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Statistical Shape Models - Understanding and Mastering Variation in Anatomy[5]

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Statistical Shape Models - Understanding and Mastering Variation in Anatomy

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Abstract

In our chapter we are describing how to reconstruct three-dimensional anatomy from medical image data and how to build Statistical 3D Shape Models out of many such reconstructions yielding a new kind of anatomy that not only allows quantitative analysis of anatomical variation but also a visual exploration and educational visualization. Future digital anatomy atlases will not only show a static (average) anatomy but also its normal or pathological variation in three or even four dimensions, hence, illustrating growth and/or disease progression.

Statistical Shape Models (SSMs) are geometric models that describe a collection of semantically similar objects in a very compact way. SSMs represent an average shape of many three-dimensional objects as well as their variation in shape. The creation of SSMs requires a correspondence mapping, which can be achieved e.g. by parameterization with a respective sampling. If a corresponding parameterization over all shapes can be established, variation between individual shape characteristics can be mathematically investigated.

We will explain what Statistical Shape Models are and how they are constructed. Extensions of Statistical Shape Models will be motivated for articulated coupled structures. In addition to shape also the appearance of objects will be integrated into the concept. Appearance is a visual feature independent of shape that depends on observers or imaging techniques. Typical appearances are for instance the color and intensity of a visual surface of an object under particular lighting conditions, or measurements of material properties with computed tomography (CT) or magnetic resonance imaging (MRI). A combination of (articulated) statistical shape models with statistical models of appearance lead to articulated Statistical Shape and Appearance Models (a-SSAMs).

After giving various examples of SSMs for human organs, skeletal structures, faces, and bodies, we will shortly describe clinical applications where such models have been successfully employed. Statistical Shape Models are the foundation for the analysis of anatomical cohort data, where characteristic shapes are correlated to demographic or epidemiologic data. SSMs consisting of several thousands of objects offer, in combination with statistical methods or machine learning techniques, the possibility to identify characteristic clusters, thus being the foundation for advanced diagnostic disease scoring.

Statistical Shape Models - Understanding and Mastering Variation in Anatomy

What do anatomists or clinicians mean by saying a structure, i.e. an organ, is normal? What does ‘normal’ mean when the term is used in anatomical descriptions? Is it “typical”, “common”, “average”, or any other attribution to the most frequently observed features of relevance? Less frequently or rarely observed features, on the contrary, are denoted as “abnormal”, “unusual”, or “atypical”. Such a terminology resulting from observations of polymorphisms indicates that the term normality is based on statistical criteria. The Latin word ‘normalis’ means conforming to a rule or pattern, where ‘norma’ is used in descriptive anatomy to indicate the standard or normal appearance of a structure (Moore, 1989). For example, ‘Norma lateralis’ is used when describing the skull to depict its typical lateral appearance.

To recognize anatomical variations it is necessary to identify patterns in size, form, relative position or orientation, or even in appearance or function. A fluctuation of such patterns within a commonly experienced range is considered as normal (natural) variation. However, anatomical variation does not only occur across subjects but also within the same subjects during growth and aging or caused by pathological changes. Occurrences beyond certain limits up to extremes are classified as anomalies or malformations (Sañudo et al. 2003). Terms for dysmorphia often reflect the exceeding of such limits by prefixes such as 'hypo', 'hyper', 'micro', 'brachy' etc. (Jones et al. 2013). The concept of “healthy” and “diseased” also fits into the notion of normal. The term malformation or anomaly, for instance, may become applicable when the structural change of an organ has a negative (up to life threatening) influence on its function. Hence, to establish a canon of normality with respect to an anatomical structure one has to thoroughly investigate its range of morphological variation first to improve diagnosis and therapeutic performance.

Statistical Anatomy

Since an existing range of variation in anatomy is a priori unknown, its definition depends on the amount of observations made. A range of variation can be narrow or wide, depending on the choice of samples that is considered for comparison as well as the anatomical variability itself (cf. Fig. 1). A well chosen and sufficiently large sample set with a Gaussian distribution of patterns can be regarded as covering a “normal” range of variation. Only if the sample set is representative the results of the statistical evaluation can be used to draw conclusions about the population as a whole and thus make general statements.

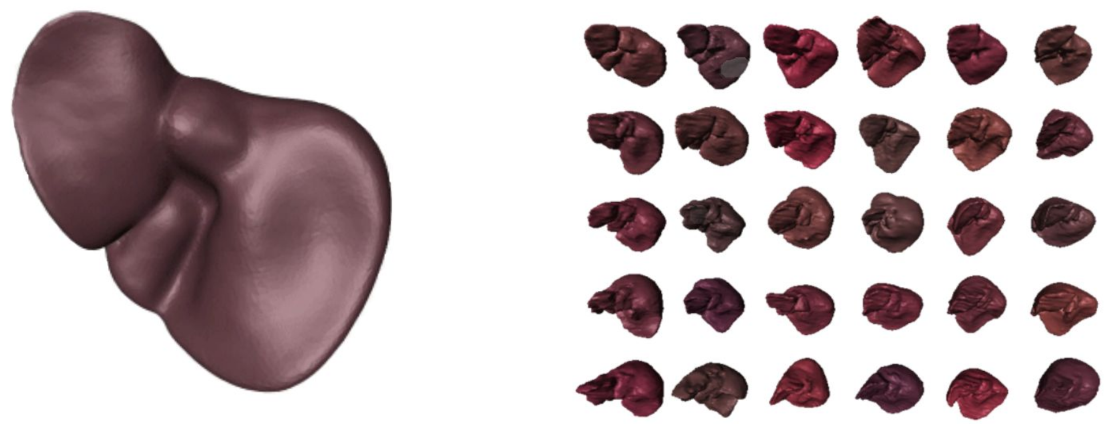

Fig. 1 Various liver shapes (right), averaged liver (left) created from 120+ liver shapes (Lamecker et al. 2002)

In product ergonomics and clothing, statistical analysis of body measurements is widespread. The entire field of anthropometry illustrates what the anatomy of the future could look like, if one is able to precisely measure anatomical structures in a similar way. In biology, very early attempts in this direction have been made by D'Arcy Wentworth Thompson (Thompson, 1917) who tried to formalize growth and form in a mathematical way. A large amount of anatomical structures is also the foundation for building so called anatomical atlases (Bookstein, 1986, Toga, 1998). Such atlases are represented by an averaged anatomy that can be regarded as a common denominator for adding additional information that is collected from various samples. In biology the use of anatomical atlases is quite common, to integrate information that is derived from several specimen into a common reference system (Rybak et al. 2010).

The advance in three-dimensional (3D) imaging techniques has opened a new field of research for descriptive anatomy (Sañudo et al. 2003). From tomographic image data, anatomical structures can be reconstructed three-dimensionally with high geometric accuracy (Zachow et al. 2007) (cf. Fig. 2).

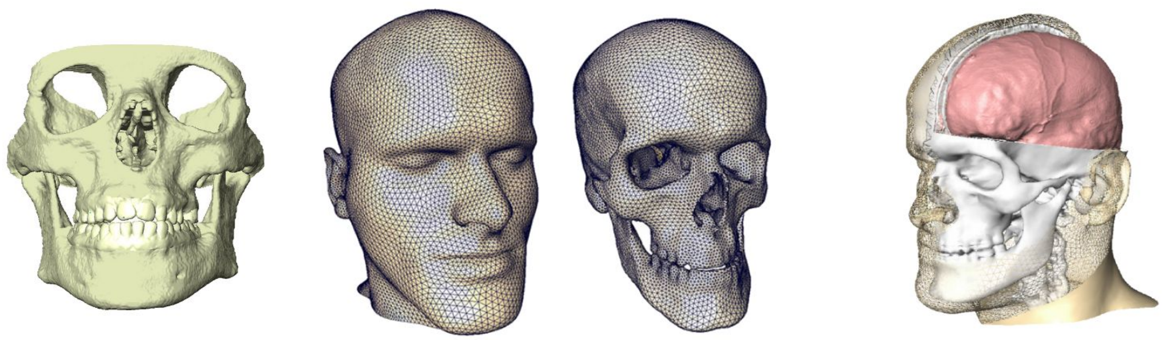

Fig. 2 Geometric reconstructions of anatomical structures, i.e. heads from CT data

The process of reconstructing anatomical 3D models from measurement data requires a so called segmentation of the data, which is tedious, time-consuming, and labor intensive. Automated methods allow a more efficient processing of large amounts of data sets (Kainmüller et al. 2007, Kainmüller et al. 2009, Seim et al. 2010, Tack et al. 2018, Ambellan et al. 2019), whereby often more than one anatomical structure can be segmented within a single tomographic data set (Fig. 3, right).

