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Introducing Anatomical and Physiological Accuracy in Computerized Anthropometry for Increasing the Clinical Usefulness of Modeling Systems

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ABSTRACT: Despite recent, important progress, current modeling environments of the musculoskeletal system do not succeed in daily clinical practice. The causes of this failure are multiple but can be summarized in one line: Today, modeling systems do not answer clinical needs and clinical constraints for a variety of reasons (lack of consensus on goals, lack of multidisciplinary communications, lack of effort and resource sharing, etc.). The author wishes to incite the biomedical community to organize and increase the clinical usefulness of results achieved in our field. This article describes the first steps of a discussion on data collection and data processing by proposing a modeling system that would be based on a detailed anatomical database of generic models, which can be customized using patient-specific data. Decision-making support should statistically analyze the final patient model to furnish probabilistic conclusions to clinical teams that can then take further action. The content of this article should then be discussed further to define the final clinical frame to develop through coordinated action organized at the international level.

KEY WORDS: musculoskeletal modeling, 3-D, anatomy, clinical decision-making, Physiome

I. INTRODUCTION

A. Context

For the last two decades, computer modeling showed important progress in the field of virtual simulation related to the analysis of the musculoskeletal system. This progress mainly concentrated on the technological aspects of modeling systems:

- More and more efficient algorithms have been developed to solve theoretical problems;
- current systems can process and register more heterogeneous data simultaneously thanks to the continuously increasing speed of available hardware;
- display technology allows stunning data visualization;
- and, last but not least, bioengineering classes enable young researchers to perform research that aims to enhance understanding of human anatomy and its many functions.

At first view, our current know-how and state-of-the-art technology may appear capable of solving most problems and producing a clinically useful technological frame. However, despite these promising aspects, serious limitations appear once the above progress is applied to the clinical setting. Problems exist for various reasons mainly related to the specific constraints clinicians meet when performing diagnosis or patient follow-ups.

The following text proposes the various components of a research frame that would allow increasing the usefulness of today's simulation systems within a clinical context. Some of these

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components are already available from the literature, others are under development or are yet to be developed. In all cases, serious clinical validation should be performed to determine the level of accuracy one can expect within a clinical context, which is usually much more constrained than the ideal experimental conditions of a research laboratory.

The goal of this article is to serve as a basis for further interdisciplinary discussions that can lead to a definition of clinical needs and long-term goals, and to find a consensus about how to answer these needs by improving the current state-of-the-art technology in the field. The readers can find more details related to the techniques discussed in the references.

B. Statement

Technologies found in modern simulation systems include advanced algorithms and state-of-the-art displays. Throughout the world, many human efforts are daily performed in the development of tools dealing with biomechanical research. Most of these answer some local, practical questions, either at the fundamental research level or, sometimes, at the clinical level. Unfortunately, most of these efforts appear to become useless once exported to other locations where local needs or local resources are different.

This poor transportability of resources (data, protocols, software codes, hardware, people, etc.) can be explained at various levels:

- complexity of the problems to be solved;
- inhomogeneity of the local resources at different locations;
- lack of a common technical language in a field including individuals from various backgrounds (engineers, physiotherapists, physicians, etc);
- lack of standardization;
- lack of optimal communication;
- lack of consensus about the goals to reach;
- and more.

In summary, numerous efforts are currently expended to answer local questions, but, in practice, only a limited number of these efforts are truly useful at a larger scale, especially in clinical practice. Better coordination and collaboration should help to reduce redundant efforts and increase resource sharing.

C. Limitations of Current Modeling Systems in Clinics

Because the above-mentioned recent progress in the field of musculoskeletal modeling allows interesting analyses to be performed at the fundamental level,[1–6] one can either study the relationship between a particular work environment and the position of specific joints and surrounding muscles or analyze the effect of a particular tendon transfer on limb dynamics (Fig. 1).

Unfortunately, these systems also show at least two serious shortcomings that limit their use within a daily clinical program. The first limitation is the lack of extensive clinical validation necessary before integrating any new tool into a clinical environment (we will not describe clinical validation here because it is too specific to national regulations and to the tool to be validated). The second main shortcoming is the difficulty in quickly integrating patient-specific information into the modeling pipeline to obtain the customized results that are needed for diagnosis or patient follow up. The remainder of this article proposes new research ideas to stimulate the field of inquiry and hopefully increase the clinical usefulness of today's available modeling systems. It is also a call to launch a debate about the best strategies for reaching this goal.

D. The Ultimate Clinical Simulation System?

One of the most challenging goals to achieve in biomechanics is found in the clinical analysis of the musculoskeletal system. The following system (Fig. 2) is the fruit of discussions that occurred recently with people from various backgrounds and expertise (mechanical engineers, orthopedists, physiotherapists, motion experts, muscle experts, physiologists, anatomists, radiologists, computer programmers, computer graphic experts, clinicians, academic researchers). Many components found in this description already exist as separate

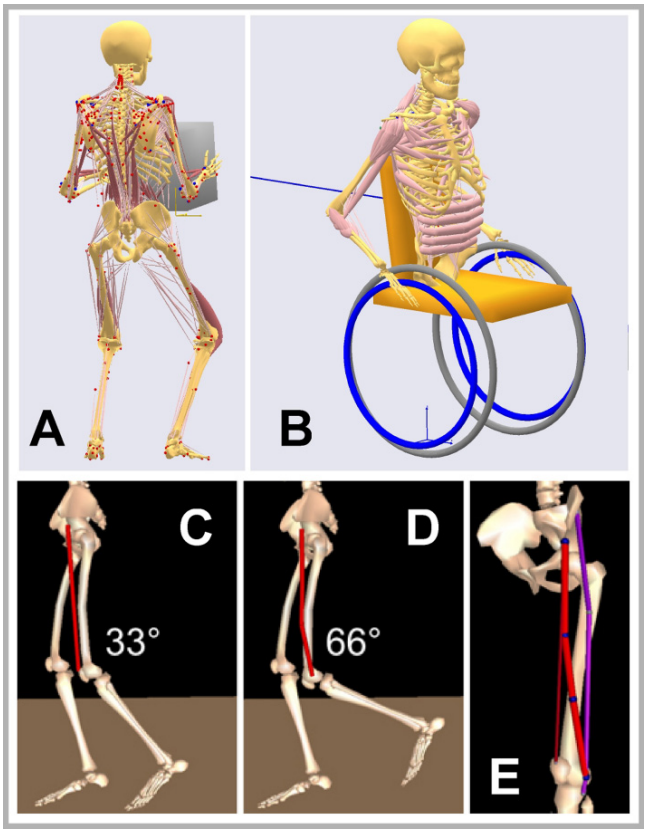

FIGURE 1. Examples of modeling environments used in real-world applications. (**A**) Lifting tasks are among the main occupational risks. Musculoskeletal modeling can analyze the influence of the workplace on the loads of different tissues. (**B**) Wheelchair users might experience shoulder pain. Such modeling can be used to optimize the design of the wheelchair to reduce this problem. (**C**) Simulation-based treatment planning for stiff-knee gait.[6] Stiff-knee gait is characterized by insufficient knee flexion during the swing phase. A muscle-driven simulation that reproduces an individual's gait dynamics can provide a scientific basis for planning treatments—for example, by predicting whether an increase in knee flexion is likely to result (**D**) following rectus femoris transfer surgery (**E**). [Figures 1A and 1B have been provided courtesy of J. Rasmussen (Anybody Research Project, Institute of Mechanical Engineering, Aalborg University, Denmark). Figures 1C, 1D, and 1E have been provided courtesy of A. Arnold (Mechanical Engineering Department, Stanford University, USA).]

entities in the literature. However, this system is yet to be developed through the improvement and combination of these components, as suggested in the remainder of the article. Unfortunately, this creation may not be feasible because of the complexity of the endeavor, unless a truly international and multidisciplinary effort is organized, as explained in the last section.

II. DESCRIPTION OF THE SYSTEM

A. Anatomical Database (*In Vitro* and *In Vivo*) (Fig. 2, Label 1)

The kernel of the system is based on a large and detailed anatomical database entirely collected from validated and objective data collection procedures. Most of the data available from the database would be collected during *in vitro* experiments. Other data, such as gait analysis or electromyography, must be obtained from volunteers during *in vivo* procedures. The following data should be available to produce anatomically sound generic models.

1. Bone Morphology

Bone morphology can be obtained from medical imaging in an accurate way using computerized tomography (CT). Existing segmentation tools perform automated or semiautomated extraction of bone information, and anatomically correct 3-D models can then be constructed and stored in a variety of formats.[7] Spatial resolution of current CT systems allows quality reconstruction of any bony structures and observation of most surface features at the bone surface (Fig. 3A). High anatomical accuracy is necessary if models have to be used for the location of anatomical landmarks, as described later.

Finite element data are requested for fine analysis of structure constraints—both in normal

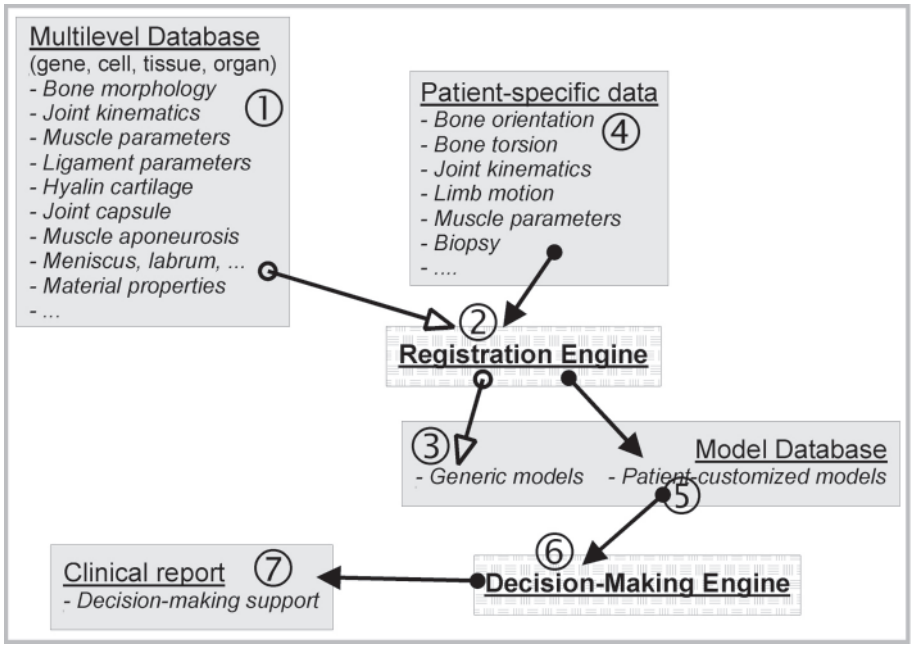

FIGURE 2. Proposal of a clinical modeling system integrating decision-making support (see further subsections for a description of each component and related data): **(1)** Detailed anatomical database, including multilevel data; **(2)** registration engine to associate and combine inhomogeneous data; **(3)** generic models built from **(1)**; **(4)** patient-specific data used to update **(3)** into patient-customized models; **(5)** patient-customized models; **(6)** knowledge-based engine processing model **(5)** for decision-making support. Two research pipelines would interact with each other (empty arrows: fundamental research pipeline; full arrows: clinical research pipeline). Fundamental modeling will create well-validated knowledge and generic models necessary to describe the normal musculoskeletal system. The available patient-specific data will be used to customize the generic models. Results of this customization are then statistically analyzed through a decision-making engine to provide support to clinical teams.

and pathological conditions. Material properties of bone, necessary for that purpose, can be obtained by biopsies or by using bone intensity in CT datasets[8] (Fig. 3B). An understanding of bone microdamage is also possible combining iodinated contrast agents and micro-CT.[9]

Such modeling should be performed for the entire skeleton (Fig. 3C), and the final database should include as many individuals as possible (Fig. 3D) to better represent the numerous anatomical variations found in the human body.

