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Soft-tissue facial anthropometry in three dimensions: from anatomical landmarks to digital morphology in research, clinics and forensic anthropology

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Summary – *The quantitative assessment of the dimensions of human facial soft-tissue structures (eyes, nose, mouth and lips, chin, ears), their reciprocal spatial positions and relative proportions, has an interdisciplinary perspective: anatomical and anthropometric descriptions, medical evaluations (clinical genetics, orthodontics, maxillo-facial and plastic surgery), forensic medicine, they all need reference three-dimensional data collected on healthy, normal individuals selected for sex, age, ethnic group, to be compared to those obtained on the single individual. The data collection technique should be non-invasive, fast, as simple as possible, performed directly on the subjects using low-cost instruments. Data should be collected in digital format, so to allow the creation of computerized data bases, and the use of the computerized techniques of visualization and simulation of treatment. Independent of classic direct anthropometry, various three-dimensional image analyzers are increasingly being used in clinical investigations and research. The instruments can be divided into two main categories: optical, non contact digitizers, and contact instruments. The first kind of instruments (mainly, laser scanners and stereophotogrammetric devices) perform a fast digitization of the face, providing a detailed analysis of the soft-tissue surface. Contact instruments (electromagnetic and electromechanic digitizers) use a landmark representation of the soft-tissue facial surface. Landmark coordinates are coupled to a mathematical and geometric model of the face, and angles, distances and ratios similar to those measured in conventional anthropometry can be obtained. Additionally, multivariate methods of analysis, obtained either from geometric morphometry or from other analytical methods, could be used. Optical instruments provide a larger amount of information but they cannot assess all the actual anatomical landmarks obtained by contact instruments. Motion artifacts are more common with contact instruments, but they can be easily transported, and they are less expensive. Overall, contact instruments seem sufficiently reliable, simple and fast to be used also in a clinical context, thus providing useful quantitative information to allow a better patient care, without submitting the subjects to potentially harmful procedures.*

Keywords – *human face, morphometrics, 3D analysis.*

Introduction

In all animals, the head forms the most complex structure of the body. This is especially important in humans: not only the head houses the central nervous system, the eyes and inner ear structures, and the first part of the digestive and respiratory apparatuses, but it is characterized by the face. The face is probably the most important source of communication and interaction with the environment (Hennessy *et al.*, 2005), and it carries information that allows the identification of a single person (DeCarlo *et al.,* 1998; Fraser *et al.*, 2003; Shi *et al.*, 2006). Bones, muscles, cutaneous and subcutaneous layers all contribute to a unique morphology in the single individual. This part of the body has been extensively studied by scientists, clinicians, artists, and they all have tried to measure and reproduce some of its characteristics, not least beauty (Kunjur *et al.*, 2006).

Artists and scientists have often used similar methods for the analysis of human face: during the Renaissance, Leonardo da Vinci in Italy, and Albrecht Dürer in Germany developed graphical methods to describe the variations in facial morphology (Peck and Peck, 1995) (Fig. 1). At the beginning of the XX Century, D'Arcy Thompson revisited this approach with his "Cartesian transformations", which were applied to clinical diagnosis in orthodontics in the 1930s by deCoster, in France, and in the 1950s by Moorrees, in North America (Ferrario *et al.,* 1996a; Moorrees and Kean, 1958).

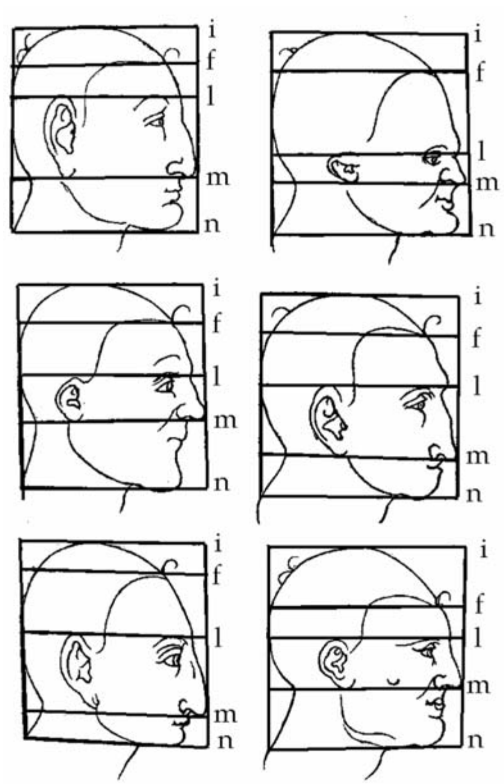

Fig. 1 - Facial proportions and disproportions by Albrecht Dürer. Modified from "Vier Bücher von menschlicher Proportion". Nuremberg: Hieronymus Formschneyder, 1528, p. 175.

The overall form (size, shape and reciprocal arrangement of the parts) and function of the face and head derive from a composite, coordinated pattern of development of separate cartilaginous, osseous, dental and soft-tissue elements. Environmental stressors model and can even alter the genetically determined outline (Breitsprecher *et al.*, 1999).

The correct assessment of this complex structure should be made with a complete morphological and functional evaluation, aimed at a global assessment of all elements classically forming beauty: precision, symmetry, coordination and functional structure (Breitsprecher *et al.*, 1999). The first elements to be considered are those describing the morphological structure, that forms the base for function. The present review will focus on the quantitative analysis of facial morphology in all three spatial dimensions, in particular dealing with data collection methods that assess non-invasively the soft-tissue structures of living human beings. Some notes on two-dimensional data collection methods currently used in research and clinics are also provided.

Some of the analytical methods that can be used to interrogate the three-dimensional data are presented. Indeed, the use of new instruments for data collection should always be coupled with the development of statistically sound and biologically meaningful methods for data analysis, in order to gain a deeper understanding of the analyzed structures and of their relationships in space and time (Hennessy and Moss, 2001).

Two-dimensional methods and their three-dimensional counterparts

Radiography

Until 1895 only the soft tissues of living individuals were assessed, but with the revolutionary discovery of x-rays made on November 8th by Wihelm Konrad Roentgen, bones also became accessible to clinicians and researchers. Interestingly, the head was one of the first structures to be extensively analyzed, and the first clinical head radiographs seem to have been taken as early as 1896 (Broadbent *et al.*, 1975).

Subsequently, the technique for head and face radiographs was refined and standardized especially by Broadbent, who modified the original craniostat developed by Todd at the Department of Anatomy of Western Reserve University making it probably the first cephalostat to be used for taking head radiographs in living individuals (Broadbent *et al.*, 1975). The method obtained separate but coordinated lateral and postero-anterior two-dimensional projections, and it was built to allow some kind of three-dimensional reconstruction of head and facial structures (Adams *et al.*, 2004; Hajeer *et al.*, 2004b). Unfortunately, all the well known technical problems of radiographic projections (enlargement, distortion, superimposition of structures belonging to different planes), together with the difficulties in the interpretation of the postero-anterior radiographs, made the three-dimensional approach almost neglected for clinical applications, even if some attempts have been made to bring the method into practical use (Brown and Abbott, 1989). Additionally, the method is very invasive, requiring a double quantity of x-rays.

Since the early 1980s, computed tomography (a x-ray based technique) and magnetic resonance imaging (a method that assess the behavior of living tissues introduced into magnetic fields) have been providing three-dimensional reconstructions of the entire craniofacial skeleton, together with the soft tissue structures (Adams *et al.*, 2004; Hajeer *et al.*, 2004b; Katsumata *et al.*, 2005; Papadopoulos *et al.*, 2002). Both systems virtually slice the analyzed structure, and a three-dimensional reconstruction is mathematically provided using the scanned slices (a plane, with two coordinate axes) and the inter-slice distance (third axis, perpendicular to the scanned surface) (Hajeer *et al.*, 2004b). Unfortunately, both methods are too expensive and have limited availability to be used outside well-selected clinical settings. Also, it seems very difficult to obtain a data base of normative values from healthy, non-patient subjects for both radioprotection concerns (computed tomography) and monetary considerations (magnetic resonance) (Sforza *et al.*, 2006). Currently, more recent radiographic methods, like the conical x-ray approach, seem to offer more affordable three-dimensional craniofacial reconstructions (Adams *et al.*, 2004), but actual in-vivo studies are still lacking.

Photography

Photographs, a non-invasive, low-cost method for soft-tissue evaluation, are also widely used in human research and clinical practice, but most often the pictures are taken for illustration purposes only, and they are less frequently used for actual measurements (Ferrario *et al.*, 1992, 1993a, 2001a; Finizio *et al.*, 2005; Gonzalez *et al.*, 2005; Guyot *et al.*, 2003; Hurwitz *et al.*, 1999; Kugu *et al.*, 2004; Kunjur *et al.*, 2006; Stephan, 2002, 2003; Stephan and Henneberg., 2003; Tangchaitrong *et al.*, 2000; Valenzano *et al.*, 2006; Wilkinson *et al.*, 2003). Obviously, they suffer the same limitations of radiographic projections, and their use in a three-dimensional setting provides only partial data (Allanson, 1997; Douglas *et al.*, 2003b), even if some attempts toward their three-dimensional use had been made in the past (Motoyoshi *et al.*, 1992). The use of proportional indices and angles would partially overcome the problem of magnification.

Current public and commercial use of video surveillance (Fraser *et al.*, 2003; Halberstein, 2001; Yoshino *et al.*, 2000) could possibly result in new quantitative applications of the method.