Fig. 3 Model-based segmentation. Left: A liver from CT data (Kainmüller et al. 2007). Right: A knee joint from MRI data (Seim et al. 2010)

The amount of acquired tomographic image data is already extremely large and it is constantly increasing. However, there is no central administration of the image data, and access for statistical analyses is not possible from an organisational or data protection point of view. To this end, attempts are being made to counter this problem by means of so-called epidemiological longitudinal studies (Osteoarthritis Initiative [OAI], UK Biobank, Study of Health in Pomerania

[SHIP], German National Cohort [GNC], etc.). The respective data of such studies will open up new possibilities for statistical anatomy. On its basis, large quantities of anatomical structures can be geometrically generated, which can then be statistically analyzed with regard to their variation in shape as well as to the correlation between shape and other attributes (age, weight, sex, smoking status, etc.). To derive an average shape from a sample and to determine shape variability one needs a concept of correspondence as well as a measure of distance between shapes. Mathematical details for shape analysis will be given in the following paragraph.

Statistical Shape Models

While humans possess an intuitive perception of shape and similarity thereof, these notions have to be formalized in order to be processed algorithmically. A first step in performing statistical analysis on shapes is therefore to convert the geometric information of an anatomy into a discrete representation thereof, e.g. a finite subset of its points or polygonal meshes describing an object's boundary (cf. Fig. 2, center). Given two or more discrete shapes, one of the fundamental problems in shape analysis is to find a meaningful relation between semantic entities and thus the entire parametrization (see Fig. 4, right). Such correspondence can be hard to estimate as it not only requires an understanding of the structure at local and global scales but also needs to take semantic information about anatomical entities or functionality into account. Due to this complexity, a plethora of methods following different approaches have been proposed over the last decades, e.g., see (van Kaick et al. 2011) and the references therein.

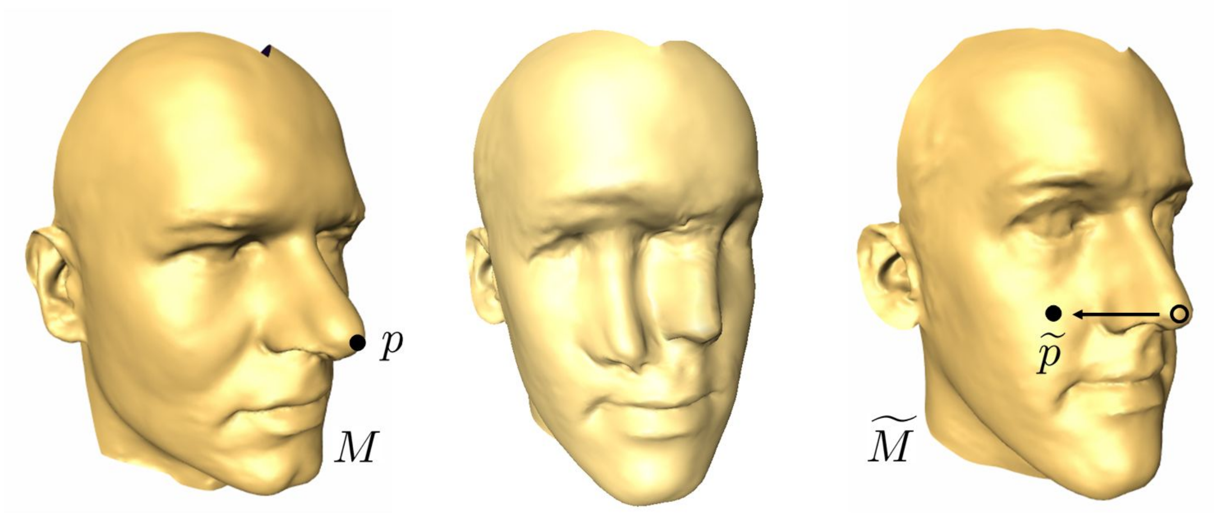

Fig. 4 When the tip of the nose (left) is wrongly set into correspondence with a point on the cheek (right), the average of the two heads reveals an implausible correspondence (center)

Most (semi-)automatic approaches actually phrase the correspondence problem as a registration between the involved shapes (see Fig. 5). For image-derived shapes, we can exploit rich local descriptors integrating color and texture (Grewe and Zachow, 2016), whereas purely shape-based descriptors are generally less distinctive. In the latter case, correspondence estimation is frequently based on the matching of a (sparse) set of features that provide a notion of similarity, and/or the proximity of points after (potentially non-rigid) alignment.

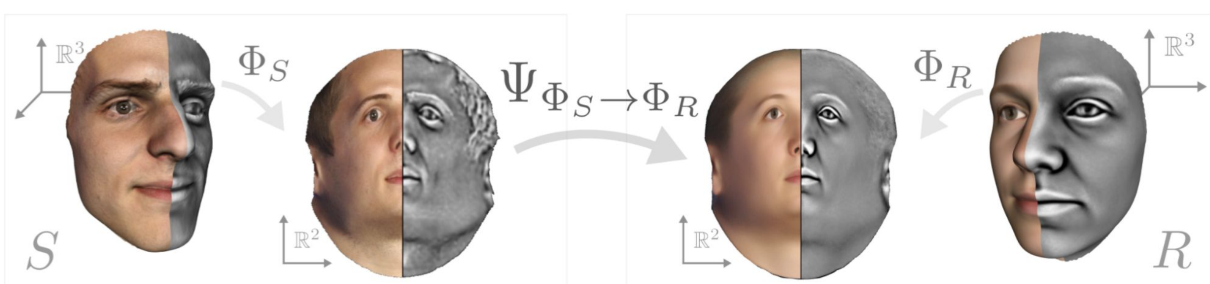

Fig. 5 Matching of a facial surface S to the reference R: Parametrizations Φ_S and Φ_R are computed and photometric as well as geometric features are mapped to the plane. The dense correspondence mapping $\Psi_{\Phi S \to \Phi R}$ accurately registers photographic and geometric features from S and R.

A common approach to compute a dense point-wise matching, is to extend a sparse correspondence defined only for a small number of homologous elements, i.e. elements with the same structure in terms of geometry, function, and appearance. In particular, extending sparse correspondences significantly reduces the computational complexity and allows to incorporate expert knowledge (Lamecker et al. 2002, Lamecker et al. 2004) (cf. Fig. 6). A specialized form of correspondence involves a group of shapes simultaneously, such that the group information can serve as an additional constraint in the solution search (Davies et al. 2002). These population-based approaches employ group-wise optimization concerning the quality of the resulting statistical model (e.g. in terms of entropy) and thus enjoy widespread application in the shape analysis community.

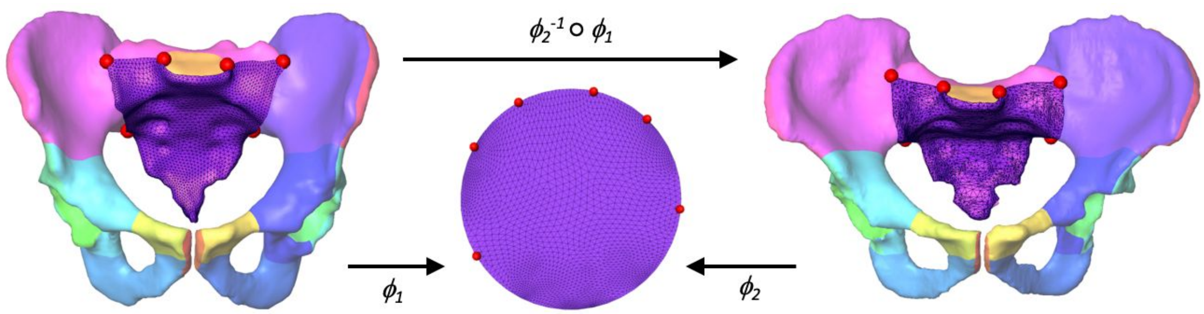

Fig. 6 Example for a consistent surface decomposition of two pelvises, where each pair of patches is set into correspondence via a common parametrization (Lamecker, 2008)

Once the discretized shapes have been put into correspondence, they can be interpreted as elements in a high-dimensional space. Points in this so-called configuration space not only represent the geometric form of an object but also its scale, position and orientation within the 3D space they are embedded in. By removing these similarity transformations, we derive the concept of shape space (Kendall et al. 2009), which is susceptible to statistical shape analysis. It is, however, this last step that introduces curvature to shape space yielding a non-trivial geometric structure. Contrary to flat spaces, shortest connecting paths in shape space are not straight lines but curved trajectories called geodesics (see Figure 7). Whereas this non-linearity ensures consistency, e.g. by preventing bias due to misalignment of shape data, it also impedes the application of classical statistical tools. As a fully intrinsic treatment of the analysis problem can be computationally demanding, a common approach is to approximate it using extrinsic distances.