2. Anatomical Landmarks

Location of landmarks is a key element in modeling of the musculoskeletal system for data registration and representation of results according to conventions (local or standardized). *In vitro* protocols can use fiducial markers implanted within the bone segments-of-interest (eg, reflective markers for motion-tracking devices or aluminum balls—Figs. 4A–4C) to characterize bone position and orientation in different heterogeneous datasets before registration.[11] The latter can then be performed using the spatial coordinates of the located markers using, for example, least-squares algorithms.[12]

Despite their usefulness for registration purposes, fiducial landmarks (FLs) cannot usually be used for anatomical representation of results because their location does not correspond to the available standards that are similar to clinical conventions. Therefore, any database related to a modeling system should include spatial coordinates of landmarks as defined by international standards[13-15] to construct anatomically meaningful reference frames. This should also facilitate data exchange and comparison.[16] Anatomical landmarks can be located using virtual palpation directly from

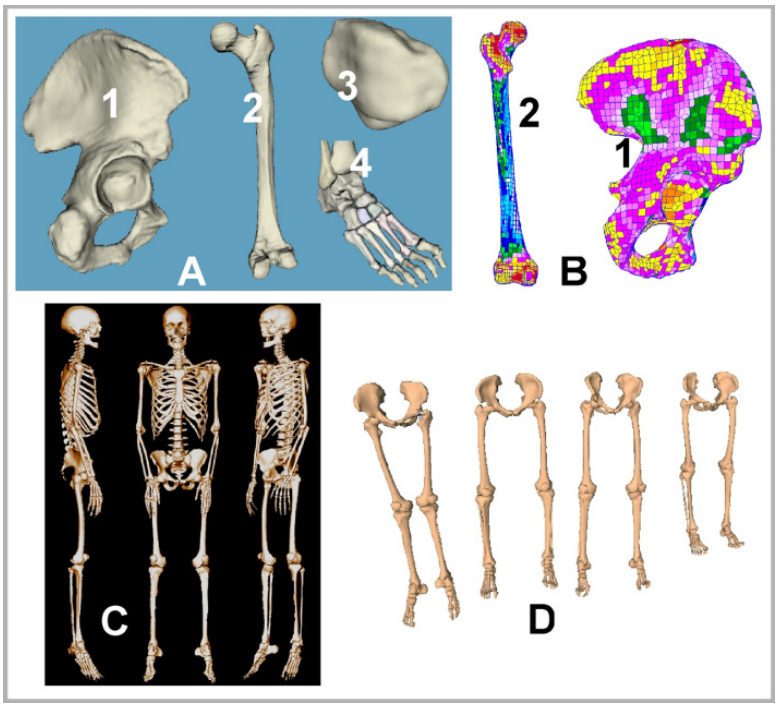

FIGURE 3. (**A**) Detailed 3-D surface model of bones: (1) iliac bone; (2) femoral bone; (3) patella; (4) foot. (**B**) Finite element models. (**C**) Fully segmented human skeleton. (**D**) Models of 4 different pairs of lower limbs. [Figure 3B has been provided courtesy of M. Viceconti (Laboratory for Medical Technologies, Istituti Ortopedici Rizzoli, Italy).] All data were obtained during the VAKHUM project.[10] (Available from: www.ulb.ac.be/project/vakhum.)

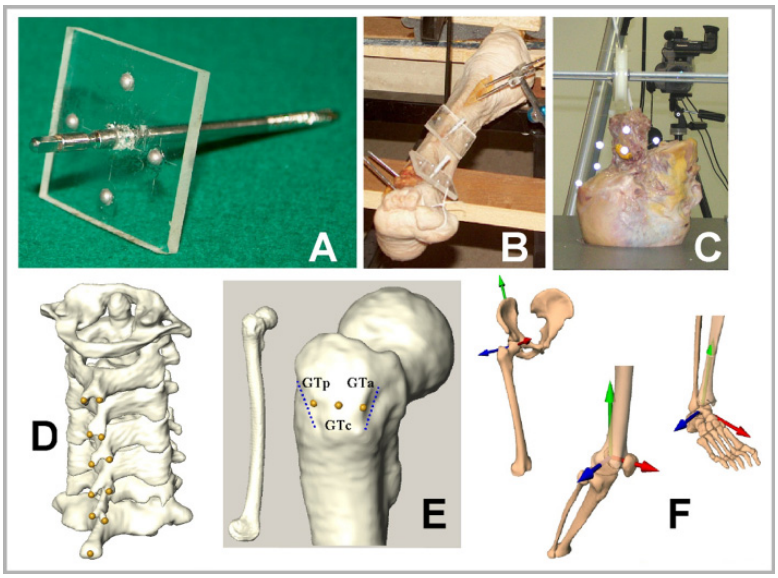

FIGURE 4. Fiducial (FL) vs. anatomical (AL) landmarks. Top row shows FLs. Bottom row shows ALs. (**A**) Aluminum balls inserted in a Plexiglas plate that is mounted on a surgical pin (aluminum is artefact-free in an X-ray field). (**B**) Two pins similar to 1 drilled into both shank and foot of a specimen. (**C**) Cluster of reflective markers inserted into the skull, first vertebra, and second vertebra. (**D**) ALs palpated on 3-D bone models of vertebrae using virtual palpation. (**E**) Virtual palpation of the great trochanter. (**F**) Local anatomical frames obtained from ALs.

3-D bone models obtained from medical imaging[7] (Figs. 4D and 4E) for accurate anatomical description (Fig. 4F). This palpation must be performed according strict anatomical definitions to achieve higher reproducibility.[17] Without detailed definitions, the comparison of results reported in even slightly different reference frames is difficult (Fig. 5). This probably explains why so many contradictory results are found in the literature; indeed, various papers related to similar topics frequently report different results, partly because the anatomical coordinate systems used to represent the kinematic results are dissimilar. Therefore, strict guidelines about accurate and reproducible anatomical landmark palpation must be developed[16] (such guidelines are currently in redaction and should be proposed in the year 2006).

3. Joint Kinematics and Motion Analysis

Joint kinematics describes the intrinsic behavior of a joint. Current data collection procedures (stereophotogrammetry, electrogoniometry) allow good

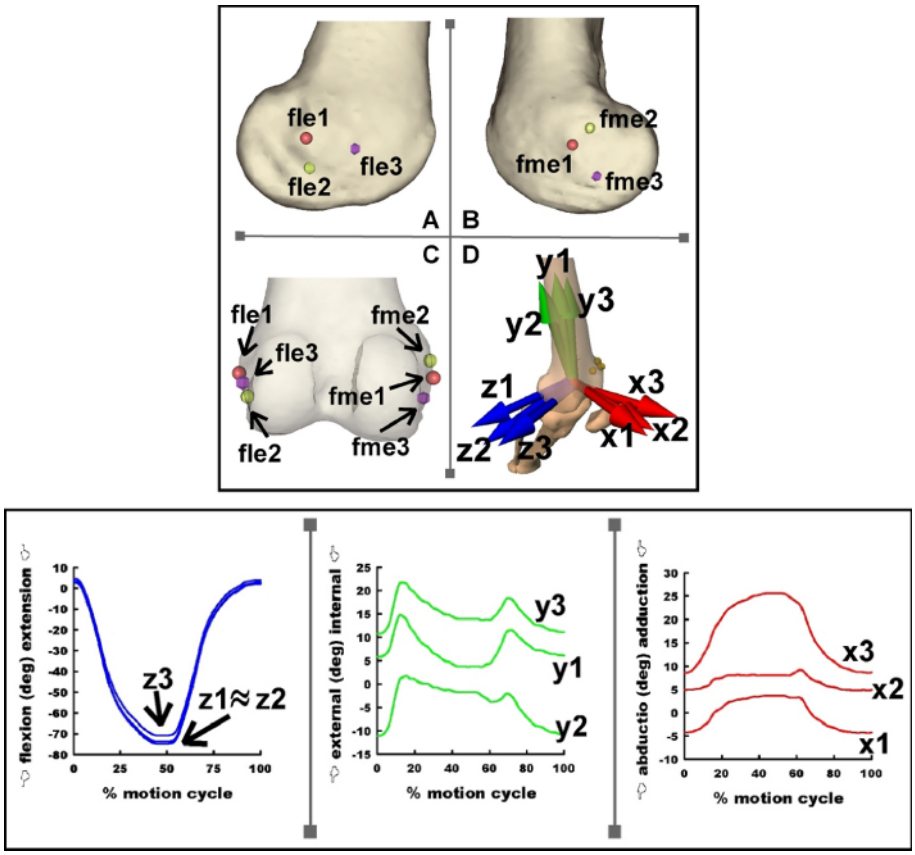

FIGURE 5. Example of discrepancies during motion interpretation to illustrate the need for accurate landmark definitions. (**A**): Lateral view; medial view. (**C**): Anterior view with semi-transparent femoral bone. (**D**): General view. (**A**), (**B**), and (**C**): Location of two anatomical landmarks (FME_i: medial epicondyle; FLE_i: lateral epicondyle) of the distal femoral knee was performed by three different experimenters (i = 1, 2, 3) without using strict definitions. Location discrepancy is observable (average discrepancy < 1 cm and < 2 cm between pairs 1–2 and pairs 1–3, respectively). For each experimenter, the corresponding joint coordinate system (JCS) was then determined (**D**).[18,19] One motion dataset (knee flexion/extension) was obtained using *in vitro* electrogoniometry,[11] registered to the above 3-D models,[11] and represented in each of the three JCSs. *Bottom:* JCSs motion graphs. Motion representation discrepancy did not appear for the main rotational degree-of-freedom (ie, flexion/extension, left graph) but is large for the associated degrees (center graph: internal rotation/external rotation; right graph: adduction/abduction). Observing these graphs in a clinical context would lead to different conclusions, whereas the collected motion dataset was the same in this example.

accuracy (error on orientation and position < 1° and 1 mm, respectively) when used *in vitro*, that is, using invasive protocols.[11] *In vivo* protocol shows lower accuracy mainly due to the interposition of soft tissue between the joint components and the landmarks used to track the motion[17]; therefore, it is advisable to use *in vitro* procedures to collect full 6 degrees-of-freedom (DOFs) data.

In vitro protocols allow invasive procedures to be used by attaching an electrogoniometer rigidly into the bone structure[11] or by drilling a marker cluster into the skeleton during data collection based on stereophotogrammetry analysis systems[20,21] or electromagnetic devices.[22] Combined with medical imaging performed on the same specimen, this method allows the production of an accurate computer simulation of the analyzed joint kinematics (Fig. 6). Anatomically meaningful results can be presented by using virtual palpation on the 3-D models obtained from medical imaging in order to generate motion graphs (Fig. 5). No matter the device used to collect joint kinematics, the obtained 6 DOFs data should represent a required basis for improved analysis of patient-specific data (see below).

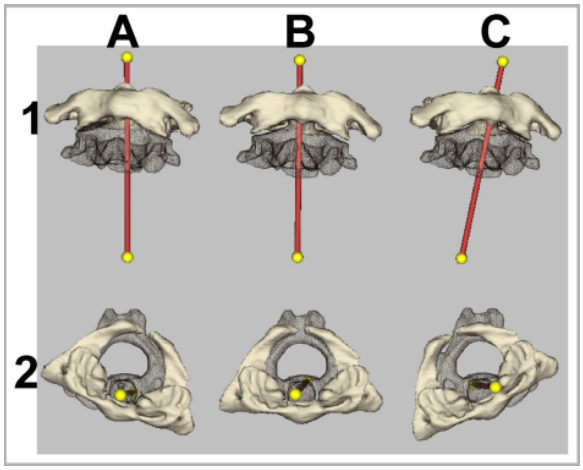

FIGURE 6. Simulation of the joint kinematics of the atlantoaxial joint, that is, between the first cervical vertebra (fully rendered) and the second vertebra (mesh rendered). *Row 1:* anterior view; *row 2:* superior view. *Column A:* right rotation; *column B:* neutral position; *column C:* left rotation. Representation of the instantaneous axis of rotation is also displayed.[23] The experimental data collection setting can been seen in Figure 4C.

Supplementary motion data must also be collected during the analysis of particular tasks (walking, sitting, stair ascending/descending, etc.) that are performed in daily life. If well standardized, this "living" motion database should represent an important normalized population usable for comparison in clinical practice, especially if combined with muscle activity and medical imaging.[24,25]

4. Muscle Parameters

Research in muscle modeling showed great progress over the last decade. Advanced modeling of the musculoskeletal system is now possible and allows researchers to quantify the effect of a tendon transfer or working environment on the dynamics of a limb.[2–6] Numerous physiological muscle parameters are included in these models[26]: origins, insertions, mass, volume, pennation, wrapping points, tendon/muscle fiber ratio, sarcomere length, etc. It has been previously mentioned that results obtained from such systems are valuable for fundamental research.

Unfortunately, these systems are built around generic models that are supposed to represent an acceptable average of the human anatomy. Despite advanced underlying technologies, current systems are unable to generate extensive customized results usable in clinical practice. There are several reasons for these limitations. First, most anatomical data within these systems have not been collected using accurate and well-validated procedures. Furthermore, the above parameters necessary for muscle modeling are frequently not available from one unique source. Researchers in the field must then obtain them from various resources (their own experiments, literature, public or commercial Internet data repositories, etc.) without extensive documentation. It is then up to the developers to find a way to combine the different pieces of the puzzle into one coherent anatomical system. In practice, data combination requires much manual tuning and data editing to achieve "acceptable" results, which are difficult to validate. Another problem is that developing teams are usually not located in premises where extensive data collection can be organized to collect all

necessary data for modeling. Therefore, optimal communication and consensus between the various actors—the data collection team and the developers—is important. Unfortunately, such communication rarely exists. A third problem is due to the numerous disparities found in the human anatomy: At all levels, muscles included, anatomical structures show many individual variations and changes (related to age and gender) that are of importance in explaining physiological differences. Such variations should be represented in modeling environments. Producing enough data to create generic models for all variations is highly utopian. The solution is the creation of customizable models built from well-validated data collection.

