# Image-Based Musculoskeletal Modeling: Applications, Advances, and Future Opportunities

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Computer models of the musculoskeletal system are broadly used to study the mechanisms of musculoskeletal disorders and to simulate surgical treatments. Musculoskeletal models have historically been created based on data derived in anatomical and biomechanical studies of cadaveric specimens. MRI offers an abundance of novel methods for acquisition of data from living subjects and is revolutionizing the field of musculoskeletal modeling. The need to create accurate, individualized models of the musculoskeletal system is driving advances in MRI techniques including static imaging, dynamic imaging, diffusion imaging, body imaging, pulse-sequence design, and coil design. These techniques apply to imaging musculoskeletal anatomy, muscle architecture, joint motions, muscle moment arms, and muscle tissue deformations. Further advancements in image-based musculoskeletal modeling will expand the accuracy and utility of models used to study musculoskeletal and neuromuscular impairments.

**Key Words:** skeletal muscle; biomechanics; human movement; muscle architecture; magnetic resonance imaging; dynamic imaging; musculoskeletal modeling

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THE OUTCOMES OF SURGERIES to correct disabling movement abnormalities are unpredictable, and sometimes unsuccessful. Theoretically, patients' abnormal

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movement patterns can be improved by identifying the biomechanical factors that contribute to abnormal movement and designing treatments accordingly. However, many factors can contribute to the abnormal movement. For example, persons with cerebral palsy exhibit disturbances in voluntary control (1), muscle spasticity (2), static muscle contractures (3), bone deformities that alter muscle paths (4), and limb malalignment (5). Current diagnostic methods do not allow clinicians to reliably differentiate between the potential causes of abnormal movement to determine the most appropriate treatment.

We believe that computer models of the musculoskeletal system can help provide a scientific basis for treating movement disorders. Models allow us to answer "what if" questions, isolate individual sources for impairment, and estimate parameters, such as muscle forces, that are difficult to measure experimentally. In recent years, computational models that characterize the three-dimensional surface geometry of bones, kinematics of joints, and the force-generating capacity of muscles have emerged as powerful tools for investigating muscle function. Models have been used to simulate orthopedic procedures, such as osteotomies (6,7), tendon transfers (8-11), tendon lengthenings (12,13), and total joint replacements (14-16). Musculoskeletal models, combined with dynamic simulation, have been used to understand normal (17) and pathological human movement (18).

These model-based studies have provided clinically useful insights and general guidelines; however, the results may have limited applicability to the treatment of individual patients. There have been limited sources for data that can be used to create musculoskeletal models and to test the predictions made by simulating treatments. The input parameters are typically based on an accumulation of cadaveric measurements from a range of studies. The predictions made by musculoskeletal models are tested with average data from unimpaired adult populations. These traits pose two important problems for using models to study individual patients.

First, the models generally represent the musculoskeletal anatomy and function of average adult subjects [e.g., Delp et al (19)]. It is not clear how musculoskeletal deformities or even simply variations in size

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and age might affect the conclusions drawn from analysis of these "generic" models. For example, how might bone deformities in children with cerebral palsy affect the anatomy and therefore function of muscles? How might altered joint kinematics in osteoarthritic knees affect the moment arms of muscles during walking? Advanced imaging techniques, combined with novel computational methods, will allow for creation of individualized models, enabling us to answer these questions.

Second, the models make several simplifying assumptions to accommodate the limited sources of data. For example, models generally assume that all fibers within muscle shorten uniformly [e.g., Zajac (20)]. Is this assumption warranted? Do some muscles shorten uniformly and others not? Dynamic imaging techniques provide an opportunity to answer these questions (21). These new sources for data have also motivated a new class of models that describe the detailed internal mechanics of muscle tissue (22). These issues may be particularly important when using models to study neuromuscular or musculoskeletal disorders, which often lead to alterations in muscle tissue properties.

In this review, we will discuss how several MR imaging techniques offer new types of in vivo data that will lead to a new pipeline for image-based musculoskeletal modeling. We will summarize image-based characterizations of musculoskeletal anatomy, complex muscle architecture, joint kinematics, muscle moment arms, and muscle tissue deformations. We suggest areas for advancement and opportunity where MR imaging can be applied directly to validating, improving, and creating new models of the musculoskeletal system. Musculoskeletal models have broad applicability and have been used to study stroke (23), spinal cord injury (24,25), osteoarthritis (26), and sports injuries (27,28). This review focuses on imaging in the context of creating musculoskeletal models that are used to study human movement. We refer the readers to other reviews that describe related applications in cartilage and ligament imaging and modeling (29-32).

# THE TRADITIONAL AND FUTURE PIPELINES FOR MUSCULOSKELETAL MODELING

Developing accurate models of the musculoskeletal system is challenging because of the intrinsic complexity of biologic systems. For example, the forces produced by muscles depend on their activation, length, and velocity. Muscles have complicated three-dimensional geometry and transmit forces through tendons, which have nonlinear properties. Tendons connect to bones that have complex shapes and span joints that have complicated kinematics.

Traditionally, the inputs to a musculoskeletal model (33) include three-dimensional bone surface geometry, mathematical descriptions of joint kinematics, parameters describing each muscle's path geometry (defined for a range of joint motions), and muscle architecture (which define the force-generating capacity of each muscle), all of which are typically derived from cadaveric studies (Fig. 1a). Bone surfaces are described as

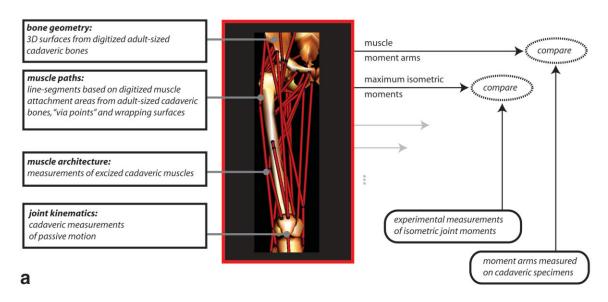
three-dimensional polygonal surfaces that have been obtained by manually digitizing or scanning cadaveric specimens. Joint models describe the transformations that relate the position and orientation of one bone to another. Some joints can be represented as a simple hinge (e.g., the elbow), whereas other joints involve three-dimensional sliding and rotation motions (e.g., the shoulder). It is challenging to determine the complex kinematic relationships for joints using external marker systems; therefore, most existing descriptions of joint kinematics are based on cadaveric studies. The path geometry of a muscle is generally characterized by a series of points that are connected by line segments. A minimum of two points (corresponding to the muscle's origin and insertion) is required to define a muscle path. To characterize muscle architecture, models generally represent the length of the muscle fibers, the length of the tendon, the orientation of the fibers with respect to the tendon, and the maximum force in the muscle (20); these parameters are also derived from cadaveric studies.