Direct facial anthroposcopy and anthropometry

Direct anthroposcopy (observation) and anthropometry (measurement) had therefore still continued to be the unique methods for in-vivo analyses of facial morphology in several basic and applied fields that cover a wide range of life and medical sciences (Farkas, 1994). Even in the XXI Century, with the advent of sophisticated techniques that can give actual insights into our genome, the direct observation and measurement of the face of human beings play an important role in the diagnosis of several dysmorphic syndromes, especially for the assessment of borderline patients (Allanson *et al.*, 1999; Douglas *et al.*, 2003a; Farkas *et al.*, 2005a; Guyot *et al.*, 2001; Hammond *et al.*, 2004; Horn *et al.*, 2004; Lane *et al.*, 1997; Meintjes *et al.*, 2002; Moore *et al.*, 2002; Skrinjaric *et al.*, 2003; Ward *et al.*, 2000; Zankl and Molinari, 2003).

For instance, abnormalities in ear dimensions and position are commonly found in several alterations of the human chromosomes and karyotype, both postnatally, and during intrauterine life, as recently reviewed (Sforza *et al.*, 2005). The prenatal developmental period of the ear is relatively long, spanning from week 12 to week 22; also, its complex shape makes it particularly prone to disturbances (Lane *et al.*, 1997). Among the others, ear length has been recently, tentatively, proposed as an additional marker for ultrasound-based prenatal screening of aneuploidy (Chitkara *et al.*, 2002). Subjects with trisomy 21, the most common autosomal aneuploidy found in humans, have smaller ears than subjects with a normal karyotype; the difference can be appreciated before birth, and it continues postnatally (Chitkara *et al.*, 2002; Sforza *et al.*, 2005).

For clinicians, the dimensions of facial soft-tissue structures (such as eyes, nose, mouth and lips, chin, ears), their reciprocal spatial positions and relative proportions, are important components in treatment planning of patients with facial alterations and deformities and in the final evaluation of results (Farkas *et al.*, 2005a; Ferrario *et al.*, 1999; Sforza *et al.*, 2006).

Conventional, direct anthropometry is currently considered the gold standard for in-vivo assessments: the method is simple, low-cost, and it does not require complex instrumentation (Allanson, 1997; Farkas, 1994; Moore *et al.*, 2002; Skrinjaric *et al.*, 2003; Zankl and Molinari, 2003; Zankl *et al.*, 2002). Unfortunately, it is time-consuming, it necessitates very well trained and experienced examiners, and it is very demanding for both the clinician and the patient (Douglas *et al.*, 2003b; Guyot *et al.*, 2003; Hurwitz *et al.*, 1999; Lane *et al.*, 1997; Meintjes *et al.*, 2002; White *et al.*, 2004). Each measurement is taken individually, a lengthy procedure prone to error (Aldridge *et al.*, 2005), and that does not leave permanent records of the facial arrangement: missing values, miscalculations or reading errors cannot be corrected once the subject has been dismissed (Allanson, 1997). Also, the method does not provide digital coordinate data that could be used to measure a new set of features, or to extract more complex calculations (surface and volume estimations, analyses of symmetry, form and shape quantification) (Douglas *et al.*, 2003a, b; Duffy *et al.*, 2000; Ferrario *et al.*, 2004d; Hammond *et al.*, 2004; Hurwitz *et al.*, 1999; Mori *et al.*, 2005; Soncul and Bamber, 2004; White *et al.*, 2004).

A further advantage of conventional anthropometry is the existence of normal databases for almost all craniofacial measurements, at least for Caucasoids (Allanson, 1997; Farkas, 1994; Zankl *et al.*, 2003), while norms for other ethnicities are more scanty (Farkas, 1994; Farkas *et al.*, 2005b).

Indeed, quantitative evaluations of the patients should be made on the basis of the comparison to global three-dimensional data collected on healthy, normal individuals of same sex, age, ethnic group.

The data collection technique should be non-invasive, fast, as simple as possible, performed directly on the subjects using low-cost instruments (Ferrario *et al.*, 1998; Hammond *et al.*, 2004; Mori *et al.*, 2005; Papadopoulos *et al.*, 2002; White *et al.*, 2004). Data should be collected in digital format, so to allow the creation of computerized data bases (Majid *et al.*, 2005), the implementation of pattern recognition algorithms (Shi *et al.,* 2006), and the use of the computerized techniques of visualization and simulation of treatment (Hajeer *et al.*, 2004b). All these requirements are nowadays met by digital, computerized anthropometry. An increasing number of clinical investigations and basic research studies is applying digital three-dimensional data collection procedures, and several facial characteristics have been quantitatively described in the three-dimensional space by using various image analyzers, as recently reviewed (Douglas, 2004; Hajeer *et al.*, 2004b; Hammond *et al.*, 2004; Papadopoulos *et al.*, 2002; Sforza *et al.*, 2006; Shaner *et al.*, 2000; Weinberg and Kolar, 2005; Weinberg *et al.*, 2004).

Several studies performed in-vivo and on inanimate models have also compared conventional and computerized anthropometric data to assess if they could be, at least in part, swapped, thus opening new possibilities to basic researchers and clinicians (Sforza *et al.*, 2004c; Weinberg *et al.*, 2006). Good in-vivo results have been obtained for soft-tissue orbital features (Douglas *et al.*, 2003b; Gonzalez *et al.*, 2005; Wilkinson *et al.*, 2003), facial profile measurements (Guyot *et al.*, 2003), mouth (Wilkinson *et al.*, 2003) and nasal dimensions

(Sforza *et al.*, 2004c), as well as for a comprehensive set of 19 antero-posterior, vertical and transverse distances (Weinberg *et al.*, 2004). These studies concluded that the conventional anthropometric and digital data seem sufficiently interchangeable, at least from a practical, clinical point of view (Gonzalez *et al.*, 2005; Sforza *et al.*, 2004c). Similar results were obtained on mannequin heads (Weinberg *et al.*, 2006). In contrast, different conclusions were reported by Shaner *et al.* (1998), who compared three-dimensional photogrammetry and caliper measurements on living persons.

From anatomical landmarks to digital morphology

Landmarks represent the key connection between the two methods of facial measurements (Douglas, 2004): conventional anthropometrics identifies soft-tissue landmarks, and places some instrument (like calipers, anglemeters, measuring tapes, protractors) over them to measure the three-dimensional distance between a pair of landmarks, or the angle comprised among three of them (Farkas, 1994). All the surface comprised between the landmarks is then neglected (Richtsmeier *et al.*, 2002), apart from observation of specific features (anthroposcopy). Basically, digital morphometry (quantitative morphology) collects a more or less wide set of landmarks from the soft-tissue surface (depending on the kind of digitizer, as detailed), and uses the spatial x, y, z coordinates as end-points for Euclidean geometry calculations: the same linear distances and angles provided by conventional anthropometrics can be obtained.

The procedure is the three-dimensional equivalent of cephalometric tracing: hard-tissue angles and distances can be obtained on the films directly with rulers and protractors, or mathematically after digitization of the x, y coordinates of the selected landmarks using a two-dimensional tablet (Battagel, 1993).

Indeed, this basic description of digital morphometry is very abridged, and it neglects the considerable possibilities of mathematics and geometrics from one side (for instance, estimations of volumes and surfaces, analyses of symmetry, detailed assessments of shape independently from size, from the same set of landmarks used by conventional anthropometry) (Aldridge *et al.*, 2005; Bookstein, 1991; DeCarlo *et al.*, 1998; Mori *et al.*, 2005; Nkenke *et al.*, 2006; Shi *et al.*, 2006), and of the enormous amount of data collected by some of the digitizers that allow detailed assessments of all inter-landmark surfaces, for instance with the development of pattern recognition algorithms (Hammond *et al.*, 2004; Hennessy *et al.*, 2005).

Types of landmarks

Landmarks (both those identified on soft tissues, and those belonging to the skeleton) possess a spatial definition and a name. The name identifies homology (biological correspondence): a landmark should have the same position in all homologous forms of the same species, and in the average form. Landmarks should be identified consistently and repeatably on the analyzed structures, with a known accuracy. Many landmarks possess a structural role as attachments of muscles and ligaments, and they are used not only to study morphology, development and evolution, but also for functional biomechanical investigations.

In classical biological investigations, several kinds of landmarks are used: anatomical landmarks (also called type I landmarks), where two different tissues or phases meet (for instance, the vermilion border of the lips); geometrically defined landmarks (type II; maximum bending of a structures, for instance the gonion landmark; they have a structural function); extremal landmarks (type III; landmarks belonging to a curve or surface those position is mathematically defined according to the geometric characteristics of the surrounding, like the tip of the nose or pronasale; Moyers & Bookstein, 1979).

According to Bookstein (1991), only the anatomical landmarks are actual biological loci: the modification of their position could be interpreted with a biological meaning (growth, development, spontaneous or assisted movement, etc). Modifications in the position of type II and III landmarks could be due to a larger number of effects: local variations but also changes of the entire structure that transform its geometric characteristics; mathematically, they possess fewer degrees of freedom because they are defined on the basis of other landmarks. Consequently, their use should be reduced to a minimum (Bookstein, 1991).