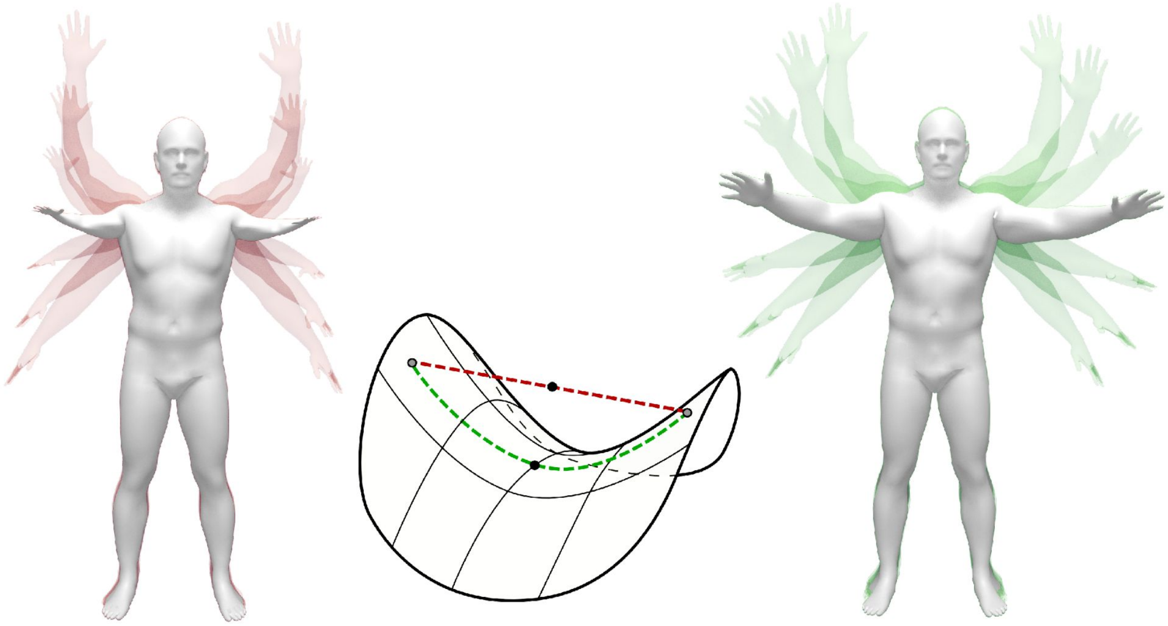

Fig. 7 Visualization of shortest paths, i.e. geodesics, connecting two body shapes w.r.t. the flat ambient space (red) and a curved shape space (green). The latter contains only valid shape instances whereas the former develops artifacts, e.g. shrinkage of the arms.

For data with a large spread in shape space or within regions of high curvature, such linearization will introduce distortions that degrade the statistical power (von Tycowicz et al. 2018). Among the many methods for capturing the geometric variability in a population, principal component analysis (PCA) and its manifold extensions remain a workhorse for the construction of statistical shape models. The resulting models encode the probability of occurrences of a certain shape in terms of a mean shape and a hierarchy of major modes explaining the main trends of shape variation (see Fig. 8).

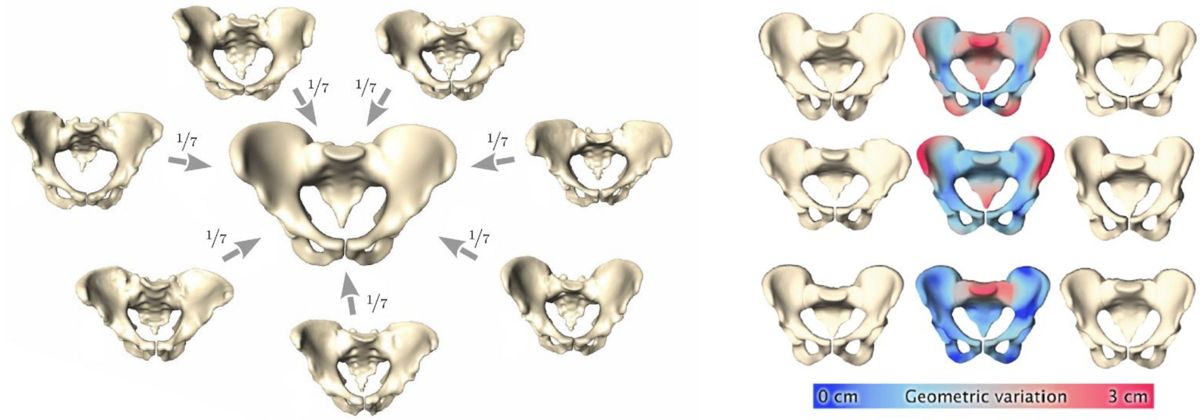

Fig. 8 Mean pelvic shape from seven instances (left) and most dominant modes of variation within a population of 150 pelvises (right)

An appealing feature of such a shape modeling approach is that the shape model itself has a generative power. Since all shape instances are in dense correspondence with respect to their geometric representation, a morphing between all shapes contained in such an SSM becomes possible (Gomes et al. 1999). This means that any weighted combination of shape instances of the SSM lead to new but plausible shapes that are not contained in the training data (cf. Fig. 9).

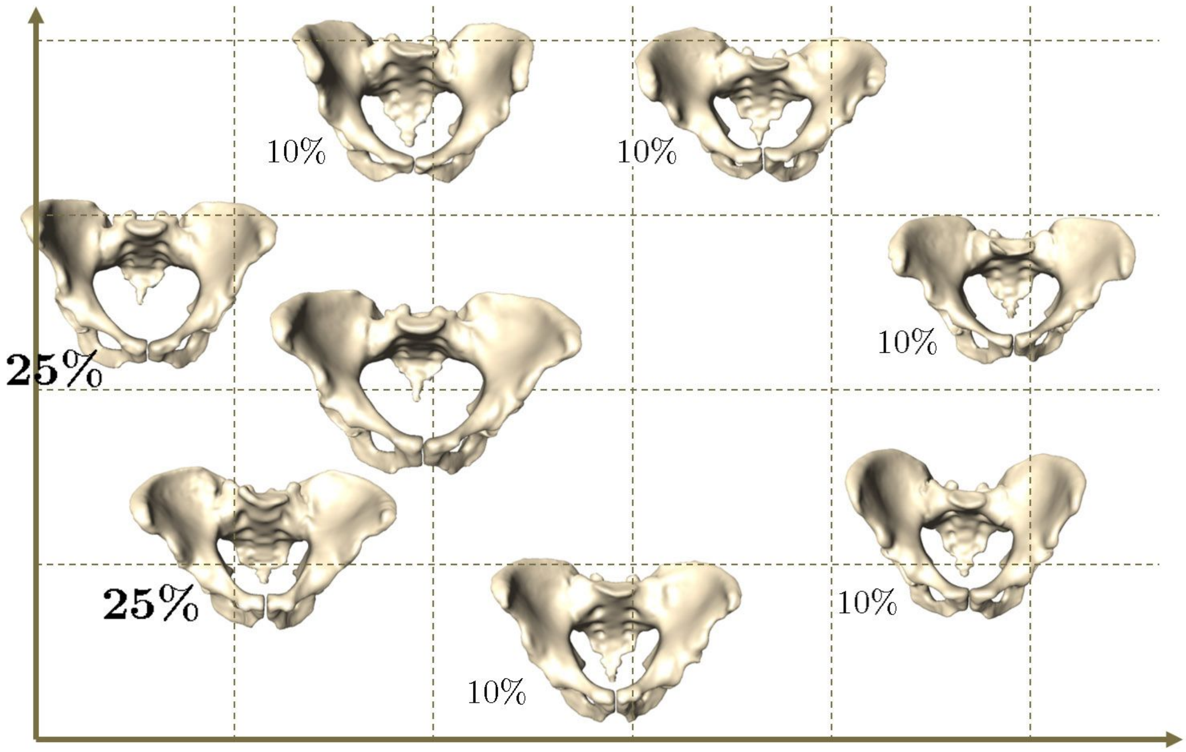

Fig. 9 Interpolation in pelvic shape space generates anatomically plausible shape instances of pelvises

Longitudinal Shape Analysis

Processes such as disease progression or recovery, growth, or aging (Fig. 10) are inherently time-dependent, requiring measurements at multiple time points to be sufficiently described. Clinical research therefore increasingly relies on longitudinal studies that track biological shape changes over time within and across individuals to gain insight into such dynamic processes. While approaches for the analysis of time series of scalar data are well understood and routinely employed in statistics and medical imaging communities, generalization to complex data such as shapes are at an early stage of research. Methods obtained for cross-sectional data analysis do not consider the inherent correlation of repeated measurements of the same individual, nor do they inform how a subject relates to a comparable healthy or disease-specific population. Integrating longitudinal shape measurements into an SSM allows to statistically analyse the temporal evolution of anatomical structures as well as a vivid visualization of the same using morphing.