Once the model is created, one can estimate muscle lengths, moment arms, muscle forces, and joint moments for any arbitrary set of joint positions, providing a powerful tool to study how muscles generate movement. At this stage, models are evaluated by 1) comparing muscle moment arms with cadaveric measurements of moment arms [e.g., Buford et al (34) and Murray et al (35)] and 2) comparing maximum joint moments with experimentally-measured joint moments [e.g., Nemeth et al (36) and Buchanan et al (37)].

With the integration of MR imaging techniques into the pipeline for musculoskeletal modeling, more individualized, detailed, and accurate models have begun to emerge (Fig. 1b). For example, the introduction of new input data—three-dimensional descriptions of muscle surface geometry—has allowed for more detailed representations of muscle geometry and architecture. By creating volumetric finite-element representations of muscle from the surface data, combined with description of the nonlinear stress-strain behavior of muscle tissue, a new formulation for representing muscle shape, geometry, and force was developed (38). This is a valuable advancement from simply representing muscles as a series of line segments because line segment approximations frequently make inaccurate assumptions about how a muscle changes shape as it interacts with underlying muscles, bones, and other structures as joints move. Volumetric finite-element representations of muscle have motivated the use of diffusion tensor imaging to characterize the three-dimensional arrangement of muscle fascicles and dynamic imaging techniques to characterize the strain fields predicted by three-dimensional muscle models.

The future image-based modeling pipeline will integrate MR measurements to build models as well as to evaluate the predictions made by models. Static MR images will be acquired to evaluate musculoskeletal anatomy of individual patients. Muscles will be defined as three-dimensional volumes and the internal architecture of muscles will be derived from diffusion tensor data. Joint kinematics will be prescribed from in vivo, dynamic, loaded measurements of individual subjects.

## Traditional Musculoskeletal Modeling Pipeline



## Future Image-based Musculoskeletal Modeling Pipeline

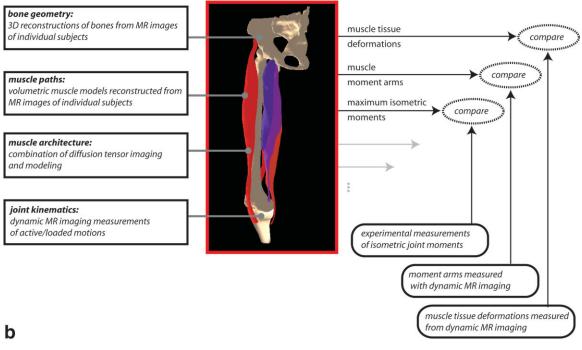


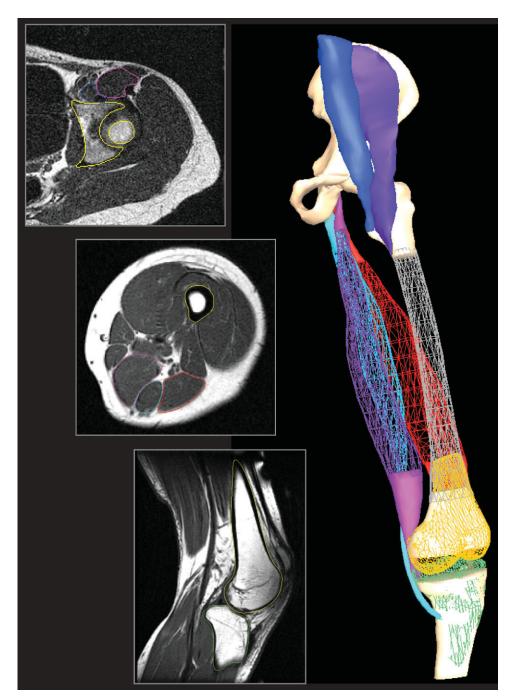
Figure 1. Traditional (a) and future (b) musculoskeletal modeling pipelines. The inputs to a musculoskeletal model have included bone surface geometry, mathematical descriptions of joint kinematics, parameters describing each muscle's path geometry, and muscle architecture, all of which have been traditionally derived from cadaveric studies. Models are traditionally evaluated by 1) comparing muscle moment arms with cadaveric measurements of moment arms and 2) comparing maximum joint moments with experimentally-measured joint moments. The future image-based modeling pipeline will use MR measurements to build models as well as to evaluate the predictions made by models. Static MR images will be acquired to characterize musculoskeletal anatomy of individual patients. Muscles will be defined as three-dimensional volumes and the internal architecture of muscles will be derived from diffusion tensor data. Joint kinematics will be prescribed from in vivo, dynamic, loaded measurements of individual subjects. Models will be evaluated by 1) comparing muscle tissue deformations predicted by volumetric muscle models with tissue deformations derived from dynamic MR imaging, 2) comparing muscle moment arms predicted by models with moment arms measured from dynamic MR imaging, and 3) comparing maximum joint moments with experimentally-measured joint moments.

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In the following sections, we will discuss how imaging has and will enhance our ability to model musculoskeletal anatomy, muscle architecture, joint motion, muscle moment arms, and muscle motion. Each section provides specific examples, discusses the key challenges, and suggests future opportunities for development and research.

# IMAGING AND SEGMENTATION OF MUSCULOSKELETAL ANATOMY

Image-based representations of musculoskeletal anatomy have been created as the basis for models of a variety of musculoskeletal structures (39–46). In general, standard pulse sequences have been used, such as T1-weighted spin-echo imaging, spoiled gradient echo imaging, and proton-density fast spin-echo imaging. Depending on the sizes of the structures of interest, images from multiple imaging series are combined to create a full limb model (Fig. 2). Occasionally, models are created from multiple image planes and merged to provide greater accuracy in particular areas of interest,



**Figure 2.** Reconstruction of muscle and bone surfaces from multiple series of MR images, as described by Arnold et al (39). Surface models of the bones and muscles are generated from two-dimensional outlines that were defined manually in images (left). Surfaces from overlapping series are registered to obtain a representation of the lower limb anatomy at one limb position (right).

such as the articular surfaces of a joint. However, as the field of view and detailed needed increase, imaging times can become longer than is practical in some patient populations.