Digital anthropometry further introduced the use of other kinds of landmarks that possess only a mathematical/ geometrical definition (also called pseudo-landmarks): sliding or interpolated landmarks (Hennessy and Moss, 2001). The sliding landmarks (a type of semi-landmarks) are "landmarks" belonging to a curve (or a surface) drawn between other landmarks; they are allowed to slide on the curve along a tangential direction. Tangential variations must be removed because homology (which defined classic landmarks) is now given to contours. The position of these landmarks is defined according to an interpolation function that optimize their closeness with the surrounding landmarks. Sliding landmarks make it possible to include outline information in the geometric morphometric analysis, and they were introduced to evaluate the surface comprised between "conventional" landmarks (Hammond *et al.*, 2004; Hennessy *et al.*, 2005). Indeed, on soft-tissue facial surfaces like the cheeks and forehead no actual landmarks (according to Bookstein, 1991) exist, and the mathematically generated landmarks can assist in the analysis (Hammond *et al.*, 2004).

Among the methods that can be used to remove the tangential variations, minimization of the thin plane spline's bending energy, and minimization of the Procrustes distance had recently been compared. Mathematical simulations performed on human dental and skeletal structures found different results (both within and between groups) as a function of the method used to obtain the sliding landmarks (Perez *et al.*, 2006). This example underlines the importance of retaining the general biological significance, using mathematics as a tool and not as the scope (Bruner, 2004; Perez *et al.*, 2006; Richtsmeier *et al.*, 2002; Shi *et al.,* 2006).

The pseudo-landmarks are mathematically generated starting from the conventional landmarks (used as control points or anchors) and low-resolution meshes; thin plate splines are used to ensure a smooth surface (Hennessy *et al.*, 2005). The complete mathematical surface (more than 5000 points) is subsequently analyzed by geometric morphometrics to extract biologically important information on shape characteristics (Bookstein, 1991; Hennessy *et al.*, 2005; Soncul and Bamber, 2004).

In other approaches, landmarks are completely neglected, and only facial areas (like the "nasal tip" or the "labiomental groove") are considered in the analysis (Soncul and Bamber, 2004). After careful superimposition and registration of two separate scans, usually made on single, well selected landmarks, longitudinal modifications can be quantified as movements within each of the selected facial areas (Chong and Mathieu, 2006; Kau *et al.*, 2006; Majid *et al.*, 2005; Soncul and Bamber, 2004).

Instruments for three-dimensional digital morphometry

The instruments available for computerized, soft-tissue three-dimensional facial anthropometry can be divided into two main categories: optical, non contact instruments (laser scanners, 3D range-cameras, optoelectronic instruments, stereophotogrammetry, Moiré topography), and contact instruments (electromagnetic and electromechanical digitizers, ultrasound probes) (De Greef *et al.*, 2006; Hajeer *et al.*, 2004b; Sforza *et al.*, 2006; Smith and Throckmorton, 2004).

Both kind of instruments are non-invasive, not potentially harmful (apart from some limitations for laser light, as detailed), do not provoke pain and do not use any energy currently considered to be potentially dangerous to the present or future health of the subjects or of her/ his offspring.

The kind of instrument to be used (optical/ contact) for the collection of soft-tissue facial features should be determined weighting benefits and limits, and also considering the kind of application and the human resources (Tab. 1).

In synthesis, among the main benefits of optical scanners there is the fast data acquisition (with low or null motion artifacts), the high information content obtained from each face, the possibility of off-line assessments of new landmarks. In contrast, landmarks cannot be directly identified on the face, but only assessed digitally (and therefore they may not correspond to anatomical loci), even if some tentative toward prior identification is being made (Weinberg *et al.*, 2004). Currently, the set of landmarks is limited to those clearly identified by inspection only. Additionally, most instruments

Tab.1 - Principal characteristics of the main three-dimensional soft tissue facial digitizers.

	Motion artifacts	Post processing	Landmarks	Information	Dimensions	Cost
Optical scanners (laser scan, stereophogrammetry)	Limited	Lengthy	Identified on the digital image	All surface; for stereophotogrammetry, also texture	Often bulky; not transportable	Expensive
Contact instruments (electromagnetic, electromechanic)	Present	Fast	Directly identified on the skin	Only selected landmarks	Movable with more or less ease	Limited

necessitates special settings, and cannot be moved with ease to meet the subjects. The cost, approximately 8-10 times larger than that of the contact instruments, could be prohibitive for most public researchers and clinicians.

The electromagnetic and electromechanic contact instruments are more prone to motion artifacts because data digitization is long; also, they cannot record all facial surface, thus losing information. The lack of a permanent trace of the facial appearance impedes off-line corrections, or to introduce new landmarks. Their strengths are the low cost, their being movable (the electromechanic with some more ease than the electromagnetic), but, most of all, their possibility to work with actual anatomical landmarks and not with their digital counterparts. The analyzed landmarks, therefore, retain all their biological significance, which may be lost when only mathematical models are used (Bruner, 2004; Richtsmeier *et al.*, 2002; Shi *et al.,* 2006).

A detailed, critical description of the two categories of instruments may allow to better appreciate benefits and limits.

Optical instruments

The optical instruments can be used for a fast analysis of facial surface, thus providing data on facial surface area and estimates of facial volume, and for indirect anthropometric assessments.

The principal instruments are laser scanners and stereophotogrammetric systems: the first illuminated the face with a laser light source while digital cameras capture the images; the depth information is obtained by triangulation geometry (Hennessy *et al.*, 2005; Majid *et al.*, 2005). During data acquisition, either the face or the laser light move to cover all the surface. While in the first scanners the laser light was not eye-safe, current instruments are stated to be not dangerous, and they could be used also for children (one cannot be completely confident in they keeping their eyelids closed). Accuracy and resolution are reported between 0.5 and 1 mm, and approximately 30 s are necessary for a complete scan (Hennessy *et al.*, 2005; Majid *et al.*, 2005). Often, not all facial surface can be scanned, and the most lateral parts of the face (namely the ears) may not be well digitally reproduced (Weinberg and Kolar, 2005). Also, shadows, local facial characteristics (hairs, nevi), as well as a dark complexion may obtrude the digitization, and motion artifacts can occur during the scan (Majid *et al.*, 2005).

In stereophotogrammetry a light source illuminates the face, and two or more coordinated cameras record the images from different points of view (Ferrario *et al.*, 1996c; Hajeer *et al.*, 2004b; Majid *et al.*, 2005). A computerized stereoscopic reconstruction is then obtained (Fig. 2). The method seems to have been first used for the clinical study of human face in 1944 (Hajeer *et al.*, 2004b), well before the advent of digital image technology. Accuracy and resolution are around 0.5 mm, and 2 ms can be sufficient for a facial scan (Aldridge *et al.*, 2005; Hammond *et al.*, 2004; Hennessy *et al.*, 2005). Surface artifacts and uneven surface coverage are limitations that stereophotogrammetry shares with laser scanning (Shaner *et al.*, 1998). Near infrared photogrammetry has also been proposed to

Fig. 2 - Wireframe range models of a female face obtained by stereophotogrammetry (modified from Hajeer et al.*, 2004b).*

overcome problems of light intensity and to permit the evaluation of both light- and dark-complexioned subjects, but current results are still preliminary (Chong and Mathieu, 2006).

Together with the abundance of data collected for each face, the main advantage of optical digitizers is the negligible time necessary to obtain a complete facial scan, thus reducing or abolishing motion artifacts, a feature particularly important for the assessment of children and disabled persons. From this point of view, stereophotogrammetry performs better than laser scanning, with appreciably faster scan times (Hajeer *et al.*, 2004b; Mori *et al.*, 2005). Motion artifacts around the lips, eyes and nose were measured when two separate right and left 0.3 s long laser scans were used for facial digitization (Kau *et al.*, 2004). Stereophotogrammetry collects also the soft-tissue texture, a useful feature during the subsequent, off-line landmark identification (Hajeer *et al.*, 2004b).

Furthermore, optical digitization needs no physical contact between the instrument and the skin, and the risk of cutaneous compression, and of potential injuries during measurements, is eliminated (Chong and Mathieu, 2006; Douglas *et al.*, 2003b; Majid *et al.*, 2005; Shaner *et al.*, 1998). One limitation is the time required for post-processing of the two-dimensional images obtained by each camera or in each of the separate scans (Hennessy *et al.*, 2005).

Even if the optical instruments provide a detailed recording of the main facial characteristics based on a wealth of soft-tissue points (a typical surface obtained by laser scanning can consists of approximately 80,000 points, Hennessy *et al.*, 2005, and 300,000-450,000 surface points have been obtained by stereophotogrammetry, Weinberg *et al.*, 2004), they do not assess single anatomical landmarks. Cutaneous landmarks are not directly identified on the subject, but they are recognized only on the digitized reconstructions of the face (Fraser *et al.*, 2003; Hammond *et al.*, 2004; Hajeer *et al.*, 2004a, b; Hennessy and Moss, 2001; Weinberg and Kolar, 2005; Weinberg *et al.*, 2004; White *et al.*, 2004). This procedure can result in some discrepancy between the actual anatomical landmarks and their digital counterparts. Indeed, several landmarks cannot be obtained by simple inspection, and only facial palpation allows their identification (for instance, gonion). Therefore, a number of standard landmarks (and subsequent measurements) should be excluded (Weinberg and Kolar, 2005; Weinberg *et al.*, 2004; White *et al.*, 2004).

