from the medial epicondyle to the olecranon tightens with passive elbow flexion, which can create nerve entrapment symptoms at end-range passive flexion. Finally, the ulnar nerve must course under the retinaculum between the two heads of the flexor carpi ulnaris. As a consequence, entrapment symptoms may increase during resistive wrist flexion–ulnar deviation as well [95].

Wrist and Hand

Only a few afflictions of the wrist and hand appear to differ between men and women. Tendon pathologies, including tenosynovitis and tendinosis, seem to be more frequent in women [96], but data related to the pathoanatomical and physiological influences on these differences have not been explored. Similarly, carpal tunnel syndrome (CTS) is more common [97, 98] and prolonged [99] in women. However, multiple factors have been elucidated, which may contribute to this difference. The etiology of carpal tunnel syndrome is multifactorial, resulting from anatomical, biomechanical, pathophysiological, neuropathological, and psychosocial influences. Anatomical factors, such as tunnel architecture and volume [100], lumbrical anatomy [101], and the shape of the hamate hook [102], have been associated with CTS. Specific anatomical and anthropometric factors appear to influence a woman's greater predisposition to CTS [103, 104]. Although carpal bone size and scaling do not appear to differ between men and women [105], hand–length ratios, space indices at the wrist, and digital features appear to differ between the sexes [103]. Along with these variations, differences in body mass index seem to predispose women to CTS because increased fatty tissue within the carpal canal leads to increased hydrostatic pressure upon the median nerve [103].

The onset and progression of CTS appear to be related to an increase in intra-tunnel pressure [106]. Different factors tend to raise this pressure, including tunnel space narrowing associated with wrist movements [107, 108], carpal instability [109], increased muscle force production [110], and trauma that produces perineural edema and fibrosis [111]. Women may be more susceptible to these influences versus men, due to reduced available space for the median nerve within the tunnel. The median nerve seems to increase in cross-sectional diameter with sustained repetitive hand movement in women as compared to men [104], thus, compromising the relative tunnel size and potentially increasing pressure within the tunnel in context with the previously discussed factors.

The individual suffering from CTS may experience sensory and/or motor changes, including paresthesias or true numbness that reflects deficits in neurological function. Women have demonstrated greater neurological dysfunction involving the median nerve when compared to men [112, 113]. However, controversy exists over the value of neurophysiological testing for the diagnosis of CTS [114]. Orthodromic median sensory latency is typically prolonged with CTS patients [115], and median nerve motor amplitudes are decreased in patients with CTS [113]. Yet, a researcher [116] discovered a poor relationship between electrodiagnostic test outcomes and final symptom consternations. Another investigator [117] found that the difference between the median and ulnar motor latencies was greater in patients experiencing CTS versus controls. The differences appear to be important for the diagnosis of CTS [112].

The presence of autonomic disturbances appears to be associated with a woman's predisposition to CTS [118]. Disturbances in neural function could be related to local sympathetic fiber stimulation and/or brachial plexus irritation associated with the double crush phenomenon, which has been observed in as many as 40% of all patients suffering from CTS [119]. As result, a vasoconstrictive event could lead to decreased perineural microvascular flow along with increased protein leakage from the vascular supply that produces epineural and perineural edema [111], as well as increased endoneural pressure plus ischemia [120], contributing to the symptoms of CTS.

1.2.2.2 Lower Extremity

Hip Joint

Women are at greater risk for both microtraumatic stress fracture [121] and macrotraumatic frank fracture at the hip [122] especially involving the femoral neck [121]. This predilection appears to be influenced by differences in bony architecture about the hip and pelvis [123]. Acetabular depth and femoral head width appear to be less in women versus men [124]. The coxadiaphyseal angle has been reported to be wider in men versus women in selected races, thus, potentially predisposing women to a higher incidence of stress reactions [125]. Women appear to have decreased femoral neck strength versus men, as evidenced by decreased femoral neck cross-sectional moment of inertia (CSMI) [126, 127]. Compressive stress (Cstress), defined as the stress in the femoral neck at its weakest cross section arising from a fall, is higher in women [127]. These features interact with women's altered estrogen level associated with menstrual irregularities [128] and menopause [122], thus, enhancing their fracture risk predisposition. Over the past decade or so, postmenopausal women have relied upon the long-acting, bone density-maintaining effects of bisphosphonate administration for reducing the rate of fragility fractures in this population [129]. However, this benefit has been accompanied by an increase in atypical subtrochanteric fractures at a younger age in response to chronic drug intake [129], especially in Asian females [130, 131]. The risk associated with bisphosphonate use continues to be controversial [132]; thus, comorbidities and management strategies should be assessed when its usage is considered [129].