Manual segmentation of bones and muscles from MR images is an arduous process. In some cases, automatic routines have been used to segment bones (47,48). However, to date, there exists no robust, automatic routine for segmenting muscle boundaries on MR images, because the boundaries between muscles are not well defined. Pulse sequences that highlight fatty tissue improve the appearance of boundaries between muscles, but muscles in some regions (e.g., the forearm) have very little intermuscular fat, making automated segmentation difficult.

Several future developments in imaging have the potential to improve our ability to efficiently and accurately create models of musculoskeletal anatomy. Because the imaging time increases as a result of imaging larger structures, advanced body or parallel imaging techniques applied to imaging the musculoskeletal system would be beneficial. Pulse sequences that distinguish between potential differences in longitudinal and transverse relaxation times or diffusion properties between neighboring muscles could enhance the ability to segment muscles. Advanced post-processing approaches that are tailored to musculoskeletal modeling will further improve the efficiency of extracting muscle anatomy from MR images. For example, Fernandez et al (49) developed a hybrid image-based modeling approach, which predefines a "reference" model and uses a free-form deformation approach to morph a highresolution model to fit a low-resolution model created from MR data.

### IMAGING MUSCLE ARCHITECTURE

Accurate characterization of the arrangement of fascicles within muscle (muscle architecture) is essential for understanding muscle function. Fascicle arrangements can be complex and vary widely across skeletal muscles (50,51). Currently, the standard methods for characterizing muscle architecture are based on cadaveric measurements (52,53) This limits the ability to represent muscle architecture in clinical populations. Fascicle length measurements from each muscle are averaged in most cadaveric studies, giving a single length estimate; therefore, models of muscle generally assume that all fascicles within each muscle have the same length (20). Models of muscle also assume that "pennation angle," defined as the angle the muscle fibers make with respect to the tendon, is constant across all fibers as well. These limitations have motivated a new class of muscle models that provide the ability to represent the threedimensional arrangement of fascicles, not assuming all fascicles have the same geometry. The challenge with these new models is acquiring the data that describe the three-dimensional arrangement of fascicles. Ultrasound techniques have been used to characterize in vivo fascicle orientations and lengths (54,55); however, they are limited to planar measurements and can only be used to study superficial muscles.

Several investigators have proven the feasibility of using diffusion tensor imaging (DTI) to show that the principle eigenvalue extracted from the diffusion tensor is aligned with the direction of fascicles within a muscle [e.g., Sinha and Yao (56)]. DTI, combined with tractography methods, have been used to extract the trajectory of fascicles with mouse skeletal muscle (57). Blemker et al (58) collected DTI data in the human calf, segmented selected muscles within the volume, and used a tractography algorithm to calculate all possible paths within the volume for each muscle (Fig. 3). The paths showed the difference between the lengths and pennation angles of the soleus muscle (a short-fibered pennate muscle) and tibialis anterior muscle (a long-fibered parallel muscle). The major challenge when using DTI to characterize the geometric arrangement of muscle fascicles is that the transverse relaxation times in muscle are relatively short; this limits the signal-to-noise ratio, increases the number of averages needed to minimize noise, and therefore extends the acquisition times.

DTI has the potential to provide input data for musculoskeletal models that are unavailable otherwise. Future developments in applying diffusion tensor imaging and tractography to characterize complex muscle architecture will provide important new data needed to advance our understanding of muscle design and improve muscle modeling.

#### IMAGING JOINT MOTION

Models of joint motion have been derived almost entirely from experimental studies on cadavers [e.g., Walker et al (59)] and external measurements of limb motions [e.g., Andriacchi et al (60)]. However, cadaver experiments cannot robustly replicate in vivo loading conditions, and motion capture techniques are based on surface anatomy and are limited in determining the internal motions of complex joints, such as the shoulder, knee, and wrist.

Using MRI to quantify joint motions has the potential to provide an entirely new and more effective paradigm for measuring motion. Kinematic MRI—that is, acquisition of static images at multiple joint positions—has been applied to studying the mechanics of the many joints (61). For example, Goto et al (62) collected a series of static MR images, and used an iterative closest point algorithm (63) to estimate the complex rotations of the carpal bones during wrist motion. For some cases, like the patellofemoral joint, these "quasi"-static conditions may not reflect the motion of the joint during certain activities where the dynamics are important. Cine phase-contrast (cine-PC) MR imaging has been shown to be a promising tool for characterizing the three-dimensional kinematics of the patellofemoral joint in dynamic conditions (64).

In vivo dynamic measurement of joint kinematics poses several challenges. First, obtaining physiological conditions is difficult within the constraints of a typical 1.5-T bore, both to obtain the weight-bearing loads and full range of joint motions. Gold et al (65) showed the feasibility of using a backrest support in a 0.5T open-MR system to study the knee under physiologic

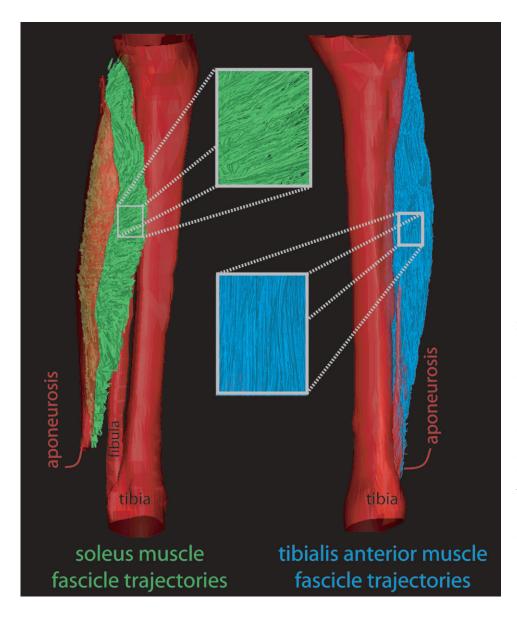


Figure 3. Tractography results that characterized the complex three-dimensional architecture of the soleus and tibialis anterior muscles. As seen in the inset zoom-ins, the soleus fascicles have a large angle with respect to the aponeurosis, and tibialis anterior fascicles run more parallel with the aponeurosis. (Reproduced from Blemker SS, Sherbondy AJ, Akers DL, Bammer R, Delp SL. Gold GE. Characterization of skeletal muscle fascicle arrangements using diffusion tensor tractography, In: Proceedings of the 13th Annual Meeting of ISMRM, Miami Beach, FL, USA, 2005, (Abstract 1539) with permission.)

loads (Fig. 4). Devices such as these are necessary to apply predictable loads and control motion. Choosing a high-quality RF coil that does not restrict motion is also a challenge; therefore, new coil designs that conform to joints and allow full ranges of motion are needed.