To overcome the problem, some landmarks can be labeled directly on the face before data acquisition (Shaner *et al.*, 1998; Weinberg and Kolar, 2005; Weinberg *et al.*, 2004), but the procedure is not feasible with most laser scanning systems because the ink used for the mark is not digitized by the scanner. Previous labeling also improves accuracy, as shown by Shaner *et al.* (1998) and Weinberg *et al.* (2004) for both indirect, digital measurements and conventional, direct anthropometry.

Other limitations of these methods are the cost of the instrumentation, and, in most instances, the dimensions and need for special settings that cannot be taken away to meet the patients. Portable sterephotogrammetric instruments have been developed, and used for low-cost screening of fetal alcohol syndrome outside a clinical setting (Meintjes *et al.*, 2002).

Portable, handheld laser scanners have also been built: their resolution and accuracy are around 1 mm, that are considered adequate for basic and clinical studies (Hennessy *et al.*, 2005). The main shortcomings are the time required to take a complete scan (approximately 30 s), and the need of metal-free environments with a carefully controlled light. From this point of view, the limitations are similar to those further described for the electromagnetic digitizer (Ferrario *et al.*, 1998): indeed, this laser scan uses part of the same technology employed for the electromagnetic digitizer.

Contact instruments

Contact instruments digitize single selected facial landmarks, thus reducing the information obtained from each face, but providing the coordinates of facial features that directly correspond to anatomical and anthropometric structures (Ferrario *et al.*, 1998, 2004a). Ultrasound probes, electromagnetic and electromechanic digitizers are currently in use, and collected data have been used for the characterization of normal individuals, and selected groups of patients.

Both electromagnetic and electromechanic digitizers are based on electromagnetic waves, while ultrasound probes use acoustic waves in the Megahertz frequency domain. Ultrasounds could image both the skeletal surface and its soft-tissue cover, in this respect being similar to computed tomography and magnetic resonance, but without any (currently) known invasiveness and biological hazard (at least at the commonly used intensities, frequency and scan duration), and with a significantly smaller price (De Greef *et al.*, 2006; Smith and Throckmorton, 2004). The method is widely used for prenatal, intrauterine imaging and diagnosis, and three-dimensional reconstructions of fetal face are into current clinical practice (Chitkara *et al.*, 2002; Sepulveda *et al.*, 2003). In contrast, the application of ultrasounds for postnatal facial morphometrics is limited, and after an initial enthusiasm for a "non invasive", ultrasound-based cephalometrics, the method had been set aside for its scarce accuracy and repeatability (Hall and Bollen, 1997; Prawat *et al.*, 1995). More recently, it has been applied to the in-vivo measurement of the thickness of facial soft-tissue drape (De Greef *et al.*, 2006; Smith and Throckmorton, 2004). At present, the method does not seem to possess any other clinical or basis research application in the field of soft-tissue facial anthropometry.

While ultrasound probes do not actually contact the cutaneous surface (a conductive gel should be interposed between the probe and the surface), electromagnetic and electromechanic digitizers provide the three-dimensional coordinates of landmarks that are actually touched one by one by the instrument's stylus (Ferrario *et al.*, 1998, 2004a). In our laboratory, they have been extensively used since 1997 (electromagnetic digitizer), and 2003 (electromechanical instrument). Currently, both instruments are being in use, and more details on their use, advantages and limitations will be provided.

The electromagnetic digitizer (3Draw, Polhemus Inc., Colchester, VT) resembles one of the classic two-dimensional tablets used for the digitization of cephalometric films (Battagel, 1993), but its electromagnetic field extends at some distance from the tablet surface, providing a working volume (three spatial coordinates). The instrument currently used in our laboratory has a resolution of 0.005 mm/mm of range, and an accuracy of 0.08 mm, with the receivers located within 76 cm of the transmitter; the operator gently touches the facial landmarks using the instrument stylus, and closes the circuit by using either a button or a pedal. The tablet is positioned behind the head of the sitting subject (see below for details), and its working volume (width 28.9 cm, length 29.9 cm, height 76 cm) well corresponds to the dimensions of the subject's head (Fig. 3a).

The calibration of the instrument can be altered by electromagnetic interferences and metal objects, and it is controlled before each data collection session using a three-dimensional object of known dimensions. To avoid interferences with the electromagnetic field, during data collection, the stylus cable never crosses the tablet, and all electromagnetic devices (computer, video, power supply of the digitizer, mobile telephones) and metal objects are positioned a minimum of 3 m from the digitizer (Ferrario *et al.*, 1998). Furthermore, all metal is removed from the head of the subject (for instance, voluminous earrings), and the operator does not wear metal arm rings or a watch on the arm using the stylus. This limits the use of the instrument outside the laboratory (for instance, when data are collected directly in hospitals or during meetings of special groups of subjects, Ferrario *et al.*, 2004a; Sforza *et al.*, 2004a), because the room for data collection should meet the above mentioned characteristics, and there should be a non-metal holder for the tablet (see below).

Data collection is relatively fast (considering the kind of instrument): with the instrument in current use, laboratory mean time for 50 facial landmarks is 48.8 s, SD 1.5 s. Overall, it is the favorite instrument for all data collections within the laboratory. Using this digitizer, more than 1000 faces of healthy, normal persons had been digitized, together with a hundred faces of disabled or diseased persons.

The electromechanical digitizer presently used in our laboratory (Microscribe G2, Immersion Corporation, San Jose, CA, USA) is a multi-joint-arm digitizer, with an accuracy of 0.38 mm (workspace 50 inc sphere, corresponding to 127 cm). Within each joint, an optical encoder works with a microchip in the base of the instrument to send the joint angle to a host computer; the three-dimensional coordinates of the stylus are therefore provided. The machine is positioned in front or on the side of the subject, and the operator lightly touches the facial landmarks using the instrument's standard tip (Fig. 3b). Calibration of the instrument is controlled before each data collection session using a three-dimensional object of known dimensions, but there is no interference with magnetic fields. The electromechanical instrument can thus work within every kind of environment, independently from the presence of metal objects. For instance, the subject could also sit in a dental chair (Nagasaka *et al.*, 2003). Data collection is somewhat less fast than with the electromagnetic tablet (current laboratory mean time for 50 facial landmarks is 51.3 s, SD 5 s), and this is the instrument of choice when we collect data outside the laboratory (Ferrario *et al.*, 2004a; Sforza *et al.*, 2004a).

Both instruments provide the files of the three-dimensional (x, y, z) coordinates of the facial landmarks, and computer programs devised in the laboratory are used for all the subsequent off-line calculations.

These instruments have two principal limitations: the reduction of information, and the time necessary for data acquisition. The acquisition of only single, selected landmarks hinders the possibility to produce life-like models of the face depicting the actual soft-tissue appearance (Ferrario *et al.*, 1998). From this point of view, the application of the method as a communication tool is difficult, in particular with the patients (Hajeer *et al.*, 2004b). Also, there are no permanent records of the facial appearance, and it is not possible to correct off-line the position of a landmark, or to introduce new landmarks.

The time necessary for data acquisition is exceedingly long when compared to that necessary for an optical facial scan (even if it is also remarkably short when compared to conventional anthropometry, Douglas *et al.*, 2003b; Farkas, 1994; Lane *et al.*, 1997; Guyot *et al.*, 2003;

Fig. 3 - a) Digitization of soft-tissue landmarks using the electromagnetic digitizer; the tablet can be seen behind the headrest. The operator gently touches the facial landmarks using the instrument stylus; b) Digitization of soft-tissue landmarks using the electromechanical digitizer; the various joints can be seen. The operator gently touches the facial landmarks using the instrument's standard tip.

Hurwitz *et al.*, 1999; Meintjes *et al.*, 2002), and movements of the facial muscles (especially those around the mouth and eyes), as well as global head movements, may occur during the approximately 60 s necessary for digitization. The data acquisition protocol has been devised to reduce the time needed, and accurate positioning of the subject's head decrease the movements. Additionally, great care is continuously taken to develop procedures provoking the minimal disturbance to the subject, especially for children, patients, and disabled persons.

Collection of three-dimensional facial landmarks using contact instruments

Data acquisition is made in a two-step procedure, followed by off-line mathematical calculations (Ferrario *et al.*, 1998). At first, a set of landmarks is directly individualized on facial skin by careful inspection and/or palpation (Ferrario *et al.*, 2003a). The identified landmarks are labeled directly on the skin with small dots made using a quick-drying, black, liquid eye-liner. The brush of the eye-liner leaves a small mark (about 1 mm in diameter), it is not toxic, and it can be cleaned out very easily. During landmark marking, the subjects sit relaxed in a position suitable for a correct identification of facial features. Usually the operator explains to the subject the procedure being performed, with a special attention to children or to disabled persons. This step usually takes less than 5 minutes in an adult, collaborative subject, but it never takes more than 10 minutes even in disabled children. The time spent by each subject is actually negligible when compared to the requirements of conventional anthropometry.

In our laboratory, we currently identify 50 soft-tissue landmarks on each face (Ferrario *et al.*, 1998). The landmarks, 12 on the midline, and 19 on each hemi-half of the face, are located on the forehead, eyes, nose, lips and mouth, chin, ears, and lateral facial surface (Fig. 4). This number of landmarks is considered a good compromise between a sufficiently detailed individuation of the anatomical characteristics of the face, and digitization time. In the laboratory, the use of a standard set of landmarks allows the consistent assessment of subjects in both longitudinal and cross-sectional studies.