The outer margin of the hip joint socket or acetabulum is completely lined with the cartilaginous labrum that serves to enlarge the articular surface [133, 134]. The labrum enhances the articular seal, fluid pressurization, load support, and joint lubrication of the hip joint [135] while also possessing a variety of sensory endings important for proprioception and nociception [136]. The labrum is vascularized in a fashion similar to the meniscus in the knee, where the outer periphery receives good vascularization, and the inner margin is lacking in blood vessels [137]. The labrum is at risk for traumatic vertical, as well as horizontal, degenerative type tears [134, 138]. The propensity for tears is increased by the deficiencies in the mechanical properties of the labral tissue, especially in women. Labral tissue obtained from male patients is stronger against tensile stress than those from female patients [139]. Moreover, labral degenerative changes may influence those same mechanical properties, adding to the risk of tearing [140, 141].

Labral tears appear to occur more frequently in the superior region of the acetabular structure, due to decreased mechanical properties accompanied by increased demand/load [140, 142]. The superior region of the labrum appears to be less well vascularized, lending to the susceptibility of that area to traumatic and degenerative tears [140, 142]. One significant mechanical contribution to this loading demand is the impact of the femoral neck against this region during full flexion of the hip [141]. Femoral neck architecture also appears to differ between men and women, where increased thickening and decreased coxadiaphyseal angulation of the neck and deformation/fullness of the neck diameter in older women predispose them to anterior acetabular labral trauma, especially when the hip is positioned in full flexion [143]. However, severity of such deformations and changes observed with imaging do not appear to correlate with the incidence of femoral–acetabular impingement and subsequent labral lesions [144], making the clinical examination paramount to diagnosis.

Knee Complex

Little evidence is available to describe sex-based differences in the patellofemoral complex of the knee. One might explain differences in terms of cartilage volume, where the female sex exhibits 33–42% of the variation with women having reduced knee cartilage area versus men [43]. However, T2 MRI examination of young, healthy volunteers did not reveal any sex-based differences in the magnitude or spatial aspect of knee cartilage [145].

Investigators have attempted to describe sex-based differences in terms of patellofemoral contact areas at various positions of knee flexion. In males, some researchers [146] reported larger contact areas of posterior patellar surfaces with the knee flexed to 30°. In addition, they observed a greater change in the female's patellar contact pressures in response to varying vastus medialis activity with the knee positioned at 0°, 30°, and 60° flexion. Although no differences were seen by another group of scientists [147] with the knee in full extension, they did observe larger contact areas in male patellofemoral joints with the knee flexed to 30° and 60°. However, the contact areas were not different when the data were normalized by patellar dimensions of height and width. Subsequently, investigators have turned their attention to the role of hip control deficits while landing in contributing to the development of anterior knee pain syndrome (AKPS), where decreases in eccentric control from the hip external rotators and abductors were shown to be associated with increased AKPS [148]. However, another set of researchers [149] found no relationship between hip control deficits and gender in subjects suffering from AKPS.

More striking is the relationship between sex and knee ligament injury. Injury to the anterior cruciate ligament (ACL) can be a devastating event, and a woman's increased risk for this injury over male counterparts is well documented [150, 151]. It has been reported that 70% of all ACL injuries result from a non-contact mechanism [150, 152], where older girls and women appear to tear their ACL two to eight times more frequently than men [153].

Since the reason for this increased ACL injury risk is unclear, investigators have explored many possible causes including anatomical, hormonal, and mechanical/neuromuscular differences. One of the classic anatomical factors attributed to sex-based differences in ACL injury is the width of the femoral intercondylar or Grant's notch. The intercondylar notch is found in the roof of the space between the femoral condyles, lending a point where the ACL could crimp up, stretch, or tear during forced rotational non-contact loading [151]. The female knee was once thought to possess a smaller notch versus men, lending them to greater vulnerability for traumatic tears [13, 15]. However, other investigators have suggested that increased female risk was based on differences in the ratio between the notch width and width of the femoral condyles (notch width index) [154].

The role of the notch width still remains controversial. Certain scientists [155] have suggested that the narrower notch width in the female knee simply reflects the smaller diameter ACL within the notch, which still must constrain the same relative loads and stresses as the male ACL. The difference in ACL diameter, along with an increase in creep deformation under sustained loading [156], subsequently renders this ligament susceptible to greater injury potential in female athletes. Some researchers [157] found no differences in notch width characteristics between the sexes, and other clinicians [14] suggested that any individual with a smaller notch width is at higher risk for injury, regardless of sex. More recently investigators have suggested that different regions of the notch may vary in width, where women appear to demonstrate greater narrowing at the base and middle of the notch versus their male counterparts. To delve into this issue further, these scientists turned to MRI three-dimensional (3D) notch volume analysis to better describe differences. They subsequently found that males exhibited a larger 3D notch volume versus females, furthering the dis-