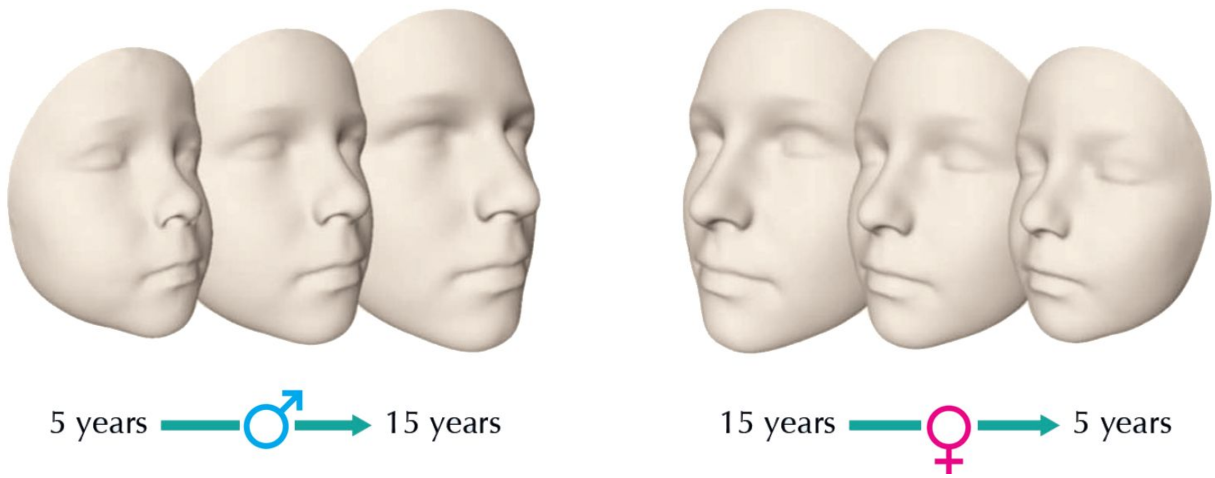

Fig. 10 Mean shape trajectories allow for an interpolation of facial aging effects (Grewe et al. 2013)

Longitudinal analysis requires a common framework based on the use of hierarchical models that include intra-individual changes in the response variable and thereby have the ability to differentiate between cohort and temporal effects. One eligible class of statistical methods are mixed-effects models (Gerig et al. 2016) that describe the correlation in subject-specific measurements along with the mean response of a population over time. At individual level, continuous trajectories have to be estimated from sparse and potentially noisy samples. To this end, subject-specific spatiotemporal regression models are employed. They provide a way to describe the data at unobserved times (i.e. shape changes between observation times and — within certain limits — also at future times) and to compare trends across subjects in the presence of unbalanced data (e.g. due to dropouts). An approach used is to approximate the observed temporal shape data by geodesics in shape space and based on these, estimate overall trends within groups. Geodesic models are attractive as they feature a compact representation (similar to the slope and intercept term in linear regression) and therefore allow for computationally efficient inference (Nava-Yazdani et al. 2018).

Articulated Statistical Shape Models

In functional analysis it is often necessary to not only consider a single anatomical shape but a shape ensemble of different interacting structures since they are in a spatial relationship that is crucial for the respective function. Very well known shape ensembles in musculoskeletal anatomy are joint structures, e.g. hip or knee joint (Fig. 11). A common method to model such joint structures statistically are so called articulated Statistical Shape Models (a-SSMs) (Boisvert et al. 2008, Klinder et al. 2008, Kainmüller et al. 2009, Bindernagel et al. 2011, Agostini et al. 2014). a-SSMs consist of an SSM for each involved anatomical structure of the joint as well as an analytical joint model that describes the degrees of freedom of the joint motion. A standard approach for modeling a hip joint (Fig. 11, left) is a ball-and-socket model, which is completely determined through its rotational center (and a global frame). The connection to the statistical part of the model is established via the coordinates of the rotational center that are included in the shape statistics, s.t. it becomes a component of the SSM being always placed at a plausible location. Other examples for joint models are hinge joints for the knee or the elbow (Fig. 11, center), often coupled with additional degrees of freedom for rotation and/or translation, or bicondular joints as for the temporomandibular joint (Fig. 11, right).

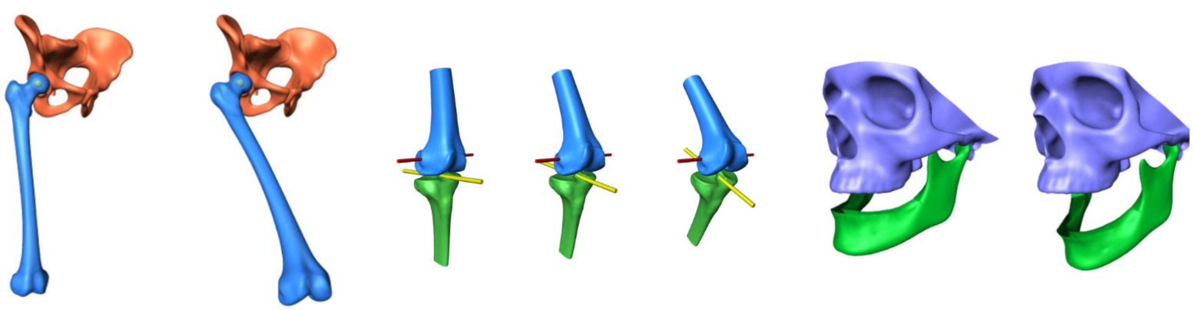

Fig. 11 Examples of articulated SSMs: hip, knee, jaw (Kainmüller et al. 2009, Bindernagel et al. 2011)

The charming aspect of an articulable ensemble of statistical shape models lies in the fact that shape and joint positions can be varied independently of each other, whereby the relationship between articulation and statistical variation of anatomical relations always leads to a plausible result. In addition, degrees of freedom of joints can still be modeled statistically to analyse motion patterns within a population sample.

Statistical Appearance Models

An organ or an anatomical structure varies not only in its shape, but also in its internal structure and appearance. For example, bone can have different degrees of mineralization or the appearance of the skin can differ. In medical imaging, different tissue types also yield to different measurements depending on the imaging modality. In addition to the statistical examination of shape, there are therefore good reasons to also consider the internal structure and the respective appearance when examining anatomical variation (Fig. 12).