Organizing extensive data collection at one location by a large team that encompasses various fields of expertise can solve the first above-mentioned problem. A maximum number of parameters would be collected during the same validated protocol and on the same specimen. A large dataset of naturally linked physiological parameters would then be available for further processing and developments. Such efforts have already been performed[27,28] but were unfortunately limited in scope (also see http://www.fbw.vu.nl/research/Lijn_A4/shoulder/VUstudy_intro.htm). More recently, a feasibility study performed at the Université Libre de Bruxelles (ULB) investigated the possibility of processing a whole specimen (Fig. 7).

The feasibility study presented in Figure 7 is extremely promising but is, unfortunately, still incomplete. Indeed, important parameters such as the sarcomere length and tendon stiffness have not been processed.[29,30] Supplementary protocols to achieve more detailed collection should be put into place. Joint kinematics (see previous section) of the same specimen should also be performed to obtain a final model that would include all requested information needed from musculoskeletal analysis from one unique subject and source.

Processing one specimen will, of course, not solve the problem of the current lack of representation of individual anatomical variations. Specimens of both genders and various ages (children, young adult, elderly) should be processed, probably at various locations, to share this time-consuming effort. It is, therefore, important that collaborations between multiple research departments are organized (this problem is tackled in the last section of this article). This should ensure that the data collection protocol is similar for all partners to facilitate data registration and data exchange.

It is highly probable that not all existing anatomical variations can be directly measured on all specimens because they are too numerous (see a detailed anatomy textbook for a description of anatomical variations). The amount of work would be highly time-consuming. Alternatives should be found in more specialized work regarding which data would be integrated into a general model. For example, supplementary information about the insertion variations of some muscles could be introduced into a full model similar to the one illustrated in Figure 7.

Muscle activity data collected during *in vivo* experiments is also of importance to create a reference database for further dynamics work. For that purpose, electromyography (EMG) associated with motion analysis (see above) should be performed during well-standardized *in vivo* protocols.[31] Unfortunately, EMG techniques are stil lacking accuracy for deep muscles, or within areas where several muscles are close to each others (ie, cross-talk phenomenon). Further work on that specific topic is necessary.[32,33]

5. Intermediate Joint Components, Hyalin Cartilage, Meniscus, Labrum

Current biomechanical musculoskeletal models rarely include full morphological joint data. Joint descriptions are usually limited to the shape of the underlying bone surface. However, joint components are numerous and important to explain particular joint behavior. The components that can be found in a particular joint will depend on the joint type.[34] Joints are usually classified according to the nature of the intermediate element found within the joint cavity, that is, the space between the bony elements articulating to each other. The intermediate element can be bony (eg, between skull bones), fibrous (eg, inferior tibiofibular joint), cartilaginous (eg, costal cartilage), or synovial (the most commun joint type). Anatomically correct modeling should represent this intermediate element if our understanding of joint physiology is to improve.

Synovial joints are covered with hyalin cartilage, which sometimes exhibit a different shape

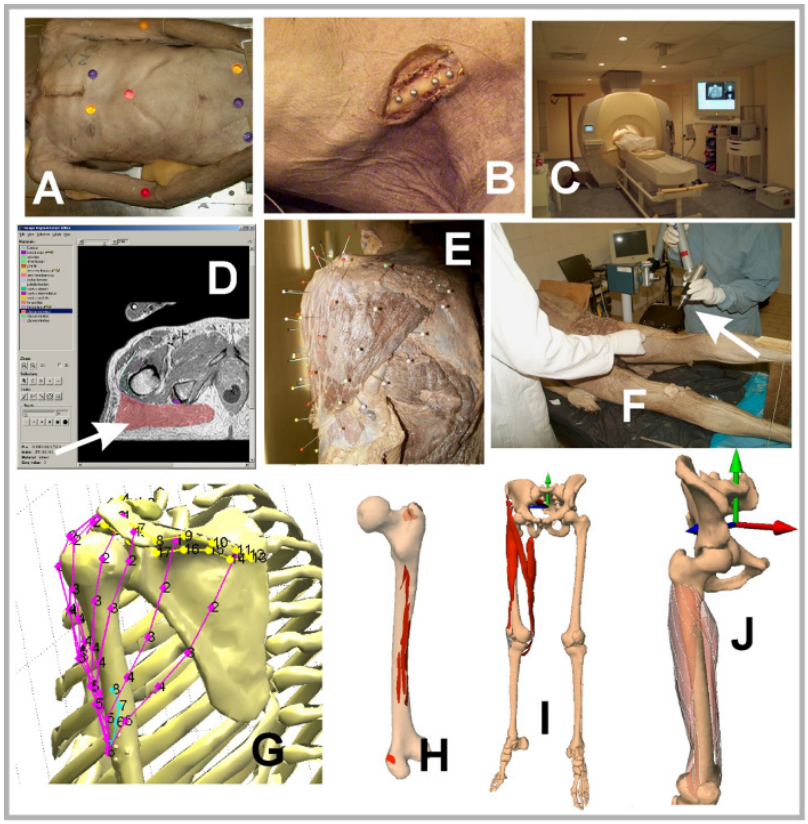

FIGURE 7. Digitization of a full musculoskeletal system (from left to right and from top to bottom). (**A**) A specimen (male, 59 years old) of average size (172 cm) and weight (69 kgs) was selected from the Body Donation program of ULB. No visible problem related to the musculoskeletal system was apparent. Large balls filled with an oily solution were set at different locations on the skin surface. These balls were visible in both CT scan and magnetic resonance imaging (MRI). (**B**) In each major bone (here a left clavicle), four aluminum balls (diameter: 4 mm) were inserted and glued. These balls were visible in the CT scan and remained in place during further dissection. (**C**) Both full-body MRI and CT scan imaging were performed the same day. A special jig ensured that the body position was similar in both medical imaging datasets. (**D**) Slices obtained from MRI allowed extracting information related to muscle volume and location of the oily balls using so-called segmentation operations. On this image, segmentation of the gluteus major muscle is highlighted (see arrow). Each segmented structure was then reconstructed three dimensionally. Segmentation of the CT data (not shown) enabled the attainment of 3-D models of the entire skeleton. Spatial location of all visible balls (oily balls and aluminum balls) was also processed. (**E**) During dissection of the specimen, each dissected muscle (here a left deltoid muscle) was carefully cleaned, and needles were inserted into the muscle following selected muscle fiber paths, including the tendon and the musculotendinous junction (if any). (**F**) The spatial position of each needle inserted into the muscle was digitized using a 3-D digitizer (arrow). The location of the bones-of-interest was also processed by digitizing the aluminum balls glued into those bones. After muscle fiber digitizing, the muscle was removed and its bone origins and insertions were digitized, as well. Weight and volume of each muscle were also obtained. (**G**) Registration of the digitized muscle fiber coordinates with the CT skeleton looks anatomically correct [here the left deltoid muscle shown in (**E**)]. (**H**) Registration of the digitized muscle origins and insertions toward the 3-D skeleton lead to anatomical cartography (view of the posterior aspect of the femoral bone). (**I**) MRI volume models registered with the CT skeleton were also performed (displayed muscles: sartorius, rectus femoris, and gracilis). (**J**) Further processing allows combining MRI volume data with the digitized fiber path and CT skeleton (displayed muscle: vastus lateralis and vastus medialis).

from the underlying bone, and important viscoelastic properties. These joints may also include supplementary structures, such as the meniscus (knee joint) or labrum (shoulder joint, hip joint), which mainly aim to increase joint stability and decrease local joint constraints.

Dissection similar to the one illustrated in Figure 7 allows data collection on structures such

as the meniscus (Fig. 8, bottom). From an imaging point of view, MRI is the best available technology and allows accurate visualization and anatomical representation. Ultrasound also shows potential but needs further development before extensive use within biomechanical applications, mainly to improve registration abilities of ultrasound data and 3-D reconstruction.

Morphological data on hyalin cartilage can be collected by dissection and digitizing, and registered to bone models. Unfortunately, hyalin cartilage is often too thin to be digitized during dissection (eg, cartilage is a few millimeters thick at the hip joint level). Digitizing accuracy is becoming an issue for automated registration ("automated registration" means that no manual human intervention is necessary to correct registration imperfections). A good alternative is found in MRI combined with an injection of contrast agent in the joint cavity (Fig. 9). Special MRI sequences then produce quality data about the hyalin cartilage that can be reconstructed three dimensionally.[35-36] Arthro-CT (ie, CT imaging with contrast agent in the joint cavity) can also be used for that purpose but is less accurate then MRI.[37-40] Recent MRI systems do not need contrast agents anymore, which facilitates cartilage data collection.

If material properties of hyalin cartilage must be assessed, then biopsies at various locations of the cartilage volume must be performed. Indeed, cartilage thickness is not homogoneous,[41] and it can be expected that cartilage mechanical properties might be locally different between high and low loading areas.[36] Viscocity analysis of the synovial fluid should also be performed to analyze its lubrification properties and the mechanism of hyalin cartilage nutrition (ie, the imbibition mechanism).[41,42]

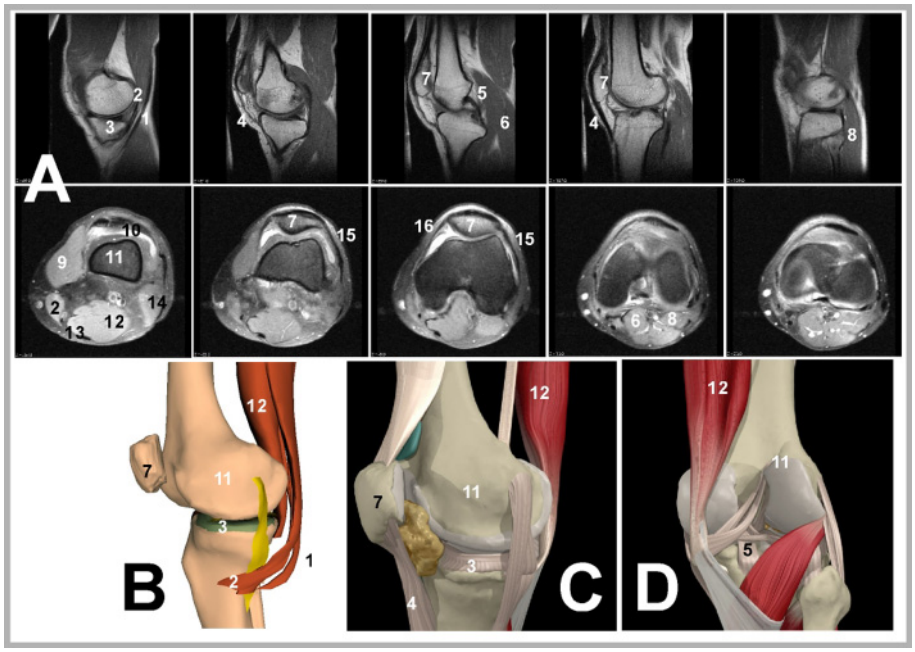

FIGURE 8. Example of soft tissue modeling (right knee joint). (**A**): MRI dataset (sagittal view and horizontal view). (**B**), (**C**), and (**D**): 3-D reconstruction. (**B**) and (**C**): medial view, (**D**): posterior view. (1): semitendinosus muscle (m.); (2): sartorius m.; (3): internal meniscus; (4): patellar ligament; (5): posterior cruciate ligament; (6): medial gastrocnemius m.; (7): patella; (8): lateral gastrocnemius; (9): vastus medialis m.; (10): femoro-patellar joint cavity; (11): femoral bone; (12): semimembranosus m.; (13): semitendinosus m.; (14): biceps cruralis m.; (15): lateral patellar retinaculum; (16): medial patellar retinaculum. (**B**): Bone model has been obtained from CT imaging; muscle modeling was performed using MRI [see (**A**)]; ligament and meniscus modeling was from dissection. All data in (**B**) came from the same specimen (Figure 7) and were registered together. (Figures 8C and 8D have been provided courtesy of © Primal Pictures Ltd. They indicate the results of realistic rendering of data obtained from MRI.)