Most dynamic images of knee motion have used cine-MR techniques, which require a relatively large number of repeated joint motions, limiting the ability to examine joint motion with substantial loads. Furthermore, since cine MR requires subjects to perform repeatable motion cycles, it cannot be easily used to study patients with neurological or musculoskeletal impairments who have difficulty performing repeated motions. Real-time imaging can greatly expand the opportunity for imaging of joint kinematics. Nayak et al (66) imaged cardiac and vascular flow at 20 frames per second. With further developments, such as implementation of a real-time imaging paradigm in an open-MR system, this technology could allow for rapid and reliable measurement of joint motions during dynamic and loaded movements.

The complexity of the motion of some joints presents a challenge for imaging dynamic joint motion. For example, the motion of the shoulder is complex: the humerus, scapula, and clavicle all move simultaneously in nonorthogonal planes. Multi-slice real-time imaging has great application to imaging dynamic motion of complex joints (67). The problem of tracking bone motion once quality dynamic image data has been collected is also difficult. Some investigators use phase-contrast imaging to encode bone velocities, which can be integrated over time to estimate positions (64). This approach can be problematic, depending on the quality of the images and the complexity of the motion. Registration of three-dimensional models with dynamic images is another approach. The combination of velocity tracking and registration has also provided some promising results (68).

Many recent developments in imaging joint motion show its amazing potential, and we hope that future improvement will involve integration of in vivo joint kinematic information with subject-specific musculoskeletal models.



**Figure 4.** Schematic drawing of a custom MR-compatible back support to image the knee under physiologic loads in an open MR scanner. The support is made of plastic pipes, a sliding mesh backrest, and a water-filled counterweight. The entire back support fits between the two halves of the "double doughnut" GE Signa SP system. The knee is positioned at isocenter. (Reproduced from Gold GE, Besier TF, Draper CE, Asakawa DS, Delp SL, Beaupre SG. Weight-bearing MRI of Pattellofemoral joint cartiledge contact area, J Magn Reson Imaging 2004;20:526-530, with permission of Wiley-Liss, Inc, a subsidiary of John Wiley & Sons, Inc.)

#### IMAGING MUSCLE MOMENT ARMS

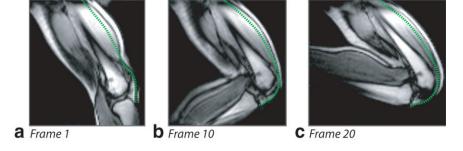
The moment arm of a muscle equals the perpendicular distance from the muscle's line of action to the joint center, and determines the muscle's ability to generate force, produce joint moments, and actuate movement (69). Moment arms are challenging to measure because they may vary substantially with body position and loading condition, especially for muscles that have complex geometry. The standard method for measuring

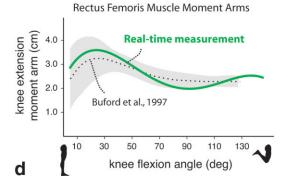
moment arms in cadavers uses the tendon displacement method, which uses the principle of virtual work, where the moment arm of a muscle is the partial derivative of the muscle-tendon length with respect to the joint angle (70). Biomechanics investigators have been using imaging techniques to estimate muscle moment arms for several years (71). Muscle moment arms have been estimated from static MR images (72–74), computed tomography (75), and ultrasound (76). These types of studies have answered questions such as: how does a muscle moment arm change between active and passive isometric conditions (77), and how are knee extensor moment arms affected by patella alta (78)?

Most previous MR-based moment arm measures are based on static acquisitions, limiting the number of measurements and loading conditions. Application of dynamic imaging techniques to measuring muscle moment arms will enable moment arms to be characterized under more physiologic conditions. However, the range of joint motions is limited in a traditional closed bore MR system, and loading conditions are limited by repetitions required by techniques such as cine-MRI. Additionally, robust measurement of moment arms requires the ability to track joint angles and the path of a muscle, which may be complex and move in and out of a single plane.

The future for measuring subject-specific moment arms is to measure muscle geometry during dynamic and loaded motions with real-time MR in open or largebore scanners. Blemker and McVeigh (79) recently demonstrated the feasibility of measuring moment arms over a full range of motion using real-time MRI in a 70-cm bore scanner (Fig. 5). Refining real-time techniques, including multiplanar measurements and adding specialized loading devices will allow for physiological measurements of muscle moment arms. MR-based moment arm measurements will be most powerful

**Figure 5.** Real-time imaging of knee huscle moment arms. Real-time images were acquired in the thigh during dynamic knee flexion-extension (a-c), and knee extension moment arms of the rectus femoris muscle (d) were determined from these images. Green dashed lines in a-c indicate the rectus femoris muscle-tendon length measurement. Knee joint angles were also measured for each frame, and moment arms were calculated through the range of motion. The moment arms are compared with Buford et al (34) (dotted lines correspond to the average values from 15 cadaveric specimens; shaded regions correspond to  $\pm 1$ SD). (Reproduced from Blemker SS and McVeigh ER, Real-time measurements of knee muscle moment arms during dynamic knee flexion-extension motion. In: Proceedings of the 14th Annual Meeting of ISMRM, Seattle, WA, USA, 2006 (Abstract 3619), with permission.)