In the second step, the digital coordinates of the landmarks are obtained using the previously labeled dots, by either the electromagnetic digitizer or the electromechanical instrument. During landmark digitization, the subject sit in a natural head position in a chair with a headrest, where a cephalostat allows to fix the subject's head. Vertically and horizontally movable systems allow to accommodate for different sitting heights and head dimensions. When the electromagnetic digitizer is used, behind the headrest, wood supports accommodate the tablet (Fig. 3a). In this instance, the chair and headframe are all metal free (wood, Plexiglas, fabric, and leather). This further limits the use of the electromagnetic digitizer outside the laboratory, because the chair should be carried together with the electromagnetic tablet.

Subject's head should also be supported and blocked when working with the electromechanic digitizer, and this can be done by fixing it with an adjustable Velcro band on any vertical rigid surface (for instance, on a wall or a wardrobe). Two operators work together during landmark digitization: the standardized sequence of landmarks is read aloud by one operator while the principal operator collects the data. This procedure allows a very fast data collection and limits errors in the landmark sequence, which has been ergonomically devised to reduce data collection time. The fastest the procedure, the smallest the probability of movement.

Before dismissing the subject, the computer performs a fast reconstruction of facial morphology using the three-dimensional coordinates of the collected landmarks, and a check between the video image and the face of the subject is made to assess the correct sequence of landmarks, and any motion artifact. The procedure can be repeated immediately if necessary. Usually, approximately 1% of acquisitions are repeated.

The use of a two-step procedure has been devised to reduce the actual data collection time and to improve accuracy, thus overcoming one of the limitations of the methods for optical, non-contact analysis of facial morphology (Hajeer *et al.*, 2004a, b; Weinberg *et al.*, 2004; White *et al.*, 2004). Accuracy is also improved by having the landmarks previously marked.

Data analysis for three-dimensional digital morphometry

The landmark data provided by the computerized instruments that assess facial morphology in three dimensions can be analyzed by classic Euclidean geometry, and angles, distances and ratios similar to those measured in conventional anthropometry can be obtained (Douglas *et al.,* 2003a; Ferrario *et al.*, 1996a; Mori *et al.*, 2005; Stromland *et al.,* 1999; White *et al.,* 2004); estimates of areas and volumes in the face in toto or in selected structures can also be provided (Douglas *et al.,* 2003a; Ferrario *et al.*, 1999; Hajeer *et al.*, 2005; Mori *et al.*, 2005; Soncul and Bamber, 2004). As an example, Table 2 reports a list of the distances, angles, areas and volumes most commonly used in our laboratory. These measurements allow a first assessment of the investigated morphology, and are mostly used within a clinical contest, but they cannot appreciate more subtle modifications in facial form.

Landmark data can also be used with other morphometric techniques, for the analysis of symmetry (Coward *et al.*, 2000; Ferrario *et al.*, 2003b; Hajeer *et al.*, 2004a; Hennessy *et al.*, 2004, 2006; Ras *et al.,* 1995; Nkenke *et al.,* 2006; Sforza *et al.*, 2006; Shaner *et al.,* 2000), as well as for separated assessments of size and shape (Ferrario *et al.*, 2003a; Sforza *et al.*, 2004b; Vidarsdottir *et al.*, 2002).

Three principal approaches for the statistical analysis of shape have been developed: superimposition methods, deformation methods, and methods based on the analysis of interlandmark distances (Richtsmeier *et al.*, 2002; Rohlf, 2000).

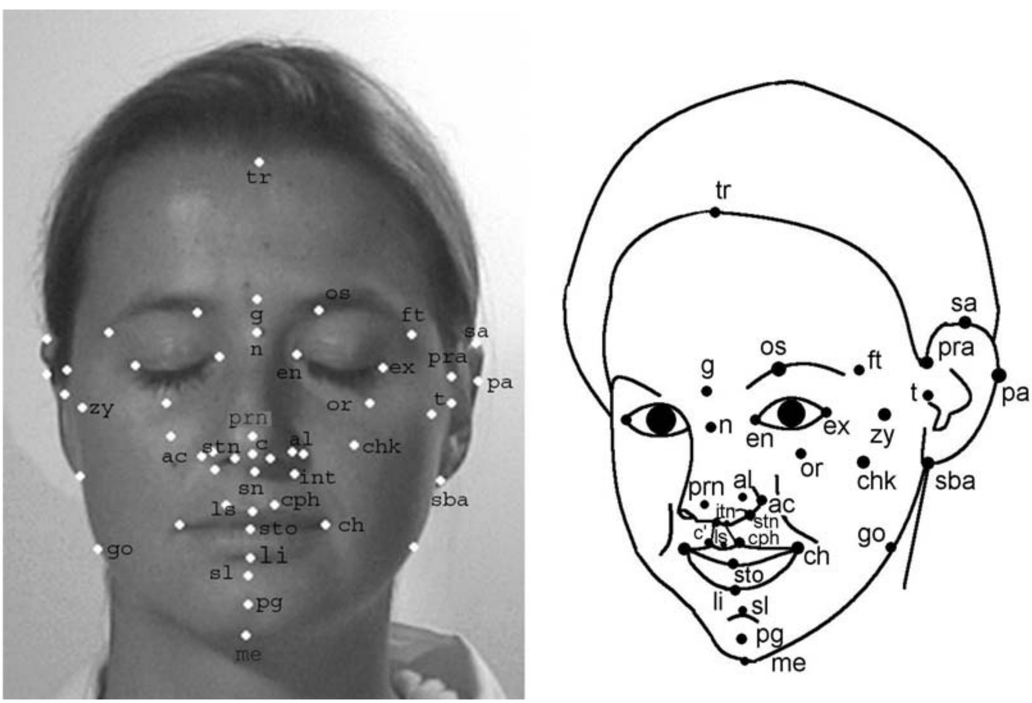

Fig. 4 - Soft-tissue landmarks identified on the face of a subject. Midline landmarks: tr, trichion; g, glabella; n, nasion; prn, pronasale; c′, columella; sn, subnasale; ls, labiale superius; sto, stomion; li, labiale inferius; sl, sublabiale; pg, pogonion; me, menton. Paired landmarks (right and left side): ex, exocanthion; en, endocanthion; os, orbitale superius; or, orbitale; ft: frontotemporale; chk, cheek; zy, zygion; t, tragion; al, alare; ac, nasal alar crest; itn, inferior point of the nostril axis; stn, superior point of the nostril axis; cph, crista philtri; ch, cheilion; go, gonion; pra, preaurale; sa, superaurale; pa, postaurale; sba, subaurale.

***Table 2**. Digital anthropometric measurements currently made in our laboratory. R: right; L: left.*

	Distances (mm)	Angles (degrees)	Volumes (mm^3)	Areas (cm^2)	Reference
Head	Forehead height; skull base width				Ferrario *et al.*, 1998
Face	Total, upper and lower face height; height of mandibular ramus; face width; width of the mandible; upper, mid and lower face depth; mandibular corpus length	Midfacial to mandibular plane; R & L gonial angles; upper, middle, and lower facial convexity in the horizontal plane; horizontal plane mandibular corpus convexity; sagittal facial convexity excluding/ including the nose	Total facial volume; upper, middle, and lower third facial volumes		Ferrario *et al.*, 1998, 1999
Eyes and orbits	Biorbital width; intercanthal width; R & L height of the orbit; R & L length of the eye fissure	R & L inclination of the eye fissure; R & L inclination of the orbit; R & L inclination of the orbit relative to soft tissue Frankfurt plane; relative position of the exocanthia and nasion in the horizontal plane		R & L external orbital surface area	Ferrario *et al.*, 2001b
Nose	Nasal width; nasal tip protrusion; height of the nose; length of the nasal bridge; R & L length of the nostrils; superior and inferior widths of the nostrils; alar base width	Alar slope; nasal tip; nasal convexity or nasal prominence	Nasal volume	External nasal surface	Ferrario *et al.*, 2004d
Mouth and lips	Mouth width; width of the philtrum; vermilion heights of the upper and lower lips; cutaneous lip heights; upper and lower lip to Ricketts' E-line	Interlabial; naso-labial; maxillary prominence; mento labial	Upper, lower, and total lip volumes	Vermilion of the upper, lower and total lip	Ferrario *et al.*, 2004d
Ears	R & L ear width; R & L ear length	R & L angle of the auricle versus the facial midplane		R & L ear area	Sforza *et al.*, 2005

Analysis of interlandmark distances

The most famous method based on the analysis of interlandmark distances is Euclidean Distance Matrix Analysis (EDMA, Lele and Richtsmeier, 1991). The method compares linear distances computed between landmarks in one form with the corresponding linear distances in the target form, and assesses the differences in length of the linear distances, either as ratios or as arithmetic differences. The method requires no assumptions about superimposition rules, or mathematical functions to map one form into another (Richtsmeier *et al.*, 2002). Originally developed for two-dimensional landmark data sets (Lele and Richtsmeier, 1991), it has been extended to the third dimension for the assessment of facial soft tissue data (Ferrario *et al.*, 1994). The statistical assessment of hypotheses is performed by nonparametric methods (bootstrap procedures), and confidence intervals for individual linear distances can be calculated. The landmarks most often involved in the linear distances that vary between forms are interpreted as the most influential in the form difference.