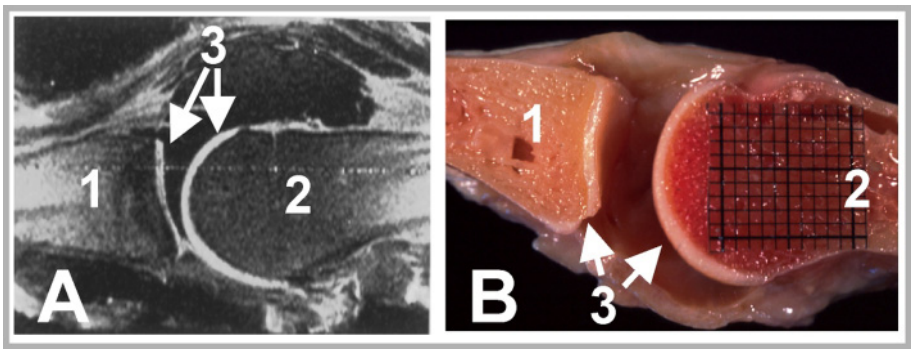

FIGURE 9. MRI imaging with contrast agent (metacarpophalangeal joint). (**A**): MRI used in combination with contrast agent to display the cartilage of a metacarpophalangeal joint (*in vitro* experiment). (**B**): Same specimen as on the left after sawing to obtain sagittal slices for comparison: (1) First phalanx; (2) metacarpal bone; (3) hyalin cartilage. A millimetric scale is displayed, as well.

6. Other Soft Tissue Parameters (Ligament, Joint Capsule, and Muscle Aponeurosis)

Besides muscle information, biomechanical models do not include detailed information on other soft tissues, despite their importance for fundamental and clinical research. Ligaments are important because they keep joints together, and their tension both limits and guides joint motions.[43,44] Accurate joint modeling should therefore include extensive ligament data. Some ligaments are actually reinforcements of joint capsule, and therefore modeling of the latter is interesting to increase our understanding about how important joint capsule architecture is for normal joint physiology. Another anatomical structure, whose role is usually largely underestimated, is muscle aponeurosis. Muscle aponeurosis has two functions: muscle contention and muscle attachment. The first function is probably less important for biomechanical applications, although it can be involved in the clinical context (see below). On the other hand, aponeurosis can host large muscle attachment areas (Fig. 10). However, current models include muscle bone attachments only, and no relationships between muscles and aponeurosis are described, whereas for some muscles, aponeurosis attachment is important. Integrating muscle aponeurosis attachment in musculoskeletal models should improve current modeling systems.

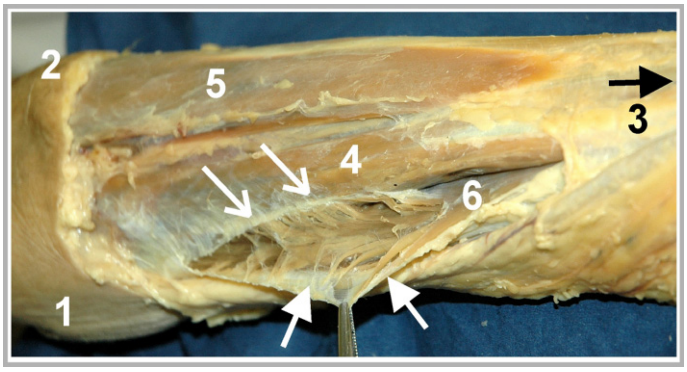

FIGURE 10. Example of large muscle attachment on aponeurosis (left forearm, anterior view): (1) medial epicondyle; (2) lateral epicondyle; (3) towards the wrist joint; (4) flexor carpi radialis muscle (m.); (5) brachioradialis m.; (6) flexor digitorum superficialis m. (Note that no palmaris longus m. was observed on this specimen.) Muscle 6 shows two kinds of aponeurosis attachment on this dissection: on the superficial aponeurosis (closed arrows) and on the aponeurosis shared with muscle 4 (open arrows).

Data collection protocols for aponeurosis are very similar to the above-mentioned tools available for joint components (Fig. 8). MRI allows visualization of collagenic fiber bundles and allows 3-D reconstruction.[45] MRI is certainly necessary for ligaments that are difficult to access by dissection only (such as the knee cruciate ligaments). Ultrasound also shows potential but is limited for the reasons mentioned previously (registration problem). Ligament deformation and ligament tension during a particular motion remain poorly quantified. This can be studied by protocols combining joint kinematic analysis with external devices inserted into the ligaments (Fig. 11).[46] Further registration with medical imaging will be of interest to better understand ligament behavior and its role in joint control.

Limited information related to joint capsule attachments can be collected using dissection. Joint capsules may indeed show complex architecture, for example, the presence of recesses, to allow optimal joint mobility. Accurate data on this architecture can be obtained using arthro-CT (Fig. 12).

Performing data collection for muscle aponeurosis remains a problem. Dissection can be performed but needs aponeurosis to be opened to access the muscle bundles located inside their limits. Such opening often disturbs the anatomical–spatial relationships between both aponeurosis and muscle structures. MRI can also be used for the thickest aponeurosis (Fig. 8). Unfortunately, some aponeuroses are too thin to be correctly identified on a MRI dataset. Ultrasound is probably an alternative, but image interpretation and efficient registration to the bone structure remains a challenge because no tool to help build biomechanical models from such data is widely available.

7. Other Parameters, Documentation, and Standards

The above list of parameters is not exhaustive. For example, future work should also focus on quantifying brain activity during central control of the musculoskeletal system. Genomics and cellular and tissular information could also be included to create a data infrastructure answering the needs of the Physiome initiative.[47]

A key element for optimal data exchange will be the availability of extensive documentation describing the whole data collection and data processing procedure for any data (including full validation and accuracy) and data formats. Standards related to the data formats must also be discussed and adopted. Once the research community agrees on a particular format, the latter must be documented to allow the development of data filters adapting the customized formats to the agreed-upon standards.

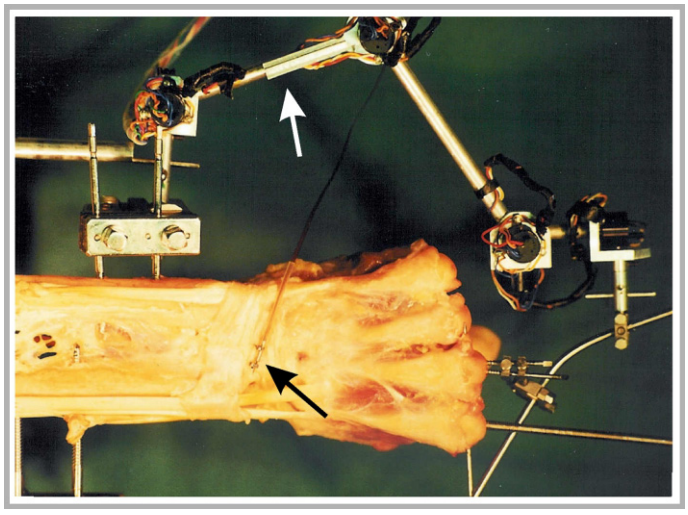

FIGURE 11. Simultaneous *in vitro* data collection of wrist joint kinematics by electrogoniometry (white arrow) and of ligament length changes with differential transducers (black arrow) inserted into the ligaments.[46]

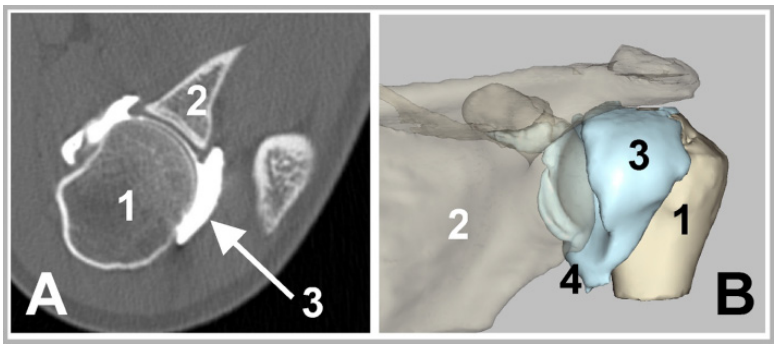

FIGURE 12. Arthro-CT of the shoulder joint: (1) humeral bone; (2) scapula; (3) joint capsule. (**A**) Original CT data (horizontal view). (**B**) 3-D model from data displayed on the left. The scapula is semitransparent (posterior view). The spatial morphology of the joint capsule can be visualized between the scapula and the humerus. Such a model also allows measuring the volume of synovial fluid within the joint. The axillary recess (4) is well observable at the lower aspect of the joint capsule. [Figure 12A: CT image data was obtained courtesy of X. Demondion (Department of Musculoskeletal Radiology, Hospital R. Salengro, CHRU Lille, France).]

In all cases, personal data related to the specimen (gender, age, weight, height, known pathology) must be given in the documentation describing the collected data. It must be stressed that ethical rules at most locations forbid stating the subject's name within the documentation. Subject identification must be organized around a coding system, the key to which must be owned by officially appointed persons (usually the scientist in charge of the data collection coordination).

B. Registration Engine and Generic Models (Fig. 2, Label 2)

Registration is an important element to guarantee that the combination of the available data is accurate enough to obtain anatomically correct and meaningful generic models. Registration is usually based on features available from the various datasets, such as anatomical or fiducial landmarks attached to the structures. In the above example (see Fig. 7), muscle volume obtained from MRI has been registered to a skeleton collected from CT scan using fiducial landmarks. Motion can be registered to a particular 3-D joint model using anatomical landmarks.[48] Other algorithms analyzed the anatomical structure volume to determine the spatial relationships of the datasets to register.[49] Such morphological algorithms can perform registration of various kinds: rigid (including both translation and rotation), scaling and shearing.[50] Spatiotemporal registration of local joint kinematics with motion analysis and 3-D bone morphology has recently been developed for the lower limb[25]: A general motion performed by a subject (eg, walking, sitting) was registered to a 3-D skeleton, including a 6 DOFs mechanism at both knee and ankle joint levels. This method allows combining anatomically accurate *in vitro* 6 DOFs joint kinematics with motion data collected from a volunteer. Application of this method to other joints should be considered. Because the underlying joint behavior of the model is accurate, further determination of muscle excursion and muscle moment arm should lead to more representative results than those obtained from modeling systems that integrated a simplified kinematic representation (Fig. 13).

The above registration procedures are mainly used for inverse kinematics and inverse simulation. Unfortunately, inverse methods require a large amount of heterogeneous data if one wants to solve related questions accurately—for example, "What are joint constraints during a particular motion?" In practice, it is often impossible to collect all required data (eg, in the previous example, the electromyography activity of all muscles crossing the joint of interest), and too many equations must be solved from too few known variables. Therefore, optimization procedures must be used in order to analyze the prob-