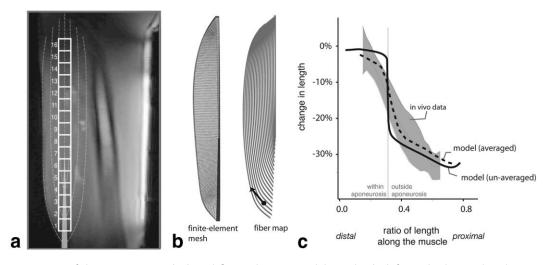
when done in conjunction with the creation of MR-based models so that comparisons between the model and image data can be made.

### IMAGING MUSCLE TISSUE DEFORMATIONS

Dynamic imaging of muscle motion has challenged the simplifying assumptions made in muscle models and provided a valuable source of data for evaluating the next-generation of muscle models. Finni et al (80) used cine-PC MRI to explore the complex deformations of the soleus muscle, and Asakawa et al (81) used cine-PC MRI to characterize the mechanics of muscles following tendon transfer surgery. Similarly, Pappas et al (21) acquired cine-PC images in the biceps brachii muscle during low-load elbow flexion and showed that some regions of the muscle shorten nonuniformly, challenging the commonly made assumption that all muscle fascicles shorten uniformly (Fig. 6). These results motivated the development of a more detailed model of muscle to explore the features of the muscle's architecture that could contribute to nonuniform strains (22). Once developed, and validated with the image data, the model revealed that the arrangement of fascicles within the muscle was a primary reason for the nonuniform shortening. Combining computational modeling and dynamic image data can deepen our understanding of how individual muscle fibers interact and function within whole muscle. Muscle pathologies are often manifested by alterations in fibers (82), connective tissue (83), and passive structures (84). Analyzing muscles using a combination of tissue-level imaging and continuum-level modeling will help us understand how these alterations due to pathology affect muscle function.

Characterizing muscle deformation using dynamic imaging poses several interesting challenges. Cine MR techniques, which require several repetitions, limit the loading conditions and applicability to persons with neurological disorders. Asakawa et al (85) demonstrated the feasibility of using real-time phase contrast MR to measure velocity in the biceps brachii. Similar to challenges in moment arm and joint motion imaging, the size of the bore in traditional imagers limits which muscles and types of motions can be studied. Application of dynamic imaging techniques to large-bore or open-MR systems will also allow for more muscles to be studied over greater ranges of motion.

The ability to accurately determine muscle motion from dynamic images is a challenge, as muscle deformations can be three-dimensional and highly complex. Most investigators have used phase-contrast techniques and numerical integration to track the displacement of specific regions over time. However, these data are averaged over several pixels, displacements are determined by integration through time, and the strains calculated are one-dimensional, so it is difficult to extract the fine resolution displacements and strain fields that are needed to describe the internal mechanics of muscles in detail. MR tagging provides useful visualizations of three-dimensional tissue motion, and has been used extensively to characterize myocardial wall motion [e.g., Declerck et al (86)]. MR imaging with displacement encoding with stimulated echoes (DENSE) directly encodes tissue displacement, and has been demonstrated to provide accurate assessment for three-dimensional strains in myocardial tissue (87). Techniques such as MR tagging and DENSE have the potential to provide the deformation data needed to improve our under-



**Figure 6.** Comparison of dynamic images (21) and finite-element model results (22) from the biceps brachii muscle. Tissue regions of interest in the first cine magnitude image of the cycle ( $\mathbf{a}$ ), and tracked until the elbow fully extended. To compliment the image data, a model of the biceps brachii was built—the model included a finite-element mesh (separating tendon, muscle, and external fascia) and a fiber map that defined the fiber direction for each element ( $\mathbf{b}$ ). Conditions similar to that of imaging experiment were imposed on the model. Changes in length between 1 cm² regions along the centerline of the muscle in the image data (shaded regions, average  $\pm$  1 SD) are compared with changes length between nodes in the model (solid lines) and 1 cm² average regions in the model (dashed lines). The model compares well with the image data ( $\mathbf{c}$ ), and the difference between the averaged and unaveraged models highlights the effects of using averaged regions to calculate strains.

standing of complex muscle motions and rigorously evaluate predictions made by muscle models.

Conclusions drawn from current dynamic measurements of muscle motion are also limited by the fact that it is difficult to accurately measure velocities or displacements within external and internal tendons. External and internal tendons play an important role in muscle mechanics (20), and the mechanics and geometry of tendons are often altered via tendon lengthening and transfer procedures in persons with neuromuscular disorders. Therefore, methods to accurately characterize the motion and deformations within tendon are needed. The key challenge is that tendinous tissue has a low transverse relaxation time, which limits the ability to obtain enough signal to encode or detect motion using cine phase-contrast, DENSE, or tagging. Ultrashort echo-time (UTE) pulse sequences have echo times that are as much as 100 times shorter than most traditional pulse sequences, and can therefore obtain signal in structures, such as tendons [e.g., Robson et al (88)], that have short transverse relaxation times. Extending UTE to dynamic imaging would allow for tendon tissue motion to be characterized and therefore enhance the applicability of dynamic imaging to studying detailed muscle mechanics.

#### CONCLUSIONS

In this review, we highlighted many imaging techniques that allow for capture of the geometry, architecture, motion, and mechanics of the musculoskeletal system. This has, and will continue to, revolutionize the fields of musculoskeletal and movements biomechanics. We provided some examples in each section of how the measurements alone can be used to answer important questions in biomechanics, and discussed how various types of image data can be integrated into a musculoskeletal modeling framework.

These measurements and models become more powerful when they are combined with other types of biomechanical tests or functional assessments. For example, Morse et al (89) combined MR-based measurements of muscle moment arms and volumes with experimental measurements of joint torques, allowing for an integrated study of how the force- and momentgenerating properties of muscle change with aging. In another example, an imaging study was integrated with clinical motion analysis data and MR-based modeling to advance the understanding of the rectus femoris transfer surgery, which is a common treatment for persons with cerebral palsy who walk with a stiff-knee gait (81,90,91). This surgery is designed to convert the muscle from knee extensor to a knee flexor; however, dynamic images acquired in these subjects showed that the muscle still functioned as a knee extensor following surgery. The subjects' postoperative gait analysis showed that many subjects still showed improvements in function from the surgery. This result indicated that the mechanism for improvement in surgical outcomes is not conversion of the muscle's action, but perhaps other effects, such as minimizing its ability to extend the knee-important information for clinicians who design and plan this treatment.