EDMA has been criticized for its lack of graphical representation of results, and for its reduced statistical power when compared to other methods provided by geometric morphometrics (Rohlf, 2000). Indeed, even some interesting graphical outputs for EDMA results have been proposed and applied to two-dimensional data (Bruner *et al.*, 2005; Ferrario *et al.*, 1993b), their use is still limited. Additionally, its statistical bases have not received the extensive amount of work that has been devoted to the analysis of landmark configurations. Nevertheless, the method is probably the most simple and honest among those used for the analysis of forms defined by landmarks: even if the information that can be obtained from the analysis is reduced in comparison to other methods of geometric morphometrics, EDMA does not relay on a priori assumptions.

Geometric morphometrics

More recently, for the analysis of biological shapes (or more correctly, of shape changes and of differences among shapes), geometric morphometrics seems to be the method that currently takes the largest advantage from the wealth of data collected by the three-dimensional digitizers (Aldridge *et al.*, 2005; Bookstein, 1991; DeCarlo *et al.*, 1998; Nkenke *et al.*, 2006; Rohlf, 2000; Shi *et al.*, 2006; Vidarsdottir *et al.*, 2002). These analytical methods were in part developed in the 1980s for the assessment of two-dimensional cephalometric data sets, and further implemented with the addition of the third landmark dimension (Bookstein, 1991). Geometric morphometrics captures the geometry of morphological structures (as identified by the relative spatial configuration of landmarks), and maintain this information throughout the analysis (Perez *et al.*, 2006; Rohlf, 2000; Vidarsdottir *et al.*, 2002).

The starting point is the definition of shape as the information about a geometric object that is invariant to overall location, size, and orientation (Perez *et al.*, 2006). A key step is the elimination of size differences among different objects/ individuals: indeed, size variations are often larger than shape differences, and may obscure more subtle discrepancies (Hennessy *et al.*, 2006). The choice of the correct size measure is essential in the procedure, since size itself is of difficult definition when objects differ in shape (Richtsmeier *et al.*, 2002). For instance, the major axis of an object may be modified together with the shape variation during some biological process. In geometric morphometrics, centroid size (the root mean square distance of the landmarks from their centroid, a measure of the dispersion of the landmarks, Hennessy *et al.*, 2006) is often used as the size measure. This measure is approximately uncorrelated with shape when landmark position vary independently and according to random error (Vidarsdottir *et al.*, 2002). Nevertheless, it has been underlined that any definition of size will affect the subsequent measurement of shape (Richtsmeier *et al.*, 2002).

Geometric morphometrics applies multivariate statistics to the theory of shape; the forms to be compared are registered and scaled using a superimposition method, and their differences are further quantified and illustrated by mathematical interpolations that “deform” one structure to match the other.

Superimposition methods

Superimposition methods assess the arrangement of landmark data between two forms: one form is considered the reference form and the other is the target form. Form difference is calculated by the displacement of landmarks in the target form from the corresponding landmarks in the reference form, according to a particular superimposition rule. Among the various superimposition methods, there are the standard cephalometric superimpositions used in orthodontics (where the sella-nasion line is usually considered the most stable line in the cranium), and the approaches based on Procrustes analysis (Richtsmeier *et al.*, 2002).

The name of this method derives from Greek mythology: Procrustes was a bandit who stretched or amputated all people passing through his land until they exactly matched his iron bed. Fortunately, the mathematical procedure is less violent than the mythological legend, and it does not damage the original landmark configuration, which can always be assessed with other, complementary methods. For instance, the original size is necessary to study allometry, the changes in shape with size (Vidarsdottir *et al.*, 2002). In Procrustes analysis, the raw landmark coordinates are superimposed by translating the configurations to a common centroid, scaling to unit centroid size, and rotating to minimize the sum of the squared distances between homologous landmarks. The resulting configuration should describe shape per se, because together with size normalization, Procrustes analysis eliminates differences in location and orientation.

Superimposition methods, in particular Procrustes distance, are widely used for the quantitative analysis of skeletal landmarks, but some recent applications for the assessment of three-dimensional soft tissue landmarks can be found (for instance, Hennessy *et al.*, 2005, 2006). Together with quantitative information, they also provide suggestive graphic outputs that can help in the interpretation of results; according to most literature, they seem to be among the best performing methods, and they are often used as a first-pass before the application of other statistical tools. Each form is then represented by a single point, and Procrustes distances can be further computed among forms in a non-Euclidean shape space known as Kendall's shape space; alternatively, the points can be projected into a linear tangent space, and this configuration of landmark coordinates can be explored by multivariate statistical analysis (Rohlf, 2000; Vidarsdottir *et al.*, 2002).

Among the statistical methods mostly applied to Procrustes coordinates, there is the Principal Component Analysis (also called relative warp analysis when applied to shape coordinates), which computes the major elements in shape variability within the sample; a reduced number of variables will simplify the explanations (Valenzano *et al.*, 2006). Indeed, modern digitizers could sample a lot of landmarks, and the resulting shape coordinates should be reduced to allow a better comprehension of the findings (Hennessy and Moss, 2001). Principal Component Analysis provides both a quantitative and a qualitative visualization of shapes and shape changes, thus permitting an easier understanding of the biological variations.

Together with the assessment of average configurations, and of differences among mean values, the variance within a single structure, and the covariation and correlation between structures, could be useful in the development and testing of hypotheses (Hennessy *et al.*, 2006; Perez *et al.*, 2006). For instance, one of the techniques is shape regression, the multivariate regression of Procrustes shape coordinates on some external variable (such as centroid size, behavioural or ecological variables), which can also be visualized as shape deformation (Hennessy *et al.*, 2005, 2006). Using this technique, a recent investigation found that verbal and visual spatial cognitive measures significantly correlated with soft-tissue facial shape and asymmetry, with different patterns in men and women (Hennessy *et al.*, 2006).

Another tool is Partial Least Squares analysis (called singular warp analysis) that assesses the pattern of covariation between two or more blocks of variables. The Principal Component Analysis of size-shape space has also been developed for developmental and discrimination studies. This method adds the centroid size to the shape variables, and allows the study of patterns of size and shape (i.e. form) together (Vidarsdottir *et al.*, 2002).

Superimposition methods have been criticized because of the arbitrariness of the superimpositions: in several instances, more than one superimposition could be chosen, leading to contrasting results (Bruner *et al.*, 2005; Richtsmeier *et al.*, 2002).

Deformation methods

Deformation methods take the area or volume of a reference form and deform it to correspond with that of the target form. These methods provide graphical representations derived from the meshes that had been used by artists since Renaissance to describe the variation of human faces (Fig. 1); these grids were introduced in scientific research by D'Arcy Thompson, and in clinical assessments by orthodontists (Ferrario *et al.,* 1996a; Moorrees and Kean, 1958; Peck and Peck, 1995). The artists' meshes, Thompson's deformation grids and the first orthodontic applications (such as the mesh diagram analysis by Moorrees) were mainly qualitative and drawn by hand; mathematical methods for a quantitative clinical application were developed only later (Moorrees *et al.*, 1975).

Geometric morphometrics provide formal algorithms to calculate the deformation grids based on homologous landmark configurations (Valenzano *et al.*, 2006). The main interpolation algorithms are finite-element scaling, a method widely used in engineering, and thin-plate splines, borrowed from material physics (Bookstein, 1991). The thin-plate spline method (the most used one) is the geometrical and mathematical equivalent of an infinitesimally thin leaf that can be modeled from the reference form to match the target form (mapping function): the quantity of energy necessary to bend and model the leaf measures the difference between the two specimens. The grid maps the actual points exactly and is as smooth as possible: mathematically, this is obtained by minimizing the "bending energy" of the deformation. The deformations can be different in the various parts of the leaf, thus accounting for by the different biological processes (Rosas and Bastir, 2002). Other functions can be chosen to match the target form, with different final results; this point is subject to the same critics of superimposition methods (Richtsmeier *et al.*, 2002).

The thin-plate spline methods provide quantitative results and useful graphic outputs of the deformations between the reference and the target forms; the landmark arrangements are often completed with drawings of the contours of the structures to allow an easier understanding, even if the actual analysis is limited to the landmarks (Valenzano *et al.,* 2006). The method is used also to obtain semi-landmarks (Hammond *et al.*, 2004; Hennessy *et al.*, 2005; Perez *et al.*, 2006).

Fourier analysis

Finally, with the optical instruments that allow detailed assessments of all inter-landmark surfaces, the contours (profiles) of the structures are becoming available, and could be investigated using Fourier analysis. Indeed, this mathematical representation does not relay on landmarks, and therefore is somehow not completely pertinent to the present review. Nevertheless, considering the more and more diffuse use of sliding landmarks (Perez *et al.*, 2006), the quantitative analysis of contours should be taken into careful consideration by all biologists. The method describes a boundary as a complex wave form which is decomposed into a series of sinusoidal waves of increasing frequency (Lu, 1965). Both standard and elliptic Fourier expansions can be usefully applied to macroscopic and microscopic biological specimens.