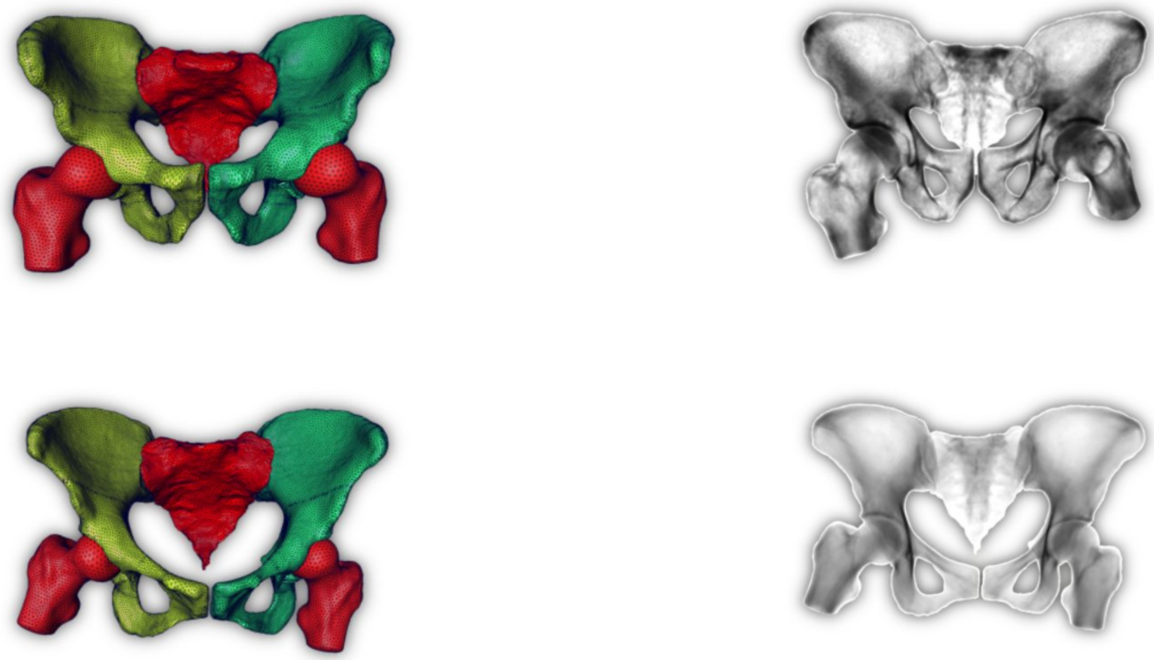

Fig. 12 Statistical variation in shape (Lamecker et al. 2006a), articulation, and bone mineral density (Yao, 2002)

Models combining shape and image statistics are known as Statistical Shape and Appearance Models (SSAM). Such models play an important role in diagnostics, where it has to be acknowledged that shape statistics alone is not in every case the solution to a problem (Mukhopadhyay et al. 2016). If we e.g. consider knee osteoarthritis (see Fig. 13) and here especially the assessment of femoral/tibial cartilage degenerations we note that the cartilage interface shows macarations before denudations emerge thereof. These macarations can be seen in MRI as the cartilage soaks synovial fluid and appears brighter than usual. If one relies on shape knowledge alone there is no chance to notice this clear sign of disease progression, i.e. shape statistics remains blind for inflammatory processes. However, it is possible to sample appearance patterns within the tibial and femoral head s.t. a statistical analysis similar to the PCA-based one on shapes can be performed on appearances to solve these ambiguities.

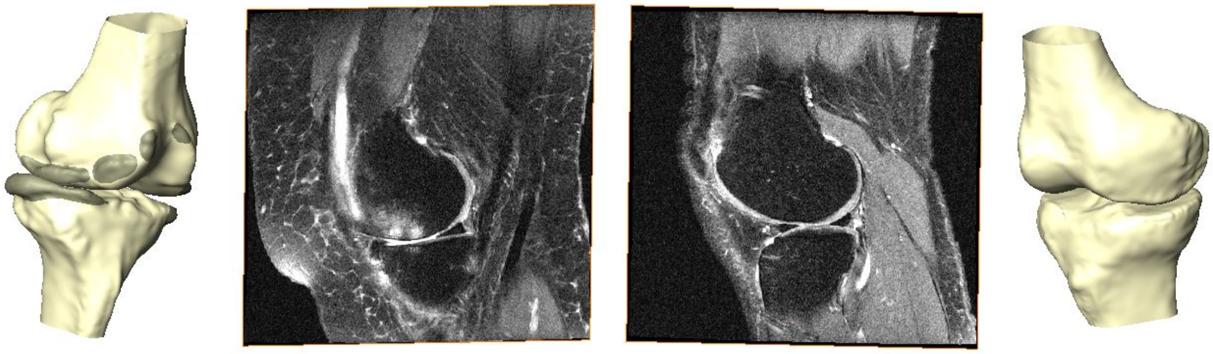

Fig. 13 An osteoarithritic knee (left) showing pathological shape and appearance features versus a healthy control (right)

Another example is the statistical evaluation of bone mineral density (BMD). SSAMs allow to analyse the relationship between BMD, bone shape, and demographic parameters, like age or sex within a large population.

Applications for Statistical Shape Models

A tremendous number of applications arose in the field of statistical shape modelling within the last decades and yet it is very likely that new ones will emerge in the future (Lamecker et al. 2005, Lamecker and Zachow, 2016). Since it would overexpand this chapter's scope we will, in the following, focus on some prominent examples with respect to anatomical shapes (Fig. 14).

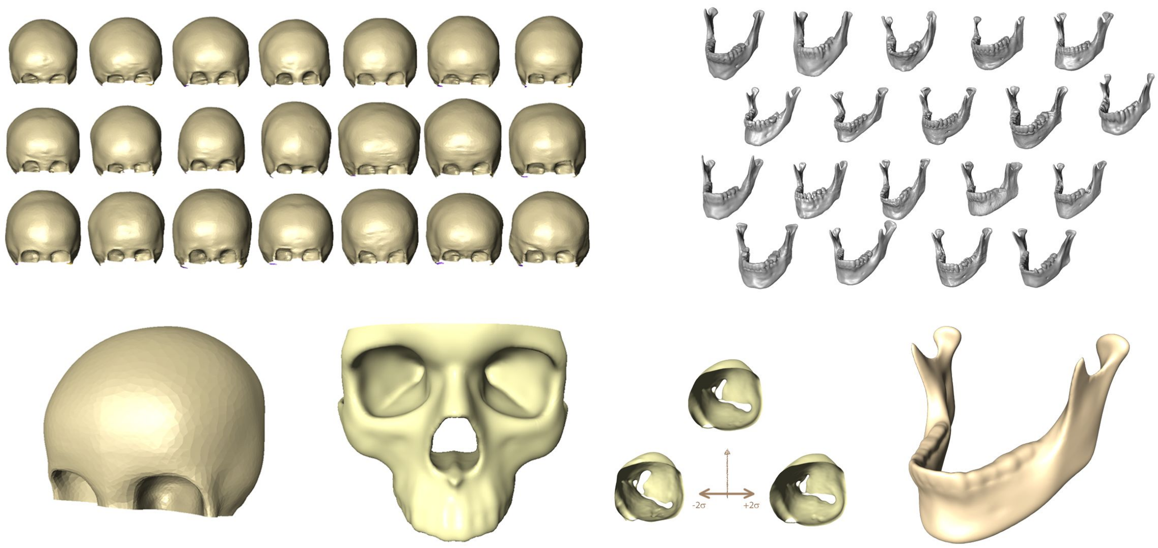

Fig. 14 Examples of statistical shape models:, neurocranium, bony orbit, midface, and mandible (Zachow, 2015)

Imaging and Metrology

Except in the case of Computer Aided Design (CAD), shapes are typically represented in a discrete form by a collection of point measurements that are distributed over the surface of an object. Shape measurements can be taken stereo-photogrammetrically, tactilely or by tomographic methods (CT, MRI) and they can either be dense or sparse, thus capturing more or less detail of a measured object. In addition, measurements may be disturbed by measurement errors and artifacts. To reconstruct an object's shape from such measurements robust algorithms are required that are able to cope with measurement errors, sparsity, or incompleteness.

With the help of (articulated) Statistical Shape and Appearance Models (a-SSAMs) geometric priors (i.e. anatomically plausible deformable templates) are given, being a valuable resource for a reconstruction of shapes from measurement data. This has been successfully demonstrated with automated geometry reconstruction approaches using a-SSAMs (Seim et al. 2010, Kainmüller et al. 2009, Tack et al. 2018, Ambellan et al. 2019) that again imply speeding up the extension of the respective SSMs. However, the benefit of using prior geometric knowledge for reconstructing shapes from measurements becomes even more valuable in cases where measurements contain severe disturbances or do not completely describe an object due to the circumstance that the measuring field is too small, the object is not fully covered by the field of view, or the anatomy of interest is simply not fully accessible to the measurement (Vidal-Migallon et al. 2015, Wilson et al. 2017, Bernard et al. 2017). In its extreme, 3D shapes may even be reconstructed from very sparse measurements in case the respective geometric prior is powerful enough to extrapolate the missing information. An example would be a geometric 3D reconstruction of anatomical structures from a few 2D radiographs or even a single one (Ehlke et al. 2013).