Other areas of imaging not discussed in the previous sections of this review also have application to musculoskeletal modeling. For example, MR elastography has been applied to characterizing the mechanical response of muscle tissue (92–94)—important information that could complement computational models of muscle. Previous investigators have demonstrated the potential utility of this technique; the major future challenge is developing the appropriate postprocessing methods to extract material properties that can be used in models of muscle.

Image-based musculoskeletal modeling will have a broad impact in improving the treatments for a variety of clinical populations. This review has provided several fruitful directions for innovative imaging research that will also serve to accelerate progress toward developing highly individualized musculoskeletal models. Areas of opportunity exist in pulse-sequence design, body imaging, dynamic imaging, diffusion imaging, coil design, and image segmentation, and many of these areas apply to multiple aspects of musculoskeletal modeling.

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### REFERENCES

- Neilson PD, O'Dwyer NJ, Nash J. Control of isometric muscle activity in cerebral palsy. Dev Med Child Neurol 1990;32:778-788.
- Gage JR. Gait analysis in cerebral palsy. London: Mac Keith Press; 1991;221p.
- Tardieu G, Tardieu C. Cerebral palsy. Mechanical evaluation and conservative correction of limb joint contractures. Clin Orthop Relat Res 1987;219:63–69.
- Laplaza FJ, Root L, Tassanawipas A, Glasser DB. Femoral torsion and neck-shaft angles in cerebral palsy. J Pediatr Orthop 1993;13: 192–199.
- Cornell MS. The hip in cerebral palsy. Dev Med Child Neurol 1995; 37:3–18
- Brand RA, Pedersen DR. Computer modeling of surgery and a consideration of the mechanical effects of proximal femoral osteotomies. St. Louis: Mosby; 1984. p 193–210.
- Schmidt DJ, Arnold AS, Carroll NC, Delp SL. Length changes of the hamstrings and adductors resulting from derotational osteotomies of the femur. J Orthop Res 1999;17:279–285.
- Lieber RL, Friden J. Intraoperative measurement and biomechanical modeling of the flexor carpi ulnaris-to-extensor carpi radialis longus tendon transfer. J Biomech Eng 1997;119:386–391.
- Murray WM, Bryden AM, Kilgore KL, Keith MW. The influence of elbow position on the range of motion of the wrist following transfer of the brachioradialis to the extensor carpi radialis brevis tendon. J Bone Joint Surg Am 2002;84-A:2203–2210.
- Herrmann AM, Delp SL. Moment arm and force-generating capacity of the extensor carpi ulnaris after transfer to the extensor carpi radialis brevis. J Hand Surg (Am) 1999;24:1083–1090.
- Delp SL, Ringwelski DA, Carroll NC. Transfer of the rectus femoris: effects of transfer site on moment arms about the knee and hip. J Biomech 1994;27:1201–1211.
- Delp SL, Statler K, Carroll NC. Preserving plantar flexion strength after surgical treatment for contracture of the triceps surae: a computer simulation study. J Orthop Res 1995;13:96–104.

 Delp SL, Zajac FE. Force- and moment-generating capacity of lower-extremity muscles before and after tendon lengthening. Clin Orthop 1992;284:247–259.

- 14. Delp SL, Komattu AV, Wixson RL. Superior displacement of the hip in total joint replacement: effects of prosthetic neck length, neckstem angle, and anteversion angle on the moment-generating capacity of the muscles. J Orthop Res 1994;12:860–870.
- Delp SL, Wixson RL, Komattu AV, Kocmond JH. How superior placement of the joint center in hip arthroplasty affects the abductor muscles. Clin Orthop 1996;328:137–146.
- Piazza SJ, Delp SL. Three-dimensional dynamic simulation of total knee replacement motion during a step-up task. J Biomech Eng 2001;123:599-606.
- Anderson FC, Pandy MG. Individual muscle contributions to support in normal walking. Gait Posture 2003;17:159–169.
- Piazza SJ, Delp SL. The influence of muscles on knee flexion during the swing phase of gait. J Biomech 1996;29:723–733.
- Delp SL, Loan JP, Hoy MG, Zajac FE, Topp EL, Rosen JM. An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. IEEE Trans Biomed Eng 1990;37: 757–767.
- Zajac FE. Muscle and tendon: properties, models, scaling, and application to biomechanics and motor control. Crit Rev Biomed Eng 1989;17:359–411.
- Pappas GP, Asakawa DS, Delp SL, Zajac FE, Drace JE. Nonuniform shortening in the biceps brachii during elbow flexion. J Appl Physiol 2002;92:2381–2389.
- Blemker SS, Pinsky PM, Delp SL. A 3D model of muscle reveals the causes of nonuniform strains in the biceps brachii. J Biomech 2005;38:657–665.
- Higginson JS, Zajac FE, Neptune RR, Kautz SA, Delp SL. Muscle contributions to support during gait in an individual with poststroke hemiparesis. J Biomech 2006;39:1769–1777.
- To CS, Kirsch RF, Kobetic R, Triolo RJ. Simulation of a functional neuromuscular stimulation powered mechanical gait orthosis with coordinated joint locking. IEEE Trans Neural Syst Rehabil Eng 2005;13:227–235.
- Paul C, Bellotti M, Jezernik S, Curt A. Development of a human neuro-musculo-skeletal model for investigation of spinal cord injury. Biol Cybern 2005;93:153–170.
- Gill HS, O'Connor JJ. Heelstrike and the pathomechanics of osteoarthrosis: a simulation study. J Biomech 2003;36:1617–1624.
- McLean SG, Su A, van den Bogert AJ. Development and validation of a 3-D model to predict knee joint loading during dynamic movement. J Biomech Eng 2003;125:864–874.
- Manal K, Buchanan TS. Use of an EMG-driven biomechanical model to study virtual injuries. Med Sci Sports Exerc 2005;37: 1917–1923.
- Fleming BC, Beynnon BD. In vivo measurement of ligament/tendon strains and forces: a review. Ann Biomed Eng 2004;32:318– 328.
- 30. Gold GE, McCauley TR, Gray ML, Disler DG. What's new in cartilage? Radiographics 2003;23:1227–1242.
- Lang P, Noorbakhsh F, Yoshioka H. MR imaging of articular cartilage: current state and recent developments. Radiol Clin North Am 2005;43:629–639, vii.
- White LM, Kramer J, Recht MP. MR imaging evaluation of the postoperative knee: ligaments, menisci, and articular cartilage. Skeletal Radiol 2005;34:431–452.
- Delp SL, Loan JP. A computational framework for simulation and analysis of human and animal movement. IEEE Comput Sci Engr 2000;2:46–55.
- 34. Buford WL, Ivey FM, Malone JD, et al. Muscle balance at the knee—moment arms for the normal knee and the ACL-minus knee. IEEE Trans Rehabil Eng 1997;5:367–379.
- Murray WM, Delp SL, Buchanan TS. Variation of muscle moment arms with elbow and forearm position. J Biomech 1995;28:513– 525
- Nemeth G, Ekholm J, Arborelius UP, Harms-Ringdahl K, Schuldt K. Influence of knee flexion on isometric hip extensor strength. Scand J Rehabil Med 1983;15:97–101.
- 37. Buchanan TS, Delp SL, Solbeck JA. Muscular resistance to varus and valgus loads at the elbow. J Biomech Eng 1998;120:634–639.
- Blemker SS, Delp SL. Three-dimensional representation of complex muscle architectures and geometries. Ann Biomed Eng 2005;33: 661-673.