Fourier method is limited to two dimensions, and three-dimensional data must be projected onto one plane before the analysis (Ferrario *et al.*, 1995). Fourier analysis allows the quantitative, mathematical reconstruction of forms, and the separate assessment of size (dimension) and shape. Indeed, Fourier reconstruction permits the analysis of shape, and not only of shape changes. Within the craniofacial complex, the method has been mostly applied to skeletal data obtained by cephalometric radiographs (Ferrario *et al.*, 1996b), but some applications to facial soft tissues have been provided (Lu, 1965). Among the others, the investigations assessed the relative contributions of genetics and environment to facial profile (Tangchaitrong *et al.,* 2000), the relationship among classic esthetic canons and mathematical representations (Ferrario *et al.*, 1992), the effect of growth, development and aging (Ferrario *et al.,* 2001a; Lu, 1965), the sexual dimorphism (Ferrario *et al.,* 1995; Lu, 1965). Recently, Fourier analysis of craniofacial contours has been coupled with Procrustes superimposition, thus using a biologically-based registration technique (Friess and Baylac, 2003).

In conclusion, deeper understandings of biological forms and form changes, together with new hypotheses on normal and abnormal development, should relay on both correct data acquisition methods, and appropriate data analysis systems, without forgetting the original biological structures that are investigated. Also, the usefulness of a method does not necessarily depend on the number of mathematical steps used to obtain the results.

Error sources in digital facial anthropometry

Technical errors of the instrument, operator's errors during digitization, motion artifacts, and landmark identification are the main error sources for both kinds of instruments. Overall, re-calibration of the instruments before each data collection session using geometrical objects of known dimensions and spatial characteristics reduces technical errors (Battagel, 1993).

Optical instruments

Incorrect landmark identification is probably the major error source for optical instruments, even if motion artifacts could also occur. Landmark identification could be obstructed by the position of the subject relative to the imaging system. This error is shared also by cephalometry (Broadbent *et al.*, 1975), and it is particularly important for the most lateral parts of the face (namely, cheeks, mandibular angle and ears) (Shaner *et al.*, 1998; Weinberg and Kolar, 2005). Additionally, the parts of the face that are likely to cast more shadows when illuminated by a laser light, such as the mouth and nose areas, are reproduced less precisely than the eyes and cheeks (Kovacs *et al.*, 2006). For a commercial stereophotogrammetric system, Lee *et al.* (2004) found that 90° degrees of rotation of an unanimated, geometric object made the relevant distances distorted between 0.2 and 13.6%.

Accurate analyses of the errors of optical digitizers can be found in the literature. For instance, Ramieri *et al.* (2006) assessed a commercial laser system, and found a mean scanning error of 1–1.2 mm and a recording error of 0.3–0.4 mm on repeated scans of five subjects. The variability of head posture and of facial expression were indicated as the primary limits of the measurement protocol.

Aldridge *et al.* (2005) recently assessed a 6-TV cameras commercial stereophotogrammetric system, and found an overall precision (average absolute difference between repeated measures of the same image) of 0.827 mm over 20 standard anthropometric landmarks identified twice in each of two repeated facial scans of 15 subjects. Glabella, left and right gonion, nasion, and left and right tragion were the landmarks with the least precision (Aldridge *et al.*, 2005). Appreciably, imprecision was greatest along the mathematical equivalents of those anatomical axes where these landmarks can physiologically vary: for instance, the largest imprecision for glabella was found in the superior-inferior axis (Aldridge *et al.*, 2005). Concurrently, errors due to digitization were negligible (less than 1% on average), as well as errors due to the imaging system (approximately 1.5%). The largest errors were found in measurements involving landmarks located with the largest imprecision (for instance gonion), landmarks belonging to the lips or the mandible (for possible movements between repeated scans), and landmarks obscured by shadows (for instance tragion) (Aldridge *et al.*, 2005). As noted by the authors, some of these errors could be reduced by marking the landmarks prior to scanning. The significant improvement in precision using this procedure has been reported by Weinberg *et al.* (2004).

Indeed, landmark gonion cannot be reliably identified in digital facial images unless it has been previously marked on the skin (Aldridge *et al.*, 2005). Even if some literature reports underline reluctance of some subjects to be marked (Aldridge *et al.*, 2005; Majid *et al.*, 2005), in our Italian experience this never occurred with either children as young as 3 years of age, or with mentally retarded persons (Ferrario *et al.*, 2003a, 2004a; Sforza *et al.*, 2004a, 2005). Nevertheless, with infants or with persons coming from different cultural environments this may be a problem.

White *et al.* (2004), after a preliminary study, did not include in their stereophotogrammetric investigation of children aged 71 to 100 days those landmarks that could not be reproducibly located within 1 mm (tragion, gonion, glabella, cheek and trichion). Of the remaining landmarks, menton and pogonion were those with the worst reproducibility (namely, 1 mm and 0.8 mm). According to their findings, duplicate digitization of problematic landmarks, together with a standardized position of the digitized images, could improve efficiency and reproducibility (White *et al.*, 2004).

The location of the most problematic landmarks is due to both biology and instrumentation: from the same work group and with the same instrument used by White *et al.* (2004), Ayoub *et al.* (2003) had previously found errors larger than 1 mm for gonion, menton, tragion and zygion during repeated digitizations in adult subjects.

Automatic landmark digitization has been proposed for three-dimensional facial reconstructions, thus paralleling the efforts currently made for automatic segmentation of digital cephalometric films (Douglas, 2004; Yamada *et al.*, 2002). Both knowledge-based methods, and learning methods (artificial intelligence, genetic programming, pattern matching) have been proposed (Douglas, 2004), but results are still scanty, and no fully automated anthropometric procedures have been proposed so far. At best, image processing algorithms can obtain the geometrical/ mathematical landmarks, that is those located on extremes of curves and contours (Douglas, 2004; Douglas *et al.*, 2003a; Shi *et al.*, 2006).

Previous marking of the landmarks on the face before data acquisition may help in devising automatic systems. Indeed, the method has been proposed to reduce digitization error (Shaner *et al.*, 1998; Weinberg and Kolar, 2005; Weinberg *et al.*, 2004), and reductions in intra-observer errors ranging between 17 and 61% have been found for a set of measurements covering all the face and obtained from coordinates digitized by a stereophotogrammetric system (Weinberg *et al.*, 2004).

Contact instruments

While landmark identification does not seem to be a major problem for contact instruments, motion artifacts are probably the principal limitation of the method. The correct identification of facial landmarks is controlled directly before data collection by the second operator; any incorrect mark can be easily cleaned using a cleansing lotion, and a new eye-liner mark placed.

Motion artifacts are limited by a careful control of the position of the subject in the chair, and especially of the subject's head. The use of the backrest and cephalostat permits an easier control of subject's motion; closing the eyes is also mandatory. Additionally, a detailed explanation of all procedures (usually given during landmark identification) gives the subjects more confidence, and greatly reduces movements. The major motion artifacts are controlled before discharging the subject by a fast computerized reconstruction of facial morphology, with an immediate visual check between the virtual video image and the actual face of the subject: if macroscopic motion artifacts occurred, the video image is distorted.

Operator's errors in the sequence of landmarks are reduced by having one operator reading aloud the standardized sequence of landmarks during data collection. The fast computerized reconstruction of facial morphology performed immediately after data collection also allows the control of landmark sequence: if the sequence is not correct, the video image is distorted.

Tests of the method error performed in the laboratory assessed the technical errors of the instruments, the identification and digitization of the landmarks, and the motion artifacts. For the technical error of the instruments (Ferrario *et al.*, 1998), the complete set of 50 facial landmarks was digitized on the stone cast of one male face; eight three-dimensional linear distances were computed. The same distances were also obtained by conventional anthropometry using a standard caliper. Differences between couples of measurements ranged between -0.65 and 1.03 mm, with a mean difference of 0.22 mm (SD 0.66) (not significantly different from the expected value of zero, $p > 0.05$).

The identification and digitization of the landmarks were assessed by repeated identifications and digitizations of 50 standardized landmarks on the same stone facial cast. Three operators performed five independent data collection procedures, and a set of distances and angles was calculated. The coefficients of variation (SD/mean x 100) of the measurements ranged between 0.28 and 1.10% (mean 0.54%), and all intraclass correlation coefficients (ICC) were larger than

0.999: results indicate a reduced variability of the measurements, with a small variance of the random measurement error.

The effect of small motion artifacts was assessed by repeated identification and digitizations of the 50 landmarks directly on the subjects' faces using the electromagnetic instrument. Facial coordinates were obtained twice in five men and five women (Ferrario *et al.*, 1998), with resulting random errors (technical error of measurement, square root of the mean sum of squared differences among repeated measurements) of 1.20 mm (men, 1.04% of the relevant nasion-mid tragion distance) and 0.95 mm (women, 1.05% of nasion-mid tragion). Overall, in vivo error with the electromagnetic instrument appeared to influence landmark coordinates of approximately 1%. In six men and six women subsequently analyzed (data not published), two independent data collection gave repeated measurements of facial distances and angles without systematic errors (paired Student's t, $p > 0.01$); random errors ranged between 0.252 and 0.319; ICC were comprised between 0.657 and 0.689. Repeated measurements on one woman and nine men with the electromechanic instrument (Ferrario *et al.*, 2004a; Sforza *et al.*, 2004a) gave a random error on the three-dimensional coordinates of the 50 facial landmarks of 1.33 mm (1.29% of the relevant nasion-mid tragion distances).