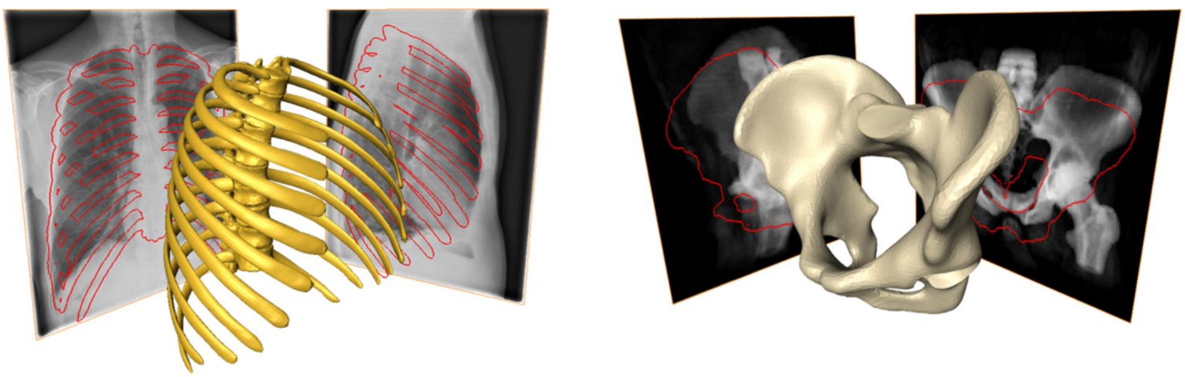

Fig. 15 SSM-based 3D reconstruction of anatomy from 2D X-ray images (Lamecker et al. 2006a, Dworzak et al. 2010, von Berg et al. 2011)

In case two or more radiographs for the same subject are given and the imaging setup, i.e. the spatial relationship between the acquired images (source, patient, detector) is known, an SSM can be fitted to the image data in such a way, that its projections (for example silhouettes) match the boundaries within the given images best (Fig. 15). This concept will be found in today's full body stereo-radiographic imaging systems, becoming an alternative to tomographic imaging in particular orthopedic applications. In cases where only a single radiograph is available, as it often is in functional imaging using fluoroscopy or in orthopedics for imaging weight-bearing situations, (a)-SSAMs offer a valuable resource for a 3D reconstruction of anatomy from the given measurements (Fig. 16). The matching between the deformable template and the image data using SSAMs not only relies on the silhouettes but also on the appearance of the complete anatomical structure within the images. That way both, shape and appearance are used to robustly drive an algorithm to select a best matching shape and pose from the statistical model.

However, it remains to be said that such 3D reconstruction from sparse measurements always requires a representative statistical model to faithfully approximate the imaged anatomy.

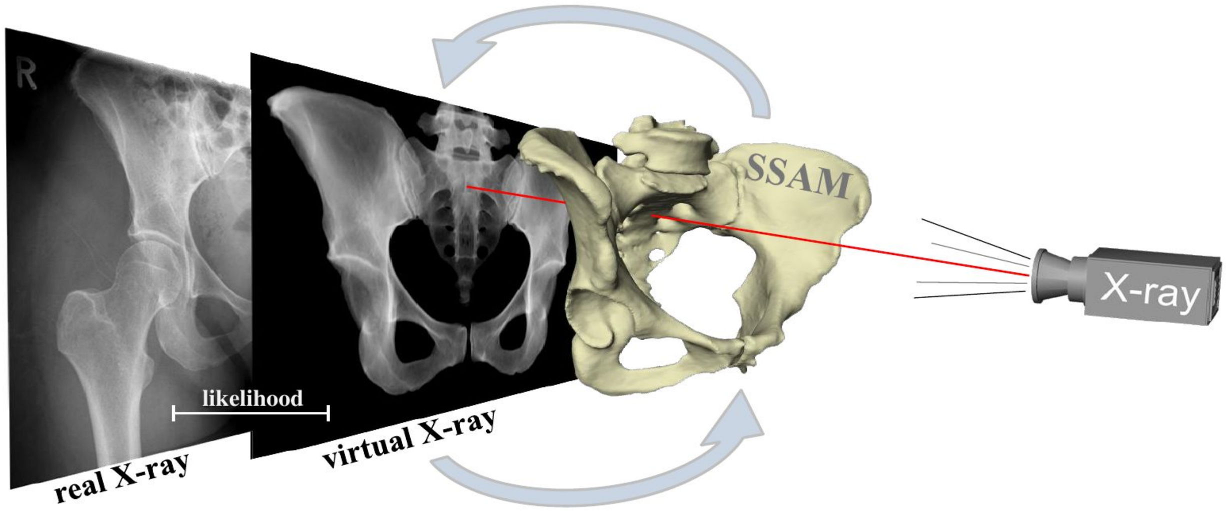

Fig. 16 Concept of SSAM-based 3D reconstruction of anatomy from a single radiograph (Ehlke et al. 2013)

Shape knowledge in combination with medical X-ray imaging (e.g. C-arm technology) also opens up new possibilities in dose reduction, since image acquisitions can be designed in such way, that a few well chosen perspectives might already be sufficient to reconstruct the anatomy of interest. This becomes especially useful for dose-critical applications as image-based positioning for radiotherapy, intraoperative, or functional imaging.

Shape Analysis

With an increasing amount of data from medical imaging and epidemiological studies as well as intensified initiatives to make such data available for research, new possibilities of morphological population analysis arise. Large longitudinal databases, in addition, offer the unique opportunity to investigate the connection between changes in anatomical shape documented through imaging at different time points and disease states rated by domain experts. Shape analysis by means of SSMs serves hereby as a valuable tool that provides a complexity reduced compact encoding for a large set of shapes. In particular, employing the coefficients representing the shapes within the basis of principal modes of variation yields highly-discriminative statistical descriptors that are able to capture characteristic changes in shape (see Fig. 17). This encoding in turn is well suited for the application of established analysis methods, e.g. employing concepts of machine learning. On the one hand, unsupervised learning can be applied to infer hidden structures and patterns in the shape data without relying on clinical variables. For example, a clustering approach could help to identify disease-specific subgroups within the data that can improve shape-based risk assessment and treatment planning (Bruse et al. 2017). In particular, clustering on SSM-based shape descriptors from a population diagnosed with coarctation of the aorta identified subgroups in aortic arch shape confirming the current clinical classification scheme (normal/crenel or gothic) and even revealed a new shape class related to age (Gundelwein et al. 2018). On the other hand, in a supervised framework, labels like disease states can be employed to train classifier systems (von Tycowicz et al. 2018) that facilitate computer-aided diagnostics of anatomical dysmorphisms.

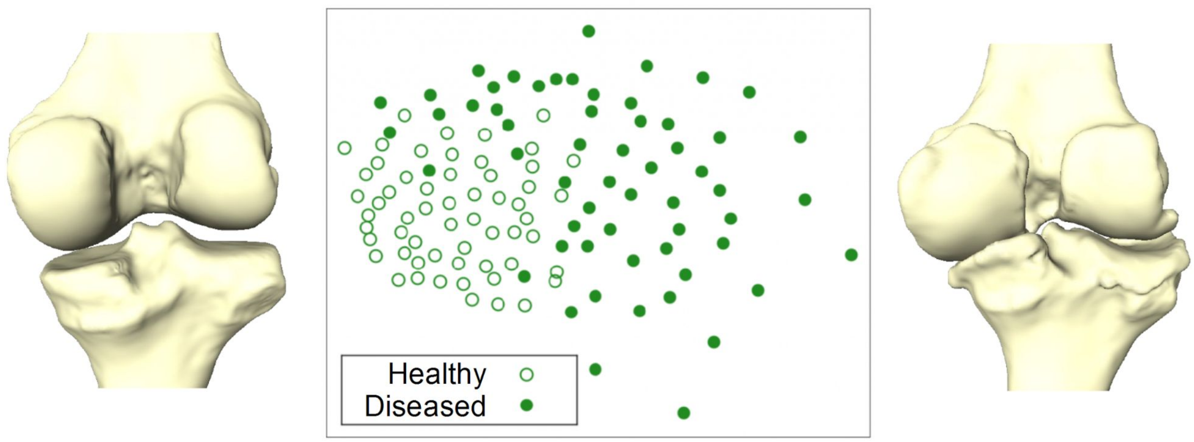

Fig. 17 Low-dimensional visualization (middle) of an SSM-derived shape descriptor used to separate healthy (left) and severely diseased knees (right), where each point is representing a subject's femoral shape.