- Arnold AS, Salinas S, Asakawa DJ, Delp SL. Accuracy of muscle moment arms estimated from MRI-based musculoskeletal models of the lower extremity. Comput Aided Surg 2000;5:108–119.
- Besier TF, Gold GE, Beaupre GS, Delp SL. A modeling framework to estimate patellofemoral joint cartilage stress in vivo. Med Sci Sports Exerc 2005;37:1924–1930.
- Chao EY. Graphic-based musculoskeletal model for biomechanical analyses and animation. Med Eng Phys 2003:25:201–212.
- 42. Penrose JM, Holt GM, Beaugonin M, Hose DR. Development of an accurate three-dimensional finite element knee model. Comput Methods Biomech Biomed Engin 2002;5:291–300.
- Pappas GP, Blemker SS, Beaulieu CF, McAdams TR, Whalen ST, Gold GE. In vivo anatomy of the Neer and Hawkins sign positions for shoulder impingement. J Shoulder Elbow Surg 2006; 15:40–49.
- 44. Tate CM, Williams GN, Barrance PJ, Buchanan TS. Lower extremity muscle morphology in young athletes: an MRI-based analysis. Med Sci Sports Exerc 2006;38:122–128.
- 45. Murray WM, Arnold AS, Salinas S, Durbhakula M, Buchanan TS, Delp SL. Building biomechanical models based on medical image data: an assessment of model accuracy. Medical Image Computing and Computer-Assisted Intervention (MICCAI '98) Lecture Notes in Computer Science. New York: Springer-Verlag;1998;1496:539–540
- Blemker SS, Delp SL. Rectus femoris and vastus intermedius fiber excursions predicted by three-dimensional muscle models. J Biomech 2006;39:1383–1391.
- Hoad CL, Martel AL. Segmentation of MR images for computerassisted surgery of the lumbar spine. Phys Med Biol 2002;47:3503– 3517.
- 48. Zoroofi RA, Sato Y, Nishii T, Sugano N, Yoshikawa H, Tamura S. Automated segmentation of necrotic femoral head from 3D MR data. Comput Med Imaging Graph 2004;28:267–278.
- Fernandez JW, Mithraratne P, Thrupp SF, Tawhai MH, Hunter PJ. Anatomically based geometric modelling of the musculo-skeletal system and other organs. Biomech Model Mechanobiol 2004;2: 139–155.
- Alexander RM, Ker RF. The Architecture of Leg Muscles. In: Winters JM, Woo SL, editors. Multiple muscle systems. New York: Springer-Verlag; 1990. p 568–577.
- 51. Lieber RL, Friden J. Clinical significance of skeletal muscle architecture. Clin Orthop Relat Res 2001;383:140–151.
- Lieber RL, Yeh Y, Baskin RJ. Sarcomere length determination using laser diffraction. Effect of beam and fiber diameter. Biophys J 1984;45:1007–1016.
- Murray WM, Buchanan TS, Delp SL. The isometric functional capacity of muscles that cross the elbow. J Biomech 2000;33:943– 952.
- 54. Fukunaga T, Ichinose Y, Ito M, Kawakami Y, Fukahiro S. Determination of fascicle length and pennation in contracting human muscle in vivo. J Appl Physiol 1997;82:354–358.
- Martin DC, Medri MK, Chow RS, et al. Comparing human skeletal muscle architectural parameters of cadavers with in vivo ultrasonographic measurements. J Anat 2001;199:429–434.
- Sinha U, Yao L. In vivo diffusion tensor imaging of human calf muscle. J Magn Reson Imaging 2002;15:87–95.
- Heemskerk AM, Strijkers GJ, Vilanova A, Drost MR, Nicolay K. Determination of mouse skeletal muscle architecture using threedimensional diffusion tensor imaging. Magn Reson Med 2005;53: 1333–1340.
- Blemker SS, Sherbondy AJ, Akers DL, Bammer R, Delp SL, Gold GE. Characterization of skeletal muscle fascicle arrangements using diffusion tensor tractography. In: Proceedings of the 13th Annual Meeting of ISMRM, Miami Beach, FL, USA, 2005 (Abstract 1539).
- Walker PS, Rovick JS, Robertson DD. The effects of knee brace hinge design and placement on joint mechanics. J Biomech 1998; 21:965–974.
- Andriacchi TP, Alexander EJ, Toney MK, Dyrby C, Sum J. A point cluster method for in vivo motion analysis: applied to a study of knee kinematics. J Biomech Eng 1998;120:743–749.
- Shellock FG. Functional assessment of the joints using kinematic magnetic resonance imaging. Semin Musculoskelet Radiol 2003;7: 249–276.
- 62. Goto A, Moritomo H, Murase T, et al. In vivo three-dimensional wrist motion analysis using magnetic resonance imaging and volume-based registration. J Orthop Res 2005;23:750–756.