Interdisciplinary implications

Basic research on human beings is currently obtaining valuable results using three-dimensional digital morphometry, and several anatomical studies have already been conducted, with quantitative descriptions of normal facial growth, development and aging (Ferrario *et al.*, 2003a; Hennessy and Moss, 2001; Mori *et al.*, 2005; Stromland *et al.*, 1999; White *et al.*, 2004; Yamada *et al.*, 2002). Normal adult morphology has also been extensively illustrated (Coward *et al.*, 2000; De Greef *et al.*, 2006; Farkas *et al.,* 2005b; Ferrario *et al.*, 1996a, 2001b, 2003a; Fraser *et al.*, 2003; Kau *et al.*, 2006; Yamada *et al.*, 2002).

Facial morphology is currently investigated to assess some hypotheses about relationships between facial shape and asymmetry, and aspects of cognition that involve the anterior brain (Hennessy *et al.*, 2006; Lane *et al.*, 1997). Considering the strict relationships between the face and anterior brain during early fetal life, the concurrence of facial and brain alterations, associated with cognitive deficits, is presently under strict scrutiny using three-dimensional digitizers (Hennessy *et al.*, 2006). The localization of facial alterations, together with the known timing of their embryological development, may offer more insights into brain development and its alterations (McGrath *et al.*, 2002; Shaner *et al.*, 2000). Recently, in schizophrenia affected patients, both conventional and digital anthropometric techniques demonstrated a peculiar facial dysmorphology with an intricate topography of three-dimensional size and shape changes (Hennessy *et al.*, 2004; Kugu *et al.*, 2004; Lane *et al.*, 1997; McGrath *et al.*, 2002).

Clinical, applied research appears promising in several fields. For instance, low-cost screening of facial morphologies linked to neuro-developmental alterations, like the fetal alcohol syndrome (Douglas *et al.*, 2003a; Meintjes *et al.*, 2002), can support the clinician with a first discrimination among putative patients, thus reducing the costs for more complex examinations (White *et al.*, 2004). Objective analysis of facial abnormalities could also help the clinician (in particular the less expert one) facing with dysmorphic syndromes that involve craniofacial alterations. The quantitative support may assist in the diagnosis of borderline patients or gene carriers (Allanson, 1997; Ferrario *et al.*, 2004a, b; Guyot *et al.*, 2001; Meintjes *et al.*, 2002; Sforza *et al.*, 2004a, b, 2005; Skrinjaric *et al.*, 2003).

As recently reviewed by Sforza *et al.* (2004c), reference data for facial morphometry are currently being collected on a wide scale using the computerized instrumentations. The assessment of normal, healthy individuals allows the creation of data banks that could be used for the quantitative assessment of patients (White *et al.*, 2004; Zankl & Molinari, 2003). Usually, the patients are seen in a clinical setting, where the computerized instruments may not be easily available, and classic, conventional anthropometry is the method of choice (Allanson, 1997; Zankl and Molinari, 2003). Computerized equipments may be used to make a complete measurement of all the craniofacial regions (head, labio-oral, nose, orbits, face, ears) in reference, normal individuals. Data banks of normal subjects could thus be created. Subsequently, data of single facial features could be singled out, and used for clinical comparisons of selected patients measured with the same digital equipment or with conventional instruments (Zankl and Molinari, 2003). Obviously, the data will not be perfectly superimposable, but they could be used for a first, low-cost screening (Douglas *et al.*, 2003a; Meintjes *et al.*, 2002). More complex examinations may be performed in a second time.

Maxillo-facial and plastic surgeons, as well as orthodontists and prosthodontists, well rely on this kind of three-dimensional information for patient assessment, treatment planning, and evaluation of results (Duffy *et al.*, 2000; Ferrario *et al.*, 1999, 2003b; Hajeer *et al.*, 2004a, b, 2005; Russel *et al.*, 2001; Sforza *et al.*, 2006; Soncul and Bamber, 2004). In reconstructive surgery, a quantitative approach is necessary to compare the outcome of different surgical procedures or intervention schedules, and it may also help in the identification of those facial areas susceptible of surgical intervention (Farkas *et al.*, 2005b; Ferrario *et al.*, 1999; Russell *et al.*, 2001; White *et al.*, 2004; Yamada *et al.*, 2002). In particular, the use of non-invasive diagnostic methods could reduce the biological burden of repeated examinations especially for children whose malformations cannot be corrected in a single time, but require several surgical interventions between birth and adult life (Duffy *et al.*, 2000; Ferrario *et al.*, 2003b; Nkenke *et al.*, 2006; Russel *et al.*, 2001; White *et al.*, 2004). Non syndromic cleft of the lip and/ or palate (an embryopathy resulting in a deficient fusion of the nasal process and palatal shelves) is one of these malformations (Breitsprecher *et al.*, 1999), found in 20 Caucasoids newborns per 10,000 (WHO, 2002).

Internal medicine dealing with general diseases affecting organs other than the face is currently finding associations between variations in facial morphology and several disorders: for instance, in adult uremic patients on chronic dialysis a positive relation between secondary hyperparathyroidism and facial soft-tissue changes has been found (Ferrario *et al.*, 2005). Nutritional disorders can modify craniofacial morphology: adult patients with undiagnosed celiac disease have significantly larger foreheads (Finizio *et al.*, 2005), while obese adolescents have transversally wider, sagittally deeper, and vertically shorter faces (Ferrario *et al.*, 2004c), than normal controls matched for sex, age, and ethnic group. Clinical applications also involve the assessment of the progression of disease (Ferrario *et al.*, 2005), the standardization of functional examinations, or the detection and quantification of side effects. For instance, laser scanning had been proposed for the estimation of facial lipodystrophy in HIV-infected patients taking highly active antiretroviral therapy (Yang and Paton, 2005); orbital and ocular dimensions are employed to standardize blood flow Doppler measurements (Ustymowicz *et al.*, 2005).

Current forensic techniques for facial reconstruction rely on traditional theories on the quantitative relationships between teeth, bones, and soft tissues, but few of them have been actually proven in present-day persons. Even if the classic rules should prove accurate (which is currently questioned, Stephan, 2002, 2003; Stephan and Henneberg, 2003; Stephan *et al.*, 2003; Wilkinson and Mautner, 2003; Wilkinson *et al.*, 2003), the secular trends in craniofacial dimensions call for new three-dimensional sex-, age-, and ethnic-based normal databases. The estimation of the age of an individual, as well as soft-tissue information for facial reconstruction from skeletal remains, both need quantitative data that should be directly collected on living subjects, and not on cadavers (Majid *et al.*, 2005; Miyasaka *et al.*, 1995; Smith and Throckmorton, 2004). For instance, ultrasound-based techniques provide direct in-vivo data on the thickness of the facial soft-tissue drape (De Greef *et al.*, 2006; Smith and Throckmorton, 2004), a basic information for facial reconstruction (Stephan, 2003). Magnetic resonance imaging has been used to measure eyeball protrusion relative to the orbit (Wilkinson and Mautner, 2003). Direct anthropometric measurements and photographic reconstructions had supplied information on the relationships between skeletal and dental characteristics, and soft-tissue ocular and mouth details (Stephan, 2002; Stephan and Henneberg., 2003; Wilkinson *et al.*, 2003).

Forensic, commercial and security identification of persons is increasingly using virtual images, like photographic or video records, and digital images could supplement conventional anthropometry (DeCarlo *et al.*, 1998; Fraser *et al.*, 2003; Halberstein, 2001; Shi *et al.,* 2006; Yoshino *et al.*, 2000) to determine the identity of probands. Recent investigations by Yoshino *et al.* (2000) and Fraser *et al.* (2003) quantified the match between three-dimensional facial images obtained by an optical scanner, and two-dimensional photographs provided by surveillance systems, finding the method useful for personal identification across different ethnicities. Landmark-based methods seem to be at the base of the best performing recognition algorithms (Shi *et al.,* 2006).

A similar field of research is the generation of computerized facial models from anthropometric measurements (De Carlo *et al.*, 1998). A set of conventional anthropometric distances and proportions is obtained, and they are used as constraints on a parameterized surface using mathematical techniques like the variational modeling (De Carlo *et al.*, 1998). These facial models are used both in medical practice (forensic medicine) and in computerized human simulations (television, cinema, virtual reality, computer games).

The manufacturing of ortheses, prostheses, as well as of safety headgears, via CAM/CAD technology is also profiting from the non invasive digitization of craniofacial characteristics in the single individual (Littlefield e al., 2005). The use of well-constructed databases could also be advantageous to the scope (Majid *et al.*, 2005).

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Info on the Web

Landmarks

http://www.getahead.psu.edu/

Instruments

http://www.polhemus.com/fastrak.htm
Electromagnetic digitizer

http://www.immersion.com/digitizer/
Electromechanic digitizer

www.fastscan3d.com
Portable laser scan

www.3dMD.com
www.genextech.com
Photogrammetric face scanner

http://www.3d-shape.com/produkte/face_e.php
Optical three-dimensional sensor based on phase-measuring triangulation

Analytical methods

http://www.virtualanthropology.com/virtual-anthropology/geometric-morphometrics/semilandmarks
http://life.bio.sunysb.edu/morph/
Definitions, applications and bibliography of geometric morphometrics

http://life.bio.sunysb.edu/morph/
Superimposition methods, thin-plate spline methods

http://www.getahead.psu.edu/
Euclidean Distance Matrix Analysis:

Examples of application

http://www.plagiocephaly.org/headshape/anthropometry.htm
Classic craniofacial anthropometry in children with plagiocephaly for lay people

http://www.cs.rutgers.edu/~decarlo/anthface.html
Generation of computerized facial models from anthropometric measurements

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