Furthermore, statistical shape descriptors (see Fig. 17) can be used to support the clinical decision-making processes as well as for the development of disease scoring mechanisms that operate fully automatically.

Product Design

For products like implants or customized instrumentation it is of utmost importance to meet the anatomy related morphological needs of a patient as precise as possible, since otherwise the outcome of a medical intervention may not fulfill the expectations (Fig. 18). In fact, there is evidence that in total knee arthroplasty patient dissatisfaction is at least partially related to a mismatch between the preoperative shape of the distal femur and its shape postoperatively, either due to the shape of the femoral component or its positioning (Akbari Shandiz, 2015, Akbari Shandiz et al. 2018).

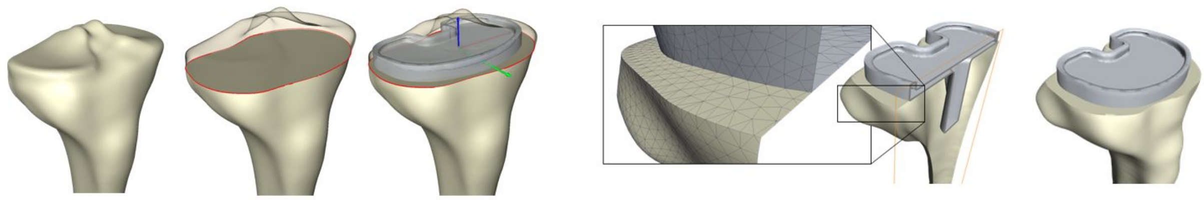

Fig. 18 Digital design and positioning of the tibial component of a knee implant (Galloway et al. 2013)

In contrast to individualized design, manufacturers and users (i.e. surgeons) are also interested in having a set of standard implants with the widest possible range of applications in terms of fit. Both, individual design as well as population-based design, do benefit from shape knowledge. Since SSMs help us to parametrize the morphological variation of anatomies and hence to visualize and to understand it in a better way, they offer - in combination with modern manufacturing techniques such as 3D printing - an immense opportunity to approach the society's need for mass customization due to a population-based design process (Fig. 19).

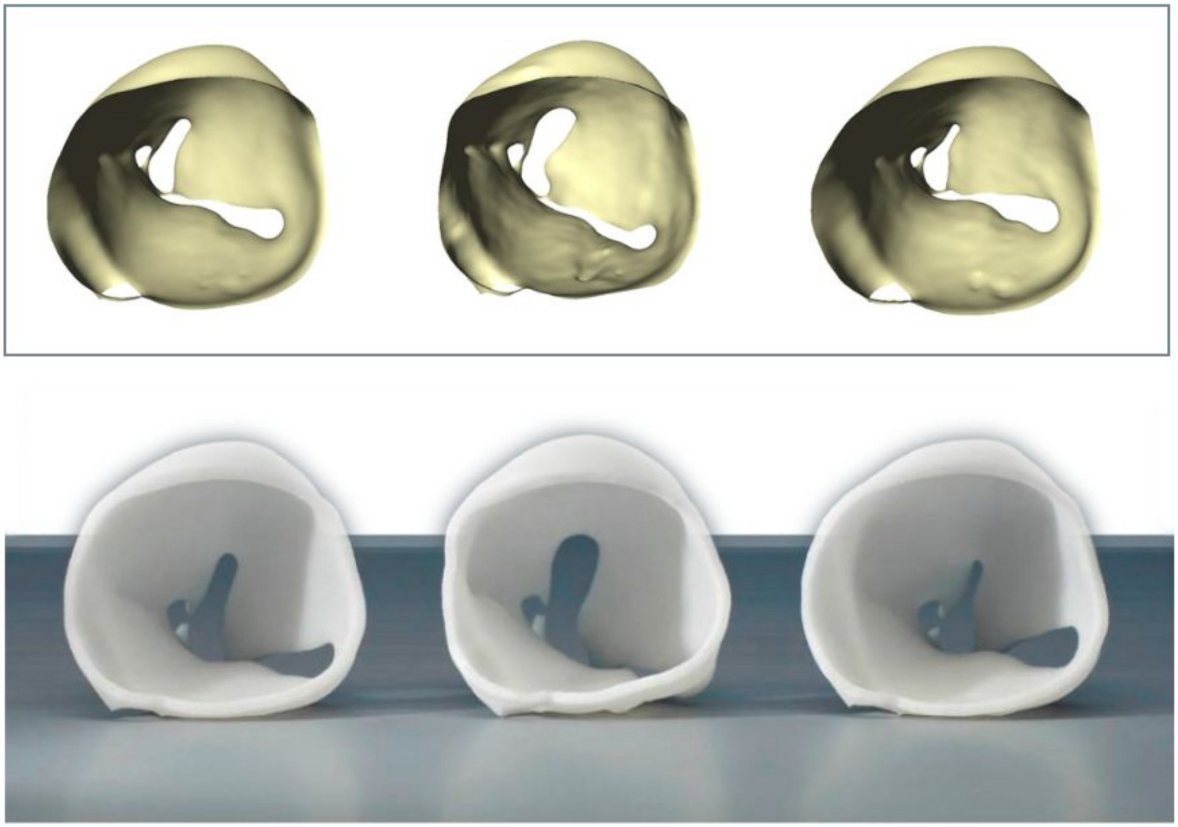

Fig. 19 Representative digital shape instances of the bony orbit derived from an SSM (top) and the corresponding physical prototypes for population-based design of orbital implants (Kamer et al. 2006)

Therapy Planning

Although the word 'normal' is probably an inappropriate one to being applied to the human body (Griffiths, 2012) we note that SSMs may help to improve anaplastology with restoring what is 'normal' patient specific anatomy. With the help of extensive shape knowledge, which is represented by statistical shape models, it is possible to plausibly complete pathological morphologies, e.g. fractured or surgically resected regions (Zachow et al. 2010). In addition SSMs may serve as an objective for plastic and reconstructive surgery to assess malformations (Zachow et al. 2005) and to surgically correct them with respect to normally developed anatomical structures (Fig. 20).

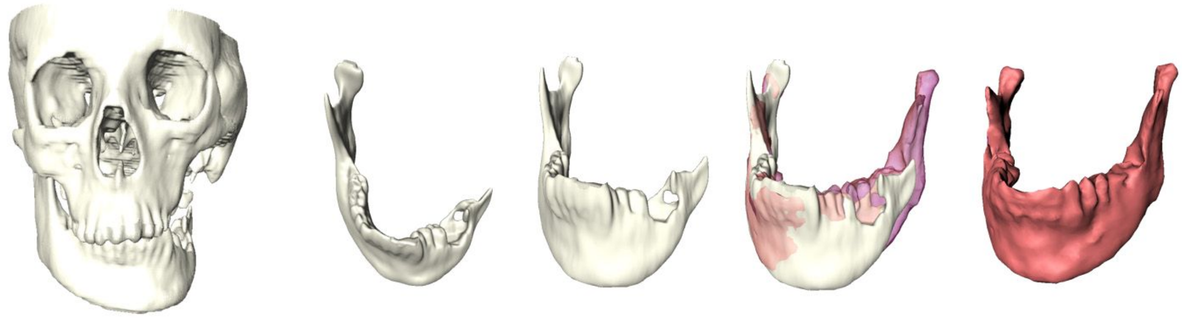

Fig. 20 Reconstruction of mandibular dysplasia using statistical shape modeling (Zachow et al. 2005)

Statistical anatomy is also extremely valuable when an objective is missing and constructive rather than reconstructive surgery is required. This is particularly true for congenital malformations such as craniosynostosis or other syndromes associated with skull development, where craniofacial (re)construction is necessary in children to surgically correct disfiguring defects. A reference for cranial remodeling would be the heads of unaffected children. Hence, an SSM of many neurocraniums has been generated and fit to the unaffected regions of an individual patient's head suffering from craniosynostosis (Hochfeld et al. 2014). The model was then fabricated, sterilized, and intraoperatively used as a template for reshaping the forehead of the patient (Fig. 21). Such a model-based planning and intervention reduces the time of surgery and thus the anesthesia as well as the possibilities of complications.