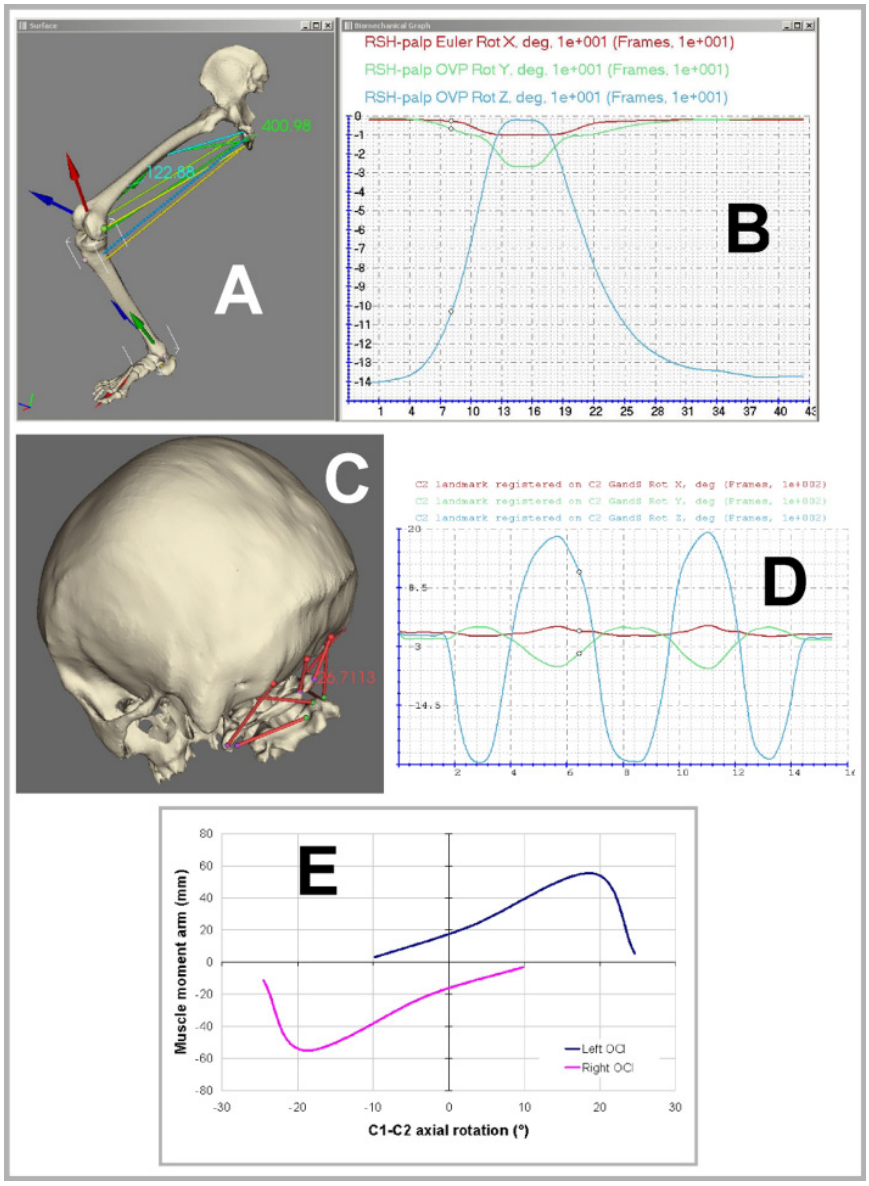

FIGURE 13. (**A**): Registration of 6 DOFs joint kinematics (*in vitro*), motion data (*in vivo*), and CT imaging (*in vitro*).[25] Attachments of the posterior muscles of the thigh have been registered from dissection results and their action lines displayed. On-line length of the action lines are processed during the motion (only two lengths are displayed here). (**B**): OVP representation of the current motion (sitting on a chair) of the shank related to the thigh observable on (**A**) (current motion frame is indicated by a dot on the curves).[51] The modeling system illustrated here is the freeware Data Manager developed by the Multimod project.[52–54] (**C**): Posterior view of a skull and the first two vertebrae: Simulation obtained from setting from Figures 4C and 6.[55] (**D**): Motion curves of the second cervical vertebrea are displayed according to Grood and Suntay convention.[18] (**E**): Moment arm of the obliquus capitis inferior muscle was estimated using the tendon excursion and joint-angle data.[56] (**D**) and (**E**): Same specimen as in (**C**).

lem based on physics-based modeling (direct dynamics).[57,58] Direct solutions prove to be useful in a fundamental research context but still need to be extensively validated to determine the anatomical and physiological accuracy of such models. A promising approach is the combination of both direct and inverse methods (Fig. 14).[59,60]

Eventually, all above-described data must be registered to generate generic models that are both anatomically correct and documented enough to allow further fundamental analysis and integration of patient-specific data within a clinical decision-making process. It must be stressed again that before clinical integration, all components of these generic models must be fully and carefully validated.

C. Patient-Specific Data (*In Vivo*) (Fig. 2, Label 4)

The use of current modeling systems is severely limited for clinical practice because they do not represent the real anatomy of the patients, or their pathological conditions. Customization of these systems is limited by the fact that data collection in clinical practice using traditional clinical tools

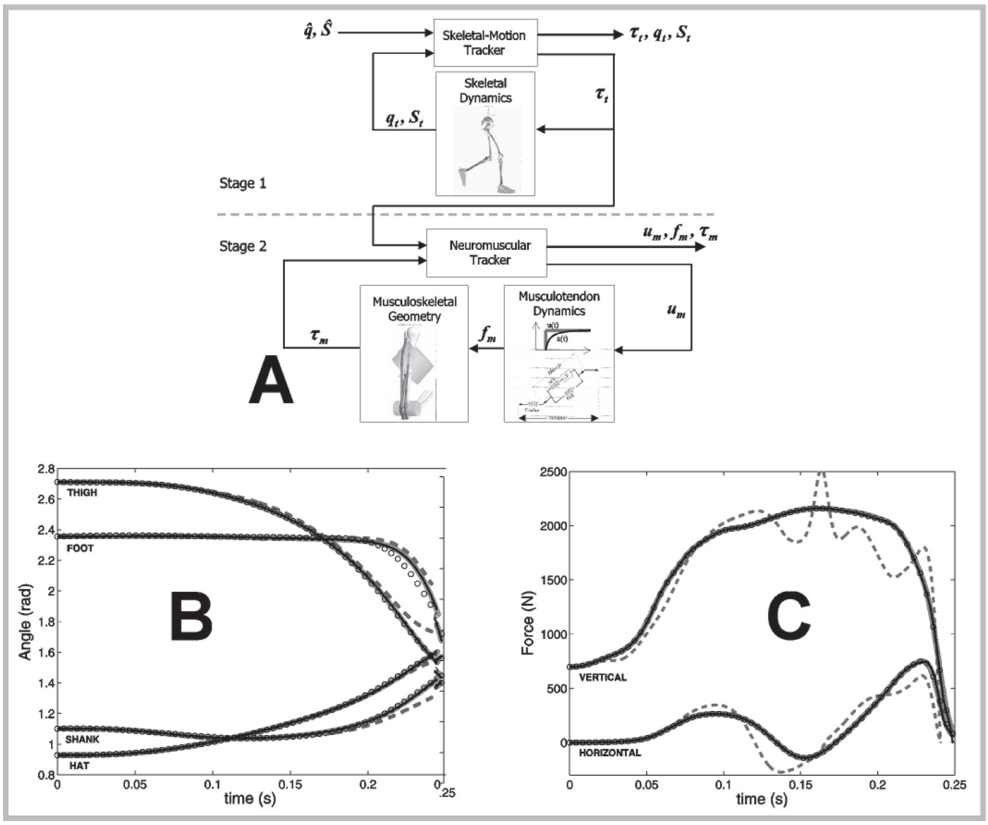

FIGURE 14. (**A**) Neuromusculoskeletal tracking (NMT) overview: Stage 1, skeletal motion tracking of experimental measurements of body kinematics and ground reaction forces ($\hat{q}$,$\hat{S}$) to determine joint torques, τ_t, which produces model-simulated kinematics, q_t, and ground contact forces, S_t (subscript *t* denotes *tracking*), in a forward simulation. Stage 2, neuromuscular tracking determines excitations, u_m, as inputs to muscle dynamics in order to determine the individual muscle forces, f_m, which produce joint moments, τ_m (subscript *m* denotes *muscle*), which track the joint torques, τ_t, from Stage 1. (**B**) Modeled segment angles obtained from tracking (gray) compared to observed data (circles) and actual segment angles (thin black). Segment angles were also obtained when the joint torques calculated from inverse dynamics were used to drive the model in a forward simulation (dashed). (**C**) Modeled ground contact forces obtained from tracking (gray) compared to observed data (circles) and actual ground reaction forces (thin black). Ground contact forces were also obtained when the joint torques calculated from inverse dynamics were used to drive the model in a forward simulation (dashed). [Figure 14 was provided courtesy of A. Seth (Department of Biomedical Engineering, University of Texas at Austin, USA) and M. G. Pandy (Department of Mechanical Engineering, University of Melbourne, Australia). It was originally presented at the ISB 2005 in Cleveland, Ohio.]

(patient palpation, medical imaging, motion analysis, etc.) did not produce data that could be directly used in current modeling engines. The latter also require too long a processing time to produce clinically relevant patient-related reports. Therefore, changing how useful data is collected for modeling in the clinical setting, and further development in modeling strategies to answer clinical constraints, should allow the speeding up of data processing and report production. Extensive clinical validation is also still missing. This should be organized on a large scale to demonstrate if such systems might become a supplementary clinical tool, without putting the patients at risk (eg, by giving inaccurate results during clinical decision making; see Fig. 5).

The above *in vitro* anatomical database can be obtained using invasive methodologies because of the nature of the *in vitro* data collection procedures. Collecting data from patients or healthy volunteers is usually performed under the terms of ethical rules guaranteeing that the subject's integrity is respected. The general attitude to adopt when developing a data collection procedure for clinical purposes must be based on ethical values and must answer the questions: "What is the quantitative individual's benefits from such procedure?" and "Do such benefits justify the potential risk related to the procedure?" In summary, *in vitro* procedures as above-described are usually too invasive to be directly applied in an *in vivo* context, especially in clinics. Alternatives must, therefore, be found.

1. Bone Morphology

Medical CT imaging is frequently performed on patients exhibiting joint problems. Therefore, individual data from bone and joint surfaces can be obtained from such imaging. One must note that CT imaging leads to X-ray radiation of the subjects. Although there is no consensus on the long-term effects of clinical diagnosis doses,[61] some ethical committees might refuse CT imaging unless benefits for the patient's are clearly demonstrated. If this is not the case, an alternative can be found with MRI, but with a loss of spatial resolution for bone reconstruction.[62] Another alternative is to consider the use of low dose CT (LDCT).[63] LDCT decreases the effective dose absorbed by the subject by more than 90% compared to standard protocols, with limited loss of quality in the data resolution for 3-D bone modeling.[64] Once patient-specific medical imaging is performed, individual skeletal architecture (eg, deformation, particular joint surface, etc.) can be introduced in the modeling system.

Customized finite-element modeling is possible using automated procedures on medical imaging datasets.[8]

2. Anatomical Landmarks

Fiducial landmarks inserted in bones are usually not available from patient-specific analysis because no invasive materials can be used, for obvious ethical reasons. On the other hand, landmarks are still needed if one wishes to perform registration, or if results must be anatomically represented. If subject-specific 3-D models are available from medical imaging then coordinates of anatomical landmarks can be located using virtual palpation under the same strict conditions as above (ie, need for strict palpation guidelines).

Manual palpation can be performed through the subject undergoing analysis (eg, joint motion analysis). Such palpation requires serious training and practice by the "palpator"—both in anatomy and palpation technique—before he or she is able to achieve a satisfactory confidence level, especially in anatomical areas where a thick layer of soft tissue (ie, fat and muscle tissues) can be found between the skin and the underlying bones. Here, too, detailed guidelines are needed to obtain satisfactory reproducibility.[16]

A common method to identify the spatial location of anatomical landmarks is to use a special palpation wand associated with stereophotogrammetry systems to decrease skin artifacts.[65] The subject is first equipped with several groups of technical markers, called *clusters of markers,* which are strapped around the joint segments. Motion analysis will later occur by tracking the trajectories of these clusters during segment displacements. The palpation wand also includes a few reflective landmarks (Fig. 15A). The architecture of the wand, that is, the spatial relationship between the wand tip and the various wand markers, must first be calibrated using an

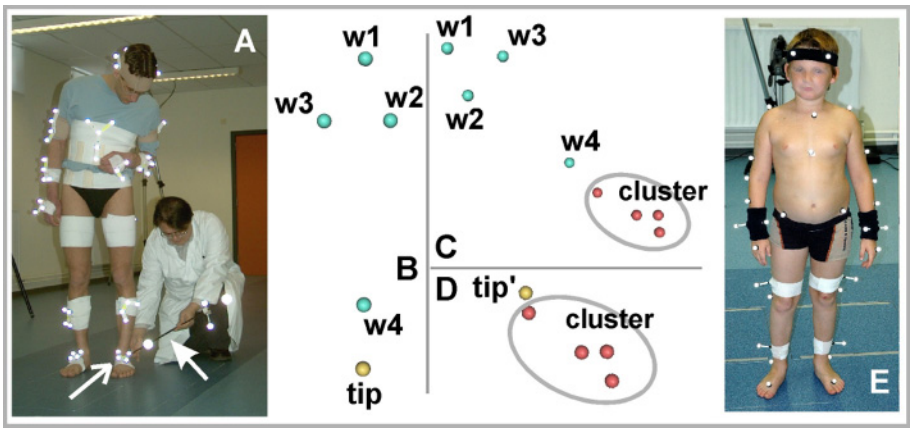

FIGURE 15. (**A**): Typical anatomical landmark calibration. Reflective markers are set on rigid plates attached to the subject's segments. The palpation wand is used here to locate a foot anatomical landmark (open arrow: foot cluster; closed arrow: palpation wand). (**B**): Wand architecture (w_n = wand markers; tip = wand extremity position). (**C**): Wand attitude during palpation with attitude of a segment cluster. [Note that only the wand markers are displayed here because the wand tip is not recorded by the system and will be interpolated later (see **D**).] (**D**): Attitude of a segment cluster together with the interpolated tip (see text for explanations). (**E**): Markers set in standardized locations (Helen Hayes configuration).

external device (Fig. 15B). For each landmark, manual palpation is then performed, and the tip of the stick is put on the palpated location (Fig. 15A). The attitude (ie, position and orientation) of both wand and technical cluster are then simultaneously recorded by the analysis system in some *reference position* during a so-called *anatomical landmarks calibration operation* (Fig. 15C). Once all anatomical landmarks are calibrated, recording of the motions can be performed.