- 63. Besl PJ, McKay ND. A method for registration of 3-D shapes. IEEE Trans Pattern Anal Mach Intell 1992;14:239–256.
- 64. Sheehan FT, Zajac FE, Drace JE. Using cine phase contrast magnetic resonance imaging to non-invasively study in vivo knee dynamics. J Biomech 1998;31:21–26.
- Gold GE, Besier TF, Draper CE, Asakawa DS, Delp SL, Beaupre GS.
  Weight-bearing MRI of patellofemoral joint cartilage contact area. J
  Magn Reson Imaging 2004;20:526–530.
- Nayak KS, Pauly JM, Kerr AB, Hu BS, Nishimura DG. Real-time color flow MRI. Magn Reson Med 2000;43:251–258.
- Gilles B, Perrin R, Magnenat-Thalmann N, Vallee JP. Bone motion analysis from dynamic MRI: acquisition and tracking. Acad Radiol 2005;12:1285–1292.
- 68. Barrance PJ, Williams GN, Novotny JE, Buchanan TS. A method for measurement of joint kinematics in vivo by registration of 3-D geometric models with cine phase contrast magnetic resonance imaging data. J Biomech Eng 2005;127:829–837.
- Pandy MG. Moment arm of a muscle force. Exerc Sport Sci Rev 1999;27:79–118.
- An KN, Takahashi K, Harrigan TP, Chao EY. Determination of muscle orientations and moment arms. J Biomech Eng 1984;106: 280–282.
- Maganaris CN. Imaging-based estimates of moment arm length in intact human muscle-tendons. Eur J Appl Physiol 2004;91:130– 139
- Rugg SG, Gregor RJ, Mandelbaum BR, Chiu L. In vivo moment arm calculations at the ankle using magnetic resonance imaging (MRI). J Biomech 1990;23:495–501.
- Jorgensen MJ, Marras WS, Granata KP, Wiand JW. MRI-derived moment-arms of the female and male spine loading muscles. Clin Biomech (Bristol, Avon) 2001;16:182–193.
- Wilson DL, Zhu Q, Duerk JL, Mansour JM, Kilgore K, Crago PE. Estimation of tendon moment arms from three-dimensional magnetic resonance images. Ann Biomed Eng 1999;27:247–256.
- Nemeth G, Ohlsen H. Moment arm lengths of trunk muscles to the lumbosacral joint obtained in vivo with computed tomography. Spine 1986;11:158–160.
- 76. Ito M, Akima H, Fukunaga T. In vivo moment arm determination using B-mode ultrasonography. J Biomech 2000;33:215–218.
- 77. Graichen H, Englmeier KH, Reiser M, Eckstein F. An in vivo technique for determining 3D muscular moment arms in different joint positions and during muscular activation—application to the supraspinatus. Clin Biomech (Bristol, Avon) 2001;16:389–394.
- 78. Ward SR, Terk MR, Powers CM. Influence of patella alta on knee extensor mechanics. J Biomech 2005;38:2415–2422.
- 79. Blemker SS, McVeigh ER. Real-time measurements of knee muscle moment arms during dynamic knee flexion-extension motion. In: Proceedings of the 14th Annual Meeting of ISMRM, Seattle, WA, USA, 2006 (Abstract 3619).

- Finni T, Hodgson JA, Lai AM, Edgerton VR, Sinha S. Mapping of movement in the isometrically contracting human soleus muscle reveals details of its structural and functional complexity. J Appl Physiol 2003;95:2128–2133.
- Asakawa DS, Blemker SS, Gold GE, Delp SL. In vivo motion of the rectus femoris muscle after tendon transfer surgery. J Biomech 2002;35:1029–1037.
- 82. Tardieu C, Huet de la Tour E, Bret MD, Tardieu G. Muscle hypoextensibility in children with cerebral palsy: I. Clinical and experimental observations. Arch Phys Med Rehabil 1982;63:97–102.
- Lieber RL, Runesson E, Einarsson F, Friden J. Inferior mechanical properties of spastic muscle bundles due to hypertrophic but compromised extracellular matrix material. Muscle Nerve 2003;28: 464–471.
- 84. Shortland AP, Harris CA, Gough M, Robinson RO. Architecture of the medial gastrocnemius in children with spastic diplegia. Dev Med Child Neurol 2002;44:158–163.
- Asakawa DS, Nayak KS, Blemker SS, et al. Real-time imaging of skeletal muscle velocity. J Magn Reson Imaging 2003;18:734–739.
- 86. Declerck J, Denney TS, Ozturk C, O'Dell W, McVeigh ER. Left ventricular motion reconstruction from planar tagged MR images: a comparison. Phys Med Biol 2000;45:1611–1632.
- 87. Kim D, Gilson WD, Kramer CM, Epstein FH. Myocardial tissue tracking with two-dimensional cine displacement-encoded MR imaging: development and initial evaluation. Radiology 2004;230: 862–871.
- 88. Robson MD, Benjamin M, Gishen P, Bydder GM. Magnetic resonance imaging of the Achilles tendon using ultrashort TE (UTE) pulse sequences. Clin Radiol 2004;59:727–735.
- Morse CI, Thom JM, Reeves ND, Birch KM, Narici MV. In vivo physiological cross-sectional area and specific force are reduced in the gastrocnemius of elderly men. J Appl Physiol 2005;99:1050– 1055.
- Asakawa DS, Blemker SS, Rab GT, Bagley A, Delp SL. Threedimensional muscle-tendon geometry after rectus femoris tendon transfer. J Bone Joint Surg Am 2004;86-A:348–354.
- Gold GE, Asakawa DS, Blemker SS, Delp SL. Magnetic resonance imaging findings after rectus femoris transfer surgery. Skeletal Radiol 2004:33:34–40.
- Bensamoun SF, Ringleb SI, Littrell L, et al. Determination of thigh muscle stiffness using magnetic resonance elastography. J Magn Reson Imaging 2006;23:242–247.
- Dresner MA, Rose GH, Rossman PJ, Muthupillai R, Manduca A, Ehman RL. Magnetic resonance elastography of skeletal muscle. J Magn Reson Imaging 2001;13:269–276.
- 94. Jenkyn TR, Ehman RL, An KN. Noninvasive muscle tension measurement using the novel technique of magnetic resonance elastography (MRE). J Biomech 2003;36:1917–1921.