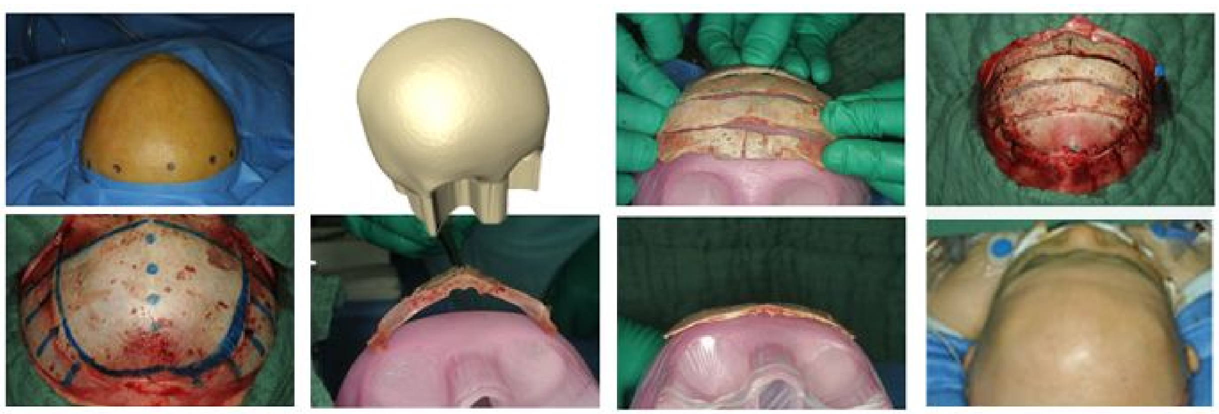

Fig. 21 Reshaping of an infant's skull based on statistical shape analysis (Lamecker et al. 2006b)
(photos taken by F. Hafner, Charitè Berlin)

Diagnosis and Follow-Up

Medical diagnostics is based on a conceptual understanding of healthy (normal) anatomical structures and their deviating (pathological) properties. A comprehensive database of anatomical shapes and appearances in combination with an appropriate classification of the associated health status provides the basis for a profound radiological assessment. The automated segmentation of medical image data using a-SSAMs in combination with machine learning opens up new and efficient possibilities for computer-aided diagnosis (Tack and Zachow, 2019). Well-trained neural networks (i.e. data-driven algorithms) can propose a classification based on such a database and thus serve as diagnostic decision support. In combination with the assessment of radiological experts, the procedures learn with each new case, so that they continuously represent the expert knowledge. As the number of cases increases, the pre-classification will correspond more and more to the expert opinion and, ideally, in a large number of cases only needs to be confirmed by the radiologist. Since the amount of medical image data is continuously increasing and the time required for radiological diagnosis is a valuable resource, computer-assisted diagnosis systems will make radiological diagnostics more efficient in the future and allow human competence in the assessment of anomalies to focus on cases of doubt. The analysis of extremely large databases can be carried out as often as required in order to retrieve requested cases within a defined range of variation for queries on disease patterns, or to analyse the data over and over again with regard to new disease patterns that have been recently learned by the algorithms. Such automated procedures form the basis for radiological screening and thus the future discipline of radiomics.

A fundamental understanding of the diversity of anatomical shapes and the possibility of quantitative shape analysis serves not only diagnostics but also the evaluation of therapeutically induced changes. For a subsequent verification of the effectiveness of a therapeutic treatment or to check whether the planned procedure has been correctly implemented, a comparison between the preoperative condition, the planning, and the therapeutic result is necessary. A morphological comparison requires a plausible dense correspondence which is inherently given by recent algorithms for shape analysis. The application of such methods within a follow-up serves not only to monitor success but also for documentation and quality assurance in future evidence-based medicine.

Education and Training

By studying anatomy, students must become aware that there is often a broad spectrum of "normal" in the shape or appearance of anatomical structures (Bergmann et al. 1988). Therefore, students must learn how to distinguish between normal and abnormal variations. Classical anatomical atlases or physical anatomical models usually show shapes of healthy structures and their relationship to each other on the basis of just one example. The range of variation occurring in a population is typically not illustrated due to a lack of precise knowledge. Also, the graphical possibilities to illustrate the range of variation of anatomical shapes and positional relationships are limited. In the best case, there are images or physical models of extremely deviant forms, whereas undefined is what exactly the "norm" means. Communicating the importance of anatomical variation to students is still considered challenging.

There is currently no systematic approach to the morphological evaluation of anatomical diversity of shapes. This is where new digital possibilities come into play. Statistical 3D shape models can be visualized vividly and with high quality by computer graphics, as in the illustrations shown in this chapter. The possibilities are extremely diverse, from photorealistic to strongly stylized. 3D organ models can be decomposed into anatomical substructures that can be displayed individually or together. Structures can be viewed, measured and annotated from all sides or arbitrarily cut to reveal inner substructures. With SSAMs even virtual medical image data such as X-rays, or tomograms can be generated to communicate varying appearances with respect to imaging. A visualization can either take place on a 2D screen or in 3D, whereas virtual reality techniques may enable an immersive viewing effect. With the help of augmented reality techniques, shapes can also be superimposed on real images in order to carry out visual comparisons.

However, the special feature of communicating the diversity of shapes is morphing, where the entire shape space of an anatomical structure can be explored by interactively varying shape parameters with an immediate visual response. The shape parameters themselves are chosen to be as compact as possible in order to keep the number of degrees of freedom as low as possible. Typically, the shapes can be varied using the main modes of variation resulting from component analysis. The animated representation of the shape variation reveals the respective shape spectrum of an anatomical structure to the observer. Statistical shape models, which have been generated from a very large and representative amount of training data, such as epidemiological studies, provide reliable representations of average shapes for anatomical structures as well as their variations within one or more standard deviations up to anomalous shapes. The statistical model can be continuously extended with each newly added shape instance. Any shape that can be generated in the respective shape space of the SSM can be visualized or manufactured as a physical model using appropriate manufacturing techniques. Such models can then be also employed for model-based training of medical procedures.

Clinical Research based on Shape Analysis

There is increasing evidence that studying shape rather than derived scalar measurements such as volume provides quantitative measures that are not only statistically significant but also anatomically relevant and intuitive. In particular, a scalar description can only capture one of the many aspects of a full structural characterization. Also, analysis of individual clinical variables using independent models for each variable do not account for correlation between the measures. Contrary, statistical shape modeling allows to account for all shape features and their correlations at once without the need to predefine discrete shape measurements. This advocates the use of SSMs for extracting clinically relevant information as required for modern precision medicine strategies.

A major theme in shape-based clinical research is to determine whether the morphological changes found in one group are significantly different to those found in another. For example, one might ask if the cardiac anatomy of patients with chronic regurgitation evolves differently than that of healthy aging subjects. As SSMs provide an estimate of the probability density function that underlies the observed shapes, group testing can be performed using suitable multivariate distances as test-statistics. In this context, permutation tests allow to build statistically powerful tests in a nonparametric fashion that do not require strong assumptions underlying traditional parametric approaches. Beyond the statistical framework, SSMs provide a generative shape model that allows to explore (within certain limits) the shapes belonging to an object class under study (see Fig. 9). For instance, the visualization of shape changes that are most dominant within a population or show a high correlation to clinical variables could help to develop an intuition about underlying mechanisms. Ideally, this would spur the development of novel hypothesis, which could be tested against new data and, hence, lead to an improved knowledge.

Future Implications of Statistical Anatomy

Statistical 3D shape models form the basis for a wide range of possible applications. The above described examples demonstrate the possibilities of shape analysis for medical applications only. SSMs also provide an interesting foundation for various other questions, such as in anthropology, biometry, evolutionary biology, biomechanics and many more. In runners, for example, it was investigated whether unusually long heel bones (Calcanei) give the calf muscles a better leverage effect and whether these runners are therefore more successful (Ingraham, 2018). In forensics, it would be conceivable to draw conclusions from the shape of the skull to the external shape of the head using statistical shape models. Products around the human body can be better tailored by means of shape analysis. The spectrum extends into the entertainment sector, where character designs can be created more intuitively and more diversely through statistical modelling than has been the case to date.

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[OAI] The Osteoarthritis Initiative, National Institute of Health, USA, https://oai.nih.gov/

[SHIP] Study of Health in Pomerania, Forschungsverbund Community Medicine at Greifswald Medical School, http://www2.medizin.uni-greifswald.de/cm/fv/ship

[GNC] German National Cohort, German federal and local state governments and the Helmholtz Association, https://nako.de/informationen-auf-englisch

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