Data processing must first interpolate the wand tip location from the known wand architecture; this gives the coordinates of the palpated landmark (Fig. 15D). The palpated landmark is then attached to one particular cluster, whose trajectory is known (the foot cluster, in this example). This is performed by *registration* of the cluster attitude in the reference position (Fig. 15C) towards the attitude of the same cluster in one of the frames (usually the first one) of the motion dataset (Fig. 15D). Such registration can be performed using least-squares algorithms.[12]

The same transformation matrix is used to register the palpated anatomical landmark, located by the wand extremity, towards the motion dataset. The latter registration leads to interpolation of the anatomical landmark trajectories. An alternative to the wand procedure can be found in 3-D digitizers.[66]

Manual palpation using a wand, or a digitizer, associated with detailed palpation guidelines has the advantage of being highly anatomical and presents good reproducibility. A high level of accuracy of the method also ensures promising results for online *in vivo* analysis.[16]

3. Joint Kinematics and Motion Analysis

Traditional motion data collection systems track the subject's segment motion from the trajectories of reflective markers set on well-standardized locations (for example the Helen Hayes configuration, see Fig. 15E). Despite well-accepted standardization, anatomical accuracy of such configurations is not high, especially if the subject shows thick layers of soft tissues (obese patients). More improvements are needed.[67] Another alternative is to adopt wand calibration of anatomical landmarks, as described in the previous section.

Current *in vivo* motion analysis protocols are unable to track the motion of particular segments using 6 DOFs, mainly because of the interposition of the subject's soft tissue between the skin and the underlying bone segments. Inhomogeneous displacement of both skin and bones[17,65] makes most DOFs unreliable (see Fig. 5 for example of discrepancy). Therefore, modeling systems usually

represent *in vivo* motion dataset using a reduced number of DOFs.

Reducing the number of available DOFs is justified because of the limitations of the data collection protocols and is acceptable if only motion analysis has to be performed. On the other hand, such limitations seriously decrease the usefulness of the data for more advanced analysis. For example, most modeling systems reduce the knee joint to a one DOF system, although it is widely accepted that the knee joint exhibits complex behavior.[68] Performing a quantitative analysis of subject-specific muscle level arm using a highly simplified joint model will show large bias. Including supplementary DOFs in the underlying models is, therefore, justified to allow better musculoskeletal analysis. Another argument for including more DOFs is the fact that one cannot predict how a particular pathology will modify a joint morphology and behavior: Rupture of the anterior cruciate ligament introduces knee anterior draw, but how is joint kinematics modified in cases of severe osteoplasy? It is therefore advisable to try integrating 6 DOFs in any joint. The analysis system will then decide which DOFs to use, according to the available input data.

Such integration has been performed for the lower limb using a so-called dubble-registration procedure.[25] In summary, the latter found the *in vitro* relationships between the main DOF of both knee and ankle joints (ie, flexion/extension) and the five other DOFs (abduction/adduction, internal rotation/external rotation, and the three translations). This relationship is then used in combination with *in vivo* motion analysis data, where the main degree-of-freedom (ie, flexion/extension) is used to register the spatiotemporal information available from the *in vitro* data (Figs. 16A and 16B). The result is the integration of patient-specific data into anatomically correct joint modeling that is useful for further and more advanced musculoskeletal analysis (Figs. 13, 16C, and 16D).

The fact that the final model includes only one DOF from the patient dataset can be seen as a drawback. Further work should integrate supplementary patient DOFs, if accuracy of *in vivo* motion analysis protocol proves to be high enough for them.

4. Muscle Parameters

Muscles are frequently involved in pathologies involving deformities of the skeleton. For example, nonphysiological muscular contracture or weakness in cerebral palsy patients lead to severe lower limb deformities and unnatural walking patterns.[69-71] Individual muscle information is therefore of importance if accurate analysis must be performed.

CT imaging can be used, but available information is often limited to the borders of the muscle bellies. Muscle pennation or tendon data cannot be obtained with current CT protocols because of limits inherent in this technology (CT is not aiming to study muscle tissue). On the other hand, MRI can be used: If well tuned, such technology can give muscle information, such as origins, insertions, muscle-tendon ratio, and even pennation (Fig. 8). Unfortunately, long muscles are often partly imaged, and, therefore, full 3-D reconstruction is not feasible. When possible, imaging of full muscles-of-interest should be performed to collect enough spatial information to create entire surface models. New developments in ultrasound technology are promising to obtain patient-specific muscle data.[72] Cost-effectiveness of the method makes it even more attractive for clinical purposes. Unfortunately, following, *in vivo,* a particular muscle fiber to determine its spatial pathway and pennation, and then integrate this information into customized musculoskeletal modeling, is still a major challenge. New techniques should be investigated, as well—for example, MRI technology based on water diffusion for fiber tracking or tractography.[73,74]

Despite their value for musculoskeletal imaging, the above medical imaging techniques have been mainly developed for clinical purposes and not for biomechanical modeling. Therefore, specific modeling needs have not been answered, and processing medical imaging data for biomechanical applications still requires a lot of manual work: Data registration between modalities is still complicated, and fiducial markers must be used, identified, and registered. It would be interesting to develop systems where advanced registration is based on anatomical features only (bone and muscle shape, anatomical landmarks).[75]

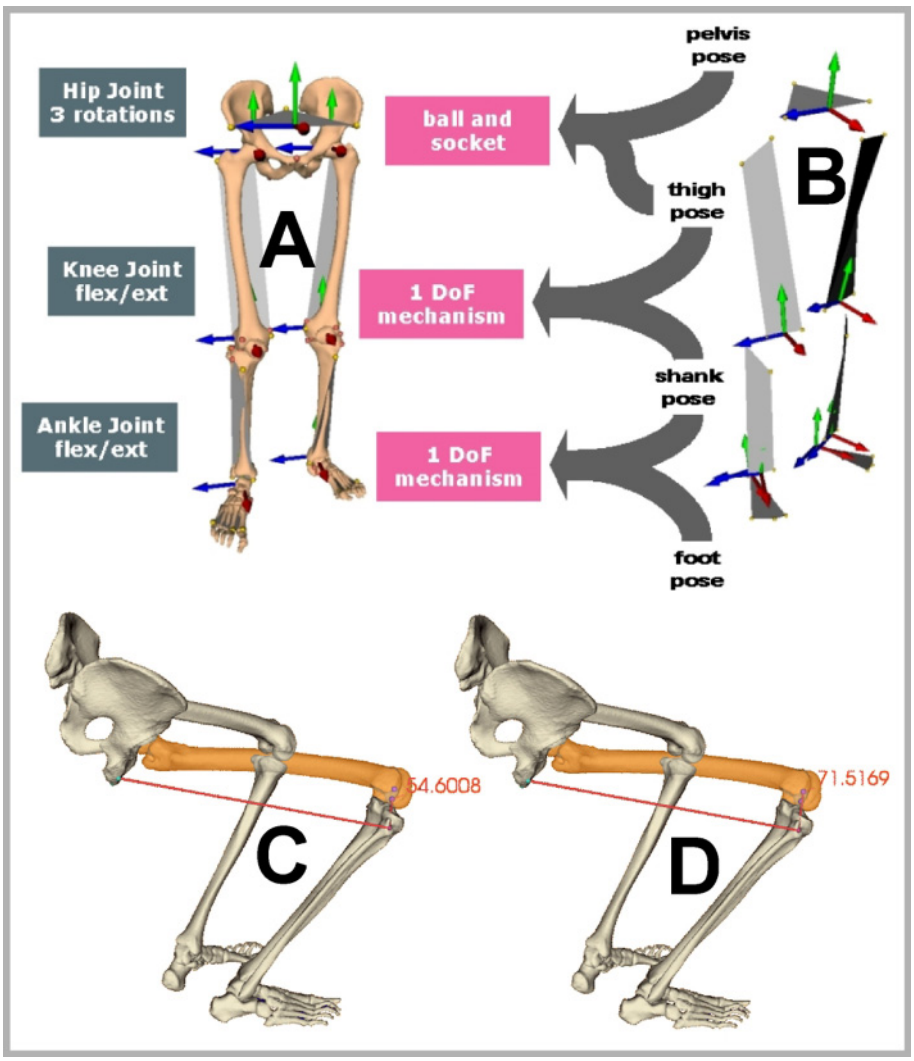

FIGURE 16. Principle of the double registration. (**A**): Joint kinematics is collected during *in vitro* experiments and allows the modeling of both knee and ankle joints as 1 degree-of-freedom mechanisms, where all DOFs are linked to flexion/extension. A 3-D skeletal model was obtained from CT imaging. (**B**): Motion data is then collected from a volunteer, and the flexion/extension DOF is used to animate the *in vitro* model. (**C**): The mechanism integrated in the model is promising for more anatomically correct determination of musculoskeletal parameters. For example, the moment arm of the biceps cruralis muscle has been processed from the double-registration method (**C**) and compared to a "traditional" model, where the center of rotation of the knee is fixed (**D**): This leads to a difference of about 24% [55 and 72 mm for (**C**) and (**D**), respectively].

5. Intermediate Joint Component, Hyalin Cartilage, Meniscus, and Labrum

All components included in a joint cavity might potentially be involved in joint traumatisms or joint degenerative pathologies. During its life, hyalin cartilage is subjected to daily loading that can change its inner properties.[76] It can be eroded (arthrosis), inflamed (arthritis), or simply age.[77,78] Synovial liquid is also of importance for correct nutrition and lubrication of the hyalin cartilage.[41,42] Other joint components, such as meniscus or labrum, can be torn or sustain degenerative pathologies.[79-82] Such pathologies may lead to nonphysiological joint behavior and joint constraints. They are also highly subject-specific (ie, a meniscus can be torn in multiple ways, which depend on the underlying trauma mechanism).

Clinical modeling should, therefore, include as many patient-specific data as possible.

Clinical data collection for such structures is similar to the above-described *in vitro* procedures. Both MRI and CT scan can be associated with contrast agents (Gadolinium and iodinated solutions, respectively) injected into the joint capsule to visualize the hyalin cartilage.[83,84] MRI can also be used for structures, such as the meniscus or labrum, especially with surface coils that increase the spatial resolution of the resulting image dataset by reducing the field-of-view.[85] Subject-specific data of quality can therefore be obtained.

Arthroscopy or biopsy would allow extracting fragments of hyalin cartilage[86] or meniscus[87] for further material property analysis. Synovial biopsy[88] through the joint capsule can collect synovial fluid for further analysis of lubrication properties.[89]

For all data, the development of registration tools to combine the above inhomogeneous data into one single model must be performed because of the shortcomings of the current state-of-the-art in the various fields involved.

6. Other Soft Tissue Parameters (Ligament, Joint Capsule, and Muscle Aponeurosis)

Soft tissues are highly involved in clinical problems. Ligaments are frequently involved in joint traumatism.[90,91] Joint capsules can be ruptured or can adhere to the surrounding environment after inflammation occurs.[92,93] The same can occur to muscle aponeurosis. Such perturbations of the soft tissue integrity can lead to serious malfunctions of the musculoskeletal system by limiting motion amplitude. Patient-specific modeling should therefore integrate clinically useful information about such structures.

Here, too, MRI surface coils enable good data for modeling to be obtained.[85] Similar to muscle observation, ultrasound is an interesting alternative[72] but with serious limitations for modeling purposes. Unfortunately, both MRI and ultrasound are mainly used as qualitative tools in clinical practice and not to perform advanced spatial measurements, such as fiber tracking or locating. Efficient registration tools of such patient data need to be developed.

7. Other Parameters and Documentation

The above description of supplementary parameters and the need for extensive documentation during fundamental *in vitro* and *in vivo* experiments (see above) also apply for any clinical *in vivo* data collection.

D. Patient-Updated Generic Model

Registration of patient-specific data toward a clinically useful generic model is probably the most challenging topic within the overall project. It is expected that registration algorithms will be similar to the ones used to generate the generic models based on anatomical landmarks (see above). Techniques based on markerless protocols[94,95] are promising, especially in a clinical environment where time constraints are of great importance (setting markers on a patient is time-consuming).

E. Decision-Making (DM): Engine and Support (Fig. 2, Label 6)

Complexity of the final models will probably be too high to be directly interpretable in a clinical context for various reasons:

- Complexity of the pathological model (ie, the patient-customized generic model)
- Time constraints clinicians face when dealing with patients
- Lack of technical training of clinical staff
- Lack of clinical reality of system developers

To solve these problems, new data representations[96,97] and case-based reasoning procedures[98,99] should be implemented in decision-making systems. A knowledge-based database will be the root of the decision-making support. Creation of this database should occur during close collaborations among senior clinicians (mostly medical doctors and physiotherapists) and developers (mostly engineers, physicists, or mathematicians). It should include all statistical data available from the validated literature that link particular anatomical, physiological, or clinical parameters to particular pathologies. Once developed, the decision-making

engine will statistically analyze the above patient-updated generic models and compare the results to the knowledge-based database. Eventually, a decision-making support report will give clinicians probability data related to their patients being analyzed. It will then be up to the clinicians, based on the report analysis, to decide whether to perform further analysis in a particular direction or start therapeutic actions.

Such an advanced analysis system is obviously not necessary for "simple" clinical cases in which the etiology of the pathology is easily understandable. On the other hand, many pathologies of the musculoskeletal systems (eg, cerebral palsy, diplegy, polyarthritis, etc) show highly complex clinical signs: muscle spaticity, bone deformation, soft tissue retraction, etc. The number of clinical signs analyzed in clinics by many different means is characterized by a non-negligible amount of inhomogeneous data that is usually mentally processed by the clinical team. Very few automated or semiautomated tools exist, making standardization difficult, and human mistakes (eg, due to fatigue) are more likely to occur. Automated support is therefore requested from the clinical practitioners.

On the other hand, one must be careful when dealing with the implementation of a modeling system in daily clinical practice. To be accepted in a clinical context, such a system will require important validation efforts, probably as important as those that drug companies are facing when developing new drugs. Only then, will clinicians be able to rely on the produced reports.

III. FEASABILITY OF THE CREATION OF AN ANATOMICALLY ACCURATE CLINICAL MODELING SYSTEM

The creation of the above-described system is a long-term endeavor; a decade is probably not overestimated. Large human and technological efforts will have to be spent before being able to bring the first version of such systems for clinical testing. An almost equally large effort will have to be spent for clinical validation.

The good news is that many elements required to build it already exist in the literature. Many data collection protocols already exist. Efficient data processing tools are already available. Current computer technology allows astonishing display and user comfort. And, last but not least, clinical preknowledge based on long-term experience is making daily progress thanks to a very systematic approach to pathologies and etymologies. Of course, the already available resources will not be sufficient to create the models as described previously. But they represent a strong basis for the whole project, and for the necessary improvements and new developments.

Progress to be made should not be limited to data collection only. Indeed, the creation of such a clinical decision-based system is, unfortunately, currently not feasible because of its complexity, as well as the multidisciplinary character of the requirements needed to build it:

- Data necessary to feed the system are numerous and highly inhomogeneous in nature.
- Protocols used for data collection are relatively accurate during *in vitro* collection but are also invasive and cannot be used during clinical practice. Therefore, noninvasive tools will have to be developed.
- Numerous inhomogeneous data lead to large numbers of processing tools. These tools can work nicely independently but should work together to achieve more complex modeling through better registration procedures.
- Inhomogeneous data also lead to different kinds of visualization tools; so the simultaneous display of disparate data must therefore be solved.
- Clinical interpretation of the results must be performed in close collaboration with clinicians. Unfortunately, communication between different professional groups (eg, engineers with physicians) is a common problem. A change in mentality is therefore required.

From this analysis, it is clear that the above-described simulation system can only be achieved through a well-coordinated and multidisciplinary effort. The amount of expertise and data is so large that such a project cannot be realized at one location. Only a long-term and continuous, international effort can achieve this. This kind of effort requires optimal communication to ensure cooperation at all levels. Although the ultimate goal of better quality healthcare is commonly

accepted, the long research challenges and strategies, and the intermediate milestones, need to come as a result of concerted efforts and consultations on issues such as the data environment (that is the nature of the data to be collected and the protocols to be used to collect and process them), how to share data (formats, repository structure, and legal issues—eg, intellectual property rights), and more.

Clearly, the first aim should be to inspire an international effort to discuss the possible future directions biomedical research should take to achieve the above goals. These directions would eventually be reported in publicly available guidelines that would serve as a roadmap for anyone who would wish to participate in such development. The roadmap would be regularly updated with new state-of-the-art developments. Such guidelines should help enable researchers to orient their research toward more clinically relevant applications and participate in the overall efforts. It is the author's belief that the above-mentioned decision-making support system might be available for clinical practice only if the understanding and participation of all stakeholders is assured along the given roadmap.

This kind of effort is close to the Physiome initiative[47] that aims to create a public-domain structure for the creation of virtual models related to the entire human organism, reflecting various anatomical levels—genetic, molecular, tissue, and organ. The European Commission (through ICT for Health, DG Information Society http://www.cordis.lu/ist/directorate_c/ehealth/index.html) is currently launching such a coordinated effort (called STEP) that aims to define the technological infrastructure necessary to develop Physiome-like projects for the creation of clinically relevant expert tools. This effort aims to increase the awareness of our community at large (politicians, academia, industry, general public) about that particular topic, and to define a general roadmap that will prioritize research challenges and applications based on in-silico human modeling for clinical use, as well as related industrial developments. A first draft document related to multilevel modeling and simulation of the human physiology is available from: http://europa.eu.int/information_society/activities/health/docs/events/barcelona2005/ec-draft-vph-white-paperv2.5.pdf.

The outcome of this roadmaping exercise will be submitted to national and international funding organizations, as well to the industrial community—that is, motion analysis, pharmaceutical, medical imaging, and medical prosthesis industries. It is up to our research community to organize itself and meet the objectives of this Great Challenge.

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REFERENCES

1. Blemker S, Delp SL. Rectus femoris and vastus intermedius fiber excursions predicted by three-dimensional muscle models. J Biomech. In press 2005.
2. Arnold AS, Liu MQ, Schwartz M, Ounpuu S, Delp SL. The role of estimating muscle-tendon lengths and velocities of the hamstrings in the evaluation and treatment of crouch gait. Gait Posture. In press 2005.
3. Arnold AS, Liu MQ, Schwartz M, Ounpuu S, Dias L, Delp SL. Do the hamstrings operate at increased muscle-tendon lengths and velocities after surgical lengthening? J Biomech. In press 2005.
4. Rasmussen J, Damsgaard M, Voigt M. Muscle recruitment by the min/max criterion—a comparative numerical study. J Biomech. 2001;34:409–15.
5. Rasmussen J, Damsgaard M, Christensen S, Surma E. Design optimization with respect to ergonomic properties. Struct Multidisciplinary Optimization 2002;24:89–97.

6. Arnold AS, Anderson FC, Liu MQ, Jonkers I, Habib A, Thelen D, et al.. Simulation-based treatment planning for gait abnormalities: vision and challenges. Proceedings of the 20th International Congress of the International Society of Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www.isb2005.org/proceedings/ISB05/search.html
7. Van Sint Jan S, Hilal I, Salvia P, Sholukha V, Poulet P, Kirakoya I, et al. Data representation for joint kinematics simulation of the lower limb within an educational context. Med Eng Phys. 2003;25:213–20.
8. Viceconti M, Davinelli M, Taddei F, Cappello A. Automatic generation of accurate subject-specific bone finite element models to be used in clinical studies. J Biomech. 2004;37:1597–605.
9. Parkesh R, Lee T, Gunnlaugsson T, Gowin W. Microdamage in bone: surface analysis and radiological detection. J Biomech. In press 2005.
10. Van Sint Jan S. The VAKHUM project: virtual animation of the kinematics of the human. In: Gielo-Perczak K, editor. Novel methods and methodologies in biomechanics as related to human systems and ergonomics theory. Theor Issues Ergonom Sci (TIES). 2005;6:3–4.
11. Van Sint Jan S, Salvia P, Hilal I, Sholukha V, Rooze M, Clapworthy G. Registration of 6-DOFs electrogoniometry and CT medical imaging for 3-D joint modeling. J Biomech. 2002;35:1475–84.
12. Challis JH. A procedure for determining rigid body transformation parameters. J Biomech. 1995;26:733–7.
13. Wu G, Cavanagh P. ISB recommendations for standardization in the reporting of kinematic data. J Biomech. 1995;28:1257–61.
14. Wu G, Siegler S, Allard P, Kirtley C, Leardini A, Rosenbaum D, et al. ISB recommendation on definitions of joint coordinate systems of various joints for the reporting of human joint motion—Part I: ankle, hip, spine. J Biomech. 2002;35:543–8.
15. Wu G, van der Helm FC, Veeger H, Makhsous M, Van Roy P, Anglin C, et al. ISB recommendation on definitions of joint coordinate systems of various joints for the reporting of human joint motion—Part II: shoulder, elbow, wrist and hand. J Biomech. 2005;38:981–92.
16. Van Sint Jan S, Della Croce U. Accurate palpation of skeletal landmark locations: why standardized definitions are necessary. A proposal. Clin Biomech. 2005;20:659–60.
17. Della Croce U, Leardini A, Chiari L, Cappozzo A. Human movement analysis using stereophotogrammetry. Part 4: assessment of anatomical landmark misplacement and its effect on joint kinematics. Gait Posture. 2005;21:226–37.
18. Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: applications to the knee. J Biomech Eng. 1983;105:136–44.
19. Cappozzo A, Catani F, Della Croce U, Leardini A. Position and orientation of bones during movement: anatomical frame definition and determination. Clin Biomech. 1995;10:171–8.
20. Leardini A, O'Connor JJ, Catani F, Giannini S. A geometric model of the human ankle joint. J Biomech. 1999;32:585–91.
21. Dugailly P, Sobczak S, Salvia P, Sholoukha V, Klein P, Van Sint Jan S, et al. Upper cervical spine modelling: in vitro 3-D kinematics. Proceedings of the 20th International Congress of the International Society of Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search.html
22. Fischer KJ, Manson TT, Pfaeffle HJ, Tomaino MM, Woo SL-Y. A method for measuring joint kinematics designed for accurate registration of kinematic data to models constructed from CT data. J Biomech. 2001;34:377–83.
23. Woltring HJ, Long K, Osterbauer PJ, Fuhr AW. Instantaneous helical axis estimation from 3-D video data in neck kinematics for whiplash diagnostics. J Biomech. 1994;27:1415–32.
24. Van Sint Jan S, Sholukha V, Hilal I, Leardini A, Salvia P, Poulet P, et al. Advanced modelling and simulation of the lower limb using medical imaging, electrogoniometry and gait analysis data. Proceedings of the 7th International Symposium on 3-D Analysis of Human Movement; 2002; Newcastle upon Tyne, UK. Newcastle upon Tyne (UK): International Centre for Life; 2002.
25. Sholukha V, Leardini A, Salvia P, Rooze M, Van Sint Jan S. Double-step registration of in vivo stereophotogrammetry with both in vitro 6-DOFs electrogoniometry and CT medical imaging. J Biomech. In press 2005.
26. Pandy M. Computer modeling and simulation of human movement. Annu Rev Biomed Eng. 2001;3:245–73.
27. Veeger H, van der Helm F, Woude L, van der Pronk G, Rozendal R. Inertia and muscle contraction parameters for musculoskeletal modelling of the shoulder mechanism. J Biomech. 1991;24:615–31.
28. van der Helm F, Veeger H, Pronk G, Woude L, Rozendal R. Geometry parameters of musculoskeletal modelling of the shoulder mechanism. J Biomech. 1992;25:129–44.
29. Klein Breteler M, Spoor C, van der Helm F. Measuring muscle and joint geometry parameters of a shoulder for modeling purposes. J Biomech. 1999;32:1191–7.
30. Langenderfer J, Jerabek S, Thangamani V, Kuhn J, Hughes R. Musculoskeletal parameters of muscles crossing the shoulder and elbow and the effect of sarcomere length sample size on estimation of optimal muscle length. Clin Biomech. 2004;19:664–70.
31. Leardini A, Astolfi L, Fantozzi S, Viceconti M, Benedetti M, Catani F. Advanced multimodal visualisation of clinical gait and fluoroscopy analyses in the assessment of total knee replacement. Comp Meth Programs Biomed. 2005;79:227–40.

32. Dimitrov G, Disselhorst-Klug C, Dimitrova N, Schulte E, Rau G. Simulation analysis of the ability of different types of multi-electrodes to increase selectivity of detection and to reduce cross-talk. J Electromyogr Kinesiol. 2003;13:125–38.
33. Byrne C, Lyons G, Donnelly A, O'Keeffe D, Hermens H, Nene A. Rectus femoris surface myoelectric signal cross-talk during static contractions. J Electromyogr Kinesiol. 2005;15:564–75.
34. Abrahams PH, Craven JL, Lumley JS, Spratt JD. Illustrated clinical anatomy. London: Hodder Arnold; 2005.
35. Hinterwimmer S, Gotthardt M, von Eisenhart-Rothe R, Sauerland S, Siebert M, Vogl T, et al. In vivo contact areas of the knee in patients with patellar subluxation. J Biomech. 2005;38:2095–101.
36. Li G, Park S, DeFrate L, Schutzer M, Ji L, Gill T, et al. The cartilage thickness distribution in the tibiofemoral joint and its correlation with cartilage-to-cartilage contact. Clin Biomech. 2005;20:736–44.
37. Eckstein F, Adam C, Sittek H, Becker C, Milz S, Schulte E, et al. Non-invasive determination of cartilage thickness throughout joint surfaces using magnetic resonance imaging. J Biomech. 1997;30:285–9.
38. Graichen H, Springer V, Flaman T, Stammberger T, Glaser C, Englmeier K, et al. Validation of high-resolution water-excitation magnetic resonance imaging for quantitative assessment of thin cartilage layers. Osteoarthritis Cartilage. 2000;8:106–14.
39. Van Berg B, Lecouvet F, Maldague B, Manghem J. MR appearance of cartilage defects of the knee: preliminary results of a spiral CT arthrography-guided analysis. Clin Imaging. 2004;28:312.
40. Schoettle P, Zanetti M, Seifert B, Pfirrmann C, Fucentese S, Romero J. The tibial tuberosity—trochlear groove distance; a comparative study between CT and MRI scanning. The Knee. In press 2005.
41. Wilson W, van Donkelaar C, van Rietbergen B, Huiskes R. A fibril-reinforced poroviscoelastic swelling model for articular cartilage. J Biomech. 2005;38:1195–204.
42. Bullough P. The role of joint architecture in the etiology of arthritis. Osteoarthritis Cartilage. 2004;12 Suppl 1:2–9.
43. Kuhlmann J, Guerin-Surville H. Anatomie descriptive et étude biodynamique du ligament collatéral médial de l'articulation trapézo-métacarpienne du pouce. Bull Assoc Anatomie. 1985;69:315–29.
44. Peña E, Calvo B, Martínez M, Doblaré M. A three-dimensional finite element analysis of the combined behavior of ligaments and menisci in the healthy human knee joint. J Biomech. In press 2005.
45. Van Sint Jan S, Van Audekerke J, Van der Linden A, Rooze M. High resolution MRI application in anatomy: the extensor digitorum muscle insertion on the first phalanx. Magn Reson Mater Phys Biol Med. 1997; 5:21–7.
46. Feipel V, Salvia P, Rooze M. A new method for measuring wrist-joint ligament length changes during sagittal and frontal motion. Clin Biomech. 1998;13: 128–37.
47. Hunter P, Borg T. Integration from proteins to organs: the Physiome project. Nat Rev Mol Cell Biol. 2003;4:237–43.
48. Van Sint Jan S, Giurintano DJ, Thompson DE, Rooze M. Joint kinematics simulation from medical imaging data. IEEE Trans Biomed Eng. 1997;44:1175–84.
49. Belsole RJ, Hilbelink DR, Llewellyn JA, Stenzler S, Greene TL, Dale M. Mathematical analysis of computed carpal models. J Orthop Res. 1988;6:116–22.
50. Foley JD, van Dam A, Feiner SK, Hughes JF. Computer graphics—principles and practice. Reading: Addison-Wesley; 1990.
51. Aranov V, Van Sint Jan S, Sholoukha V, Rooze M, Viceconti M. Implementation of interactive motion representation (IMR) within the data manager. Proceedings of the 30th Congress of the Sociéte de Biomécanique; 2005; Bruxelles, Belgium. Bruxelles: Sociéte de Biomécanique; 2005.
52. Viceconti M, Taddei F, Testi D, Leardini A, Astolfi L, Davinelli D, et al. The MULTIMOD Data Manager: an essential tool for musculo-skeletal modelling. Proceedings of the Medicon Conference; 2004; Ischia, Italy. Ischia: Medicon; 2004.
53. Van Sint Jan S, Viceconti M, Clapworthy G. Modern visualization tools for both research and education in biomechanics. Proceedings of the 8th International Conference on Information Visualisation; 2004; London, UK. Los Alamitos: IEEE Computer Society Press; 2004.
54. Van Sint Jan S, Viceconti M, Clapworhy G. A development architecture for data and algorithm exchange: MAF and Data Manager. Proceedings of the International Symposium on Computer Simulation in Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search.html
55. Dugailly P, Sobczak S, Salvia P, Sholoukha V, Feipel V, Van Sint Jan S, et al. 3-D muscle moment arms using musculoskeletal modelling of the upper cervical spine. Proceedings of the 20th International Congress of the International Society of Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search.html
56. Hughes R, Niebur G, Liu J, An K-N. Comparison of two methods for computing abduction moment arms of the rotator cuff. J Biomech. 1997;31:157–60.
57. Jonkers I, Spaepen A, Papaioannou G, Stewart C. An EMG-based, muscle driven forward simulation of single support phase of gait. J Biomech. 2002;35:609–19.
58. Camilleri M, Hull M. Are the maximum shortening velocity and the shape parameter in a Hill-type model of whole muscle related to activation? J Biomech. 2005;38:2172–80.
59. Seth A, Pandy M. Tracking ground force data improves estimates of net joint torques. Proceedings of the International Symposium on Computer Simulation in Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search.html

60. Seth A, Pandy MG A neuromusculoskeletal tracking method for estimating individual muscle forces from human movement data. J Biomech. [Submitted]
61. Van Sint Jan S, Baruffaldi F, Feipel V, Loncol T, Louryan S, Suess C, Rooze M. Customizable software assessment of effective dose in computed tomography. IEEE Trans Biomed Eng. [Submitted]
62. Udupa JK, Hirsch BE, Samarasekera S, Goncalves RJ. Joint kinematics via three-dimensional MR imaging. Proc Spie. 1992;1808:664–70.
63. Nagel H, Galanski M, Hidajat N, Maier W, Schmidt T. Radiation in computed tomography. European Coordination Committee of the Radiological and Electromedical Industries (COCIR); 2000. Available from: www.COCIR.org
64. Van Sint Jan S, Sobzack S, Dugailly P-M, Feipel V, Lefèvre P, Lufimpadio J-L, et al. Low-dose CT (LDCT) and 3-D bone modeling accuracy. IEEE Trans Biomed Eng. [Submitted]
65. Leardini A, Chiari L, Della Croce U, Cappozzo A. Human movement analysis using stereophotogrammetry. Part 3. Soft tissue artifact assessment and compensation. Gait Posture. 2005;21:212–5.
66. Van Sint Jan S, Salvia P, Dugailly P-M, Feipel V, Sobzack S, Rooze M, et al. In vivo registration of both electrogoniometry and medical imaging: development and application on the ankle joint. IEEE Trans Biomed Eng. In press 2005.
67. Houck J, Yack H, Cuddeford T. Validity and comparisons of tibiofemoral orientations and displacement using a femoral tracking device during early to mid stance of walking. Gait Posture. 2004;19:76–84.
68. Kapandji IA. Physiologie Articulaire—Membre Inférieur. Paris: Maloine; 1985.
69. Metaxiotis D, Accles W, Siebel A, Doederlein L. Hip deformities in walking patients with cerebral palsy. Gait Posture. 2000;11:86–91.
70. Maruishi M, Mano Y, Sasaki T, Shinmyo N, Sato H, Ogawa T. Cerebral palsy in adults: independent effects of muscle strength and muscle tone. Arch Phys Med Rehabil. 2001;82:637–41.
71. Zwick E, Leistritz L, Milleit B, Saraph V, Zwick G, Galicki M, et al. Classification of equinus in ambulatory children with cerebral palsy—discrimination between dynamic tightness and fixed contracture. Gait Posture. 2004;20:273–9.
72. Fry N, Gough M, Shortland A. Three-dimensional realisation of muscle morphology and architecture using ultrasound. Gait Posture. 2004;20:177–82.
73. Bonny J-M, Renou J-P. Water diffusion features as indicators of muscle structure ex vivo. MRI. 2002;20: 395–400.
74. Bammer R, Acar B, Moseley M. In vivo MR tractography using diffusion imaging. Eur J Radiol. 2003;45:223–34.
75. Frantz S, Rohr K, Stiehl H. Development and validation of a multi-step approach to improved detection of 3-D point landmarks in tomographic images. Image Vision Comput. 2005;11:956–71.
76. Wu J, Herzog W. Analysis of the mechanical behavior of chondrocytes in unconfined compression tests for cyclic loading. J Biomech. In press 2005.
77. Silver F, Bradica G, Tria A. Do changes in the mechanical properties of articular cartilage promote catabolic destruction of cartilage and osteoarthritis? Matrix Biol. 2004;23:467–76.
78. Carrington J. Aging bone and cartilage: cross-cutting issues. Biochem Biophys Res Commun. 2005;328: 700–8.
79. Ilahi O, Labbe M, Cosculluela P. Variants of the anterosuperior glenoid labrum and associated pathology. Arthroscopy: J Arthrosc Rel Surg. 2002;18:882–6.
80. Peña E, Calvo B, Martínez M, Palanca D, Doblaré M. Finite element analysis of the effect of meniscal tears and meniscectomies on human knee biomechanics. Clin Biomech. 2005;20:498–507.
81. Guanche C, Sikka R. Acetabular labral tears with underlying chondromalacia: a possible association with high-level running, Arthroscopy: J Arthrosc Rel Surg. 2005;21:580–5.
82. Hart W, Kelly C. Arthroscopic observation of capsulolabral reduction after shoulder dislocation. J Shoulder Elbow Surg. 2005;14:134–7.
83. Liess C, Lüsse S, Karger N, Heller M, Glüer C. Detection of changes in cartilage water content using MRI T_2-mapping *in vivo*. Osteoarthritis Cartilage. 2002;10:907–13.
84. Beaulé P, Zaragoza E, Motamedi K, Copelan N, Dorey F. Three-dimensional computed tomography of the hip in the assessment of femoroacetabular impingement. J Orthop Res. 2005;23:1286–92.
85. Cohen Z, McCarthy D, Kwak S, Legrand P, Fogarasi F, Ciaccio E, Ateshian G. Knee cartilage topography, thickness, and contact areas from MRI: in vitro calibration and in vivo measurements. Osteoarthritis Cartilage. 1999;7:95–109.
86. Sekiya I, Kobayashi M, Taneda Y, Matsui N. Arthroscopy of the proximal interphalangeal and metacarpophalangeal joints in rheumatoid hands. Arthroscopy: J Arthrosc Rel Surg. 2002;18:292–7.
87. Marcacci M, Kon E, Zaffagnini S, Iacono F, Pia Neri M, Vascellari A, Visani A, Russo A. Multiple osteochondral arthroscopic grafting (mosaicplasty) for cartilage defects of the knee: prospective study results at 2-year follow-up. Arthroscopy: J Arthrosc Rel Surg. 2005;21: 462–70.
88. Gerlag D, Tak P. Synovial biopsy. Best Pract Res Clin Rheum. 2005;19:387–400.
89. Mazzucco D, Scott R, Spector M. Composition of joint fluid in patients undergoing total knee replacement and revision arthroplasty: correlation with flow properties. Biomaterials. 2004;25:4433–45.
90. Lafosse L, Baier G, Leuzinger J. Arthroscopic treatment of acute and chronic acromioclavicular joint dislocation. Arthroscopy: J Arthrosc Rel Surg. 2005;21: 1017.e1–8.
91. Briggs P. The structure and function of the foot in relation to injury. Curr Orthop. 2005;19:85–93.

92. Field P, Hueston J. Articular cartilage loss in long-standing immobilisation of interphalangeal joints. Br J Plastic Surg. 1970;23:186–91.
93. Loew M, Heichel T, Lehner B. Intraarticular lesions in primary frozen shoulder after manipulation under general anesthesia. J Shoulder Elbow Surg. 2005;14:16–21.
94. Mündermann L, Anguelov D, Corazza S, Chaudhari A, Andriacchi TP. Validation of a markerless motion capture system for the calculation of lower extremity kinematics. Proceedings of the 20th International Congress of the International Society of Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search. html
95. Corazza S, Mündermann L, Andriacchi TP. Lower limb kinematics through model-free markerless motion capture. Proceedings of the 20th International Congress of the International Society of Biomechanics; 2005; Cleveland, Ohio. [CD-ROM]. Available from: www. isb2005.org/proceedings/ISB05/search.html
96. Loslever P, Barbier F. Multivariate graphical presentation for gait rehabilitation study. Gait Posture. 1998; 7:39–44.
97. Barton G, Lees A, Lisboa P, Attfield S. Visualisation of gait data with Kohonen self-organising neural maps. Gait Posture. In press 2005.
98. Bekey G, Kim J, Gronley J-A, Bontrager E, Perry J. GAIT-ER-AID: An expert system for diagnosis of human gait. Artif Intell Med. 1992;4:293–308.
99. Watelain E, Barbier F, Allard P, Thevenon A, Angué J-C. Gait pattern classification of healthy elderly men based on biomechanical data. Arch Phys Med Rehabil. 2000;81:579–86.