Soft- and hard-tissue facial anthropometry in three dimensions: what's new

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Summary - In the last few years, technology has provided new instruments for the three-dimensional analysis of human facial morphology. Currently, quantitative assessments of dimensions, spatial positions and relative proportions of distinctive facial features can be obtained for both soft- and hard- (skeletal and dental) tissues. New mathematical tools allow to fuse digital data obtained from various image analyzers, thus providing quantitative information for anatomical and anthropometric descriptions, medical evaluations (clinical genetics, orthodontics, maxillo-facial and plastic surgery), and forensic medicine.

Keywords - Human face, Morphometrics, 3D analysis.

Introduction

The quantitative analysis of the human face has always received a large attention from both scientists and artists: the face allows to communicate and interact with the environment, it is used to identify the persons, and it can carry information about the health state of an individual (Hennessy *et al.*, 2005; Tollefson & Sykes, 2007; Kochel *et al.*, 2010; Sforza & Ferrario, 2010; Smeets *et al.*, 2010; Mutsvangwa *et al.*, 2010, 2011; Fang *et al.*, 2011; Ritz-Timme *et al.*, 2011; Verzè *et al.*, 2011b).

This unique morphology is made from separate cartilaginous, osseous, dental and soft-tissue elements, where their coordinated pattern of growth, development and aging produces a never static outline that can be modeled and varied by the combined action of internal (genetic and epigenetic) and external (environmental) factors (Breitsprecher *et al.*, 1999; Hammond *et al.*, 2008; Smeets *et al.*, 2010; Aldridge *et al.*, 2011; Baynam *et al.*, 2011; Hammond & Suttie 2012). Additionally, the presence of a large number of facial (subcutaneous) muscles makes facial appearance instantaneously variable and dynamic, even producing problems for its correct representation and measurement (Kovacs *et al.*, 2006; Ferrario & Sforza, 2007; Maal *et al.*, 2008, 2010; Schimmel *et al.*, 2010; Smeets *et al.*, 2010; Sforza *et al.*, 2010a, 2010d, 2011b, 2012d; Trotman 2011; Verzè *et al.*, 2011b; Lubbers *et al.*, 2012).

In a previous review, we analyzed the state of the art for the assessment of the soft-tissue facial structures of human beings in all three spatial dimensions. Information about the instruments to be used for data collection, on the analytical methods for data analysis, as well as on the main interdisciplinary applications, were provided (Sforza & Ferrario, 2006).

In the subsequent years, new applications of the instruments for data collections have been proposed, together with new mathematical tools that allow fusing the digital data obtained from various image analyzers. A web search using the key-words "3D, face, human" retrieved 11029 Tab. 1 - Papers with the key words "3D", "face", "human" published between 1950 and 2012 divided into decades (research performed on May, 16th 2012).

YEARS	NO. OF PAPERS	
1950-1959	2	
1960-1969	1	
1970-1979	8	
1980-1989	10	
1990-1999	930	
2000-2009	7844	
2010-2012	2234	

full text papers published between 1950 and 2012 (http://search.proquest.com/, accessed on May, 16th 2012) (Tab. 1). Among these papers, 10078 were published in the current Century, about 3580 before our previous review (2000-2005), and about 6498 after it (2006-currently). Investigations and relevant literature on this topic are therefore increasing very fast, and a revision of the most recent instruments, findings and fields of application seems necessary (Fig. 1).

In the current review, some information about the new trends in soft- and hard-tissue facial analysis are provided, along with their principal fields of anatomical, anthropometric, medical and dental application.

The instruments and their use

Three-dimensional (3D) images are becoming a daily reality in several clinical and research contexts all over the world. Currently, two image analyzers can provide combined 3D reconstructions of the soft tissue structures together with the craniofacial skeleton: computed tomography (CT) and magnetic resonance (MR) imaging (Adams *et al.*, 2004; Papadopoulos *et al.*, 2002; Hajeer *et al.*, 2004; Katsumata *et al.*, 2005; Maal *et al.*, 2008; Keller & Roberts, 2009; Swennen et al., 2009; Ji et al., 2010; Fourie et al., 2011b; Papagrigorakis et al., 2011; Wang et al., 2011; Aboul-Hosn Centenero & Hernandez-Alfaro, 2012; Bechtold et al., 2012; Hammond & Suttie, 2012; Lee et al., 2012). These volumetric scanners can image both the internal body structures and the external cutaneous covering, allowing a complete assessment of facial morphology. Other scanners (namely, laser scanners and stereophotogrammetric systems) can record and reproduce only the external body surface, permitting 3D measurements of the external (soft tissues, in the living persons) structures (Gwilliam et al., 2006; Heike et al., 2010; Friess, 2012).

To overcome problems related to facial illumination, near infrared light can be used to scan facial surface (Li *et al.*, 2007). A new kind of instruments are those using the terahertz radiation of the electromagnetic field. These scanners can image several millimeters of tissue with low water content (e.g., fatty tissue), detecting differences in tissue density. Another promising field of application is the 3D imaging of teeth (Jalil *et al.*, 2012).

Computerized tomography

CT provides 3D digital reconstruction of the entire craniofacial skeleton from axial slices allowing to evaluate all internal structures. CT can be efficiently used also to assess, archive and measure archaeological specimens (Badawi-Fayad & Cabanis, 2007; Papagrigorakis *et al.*, 2011; Kullmer, 2008; Friess, 2012). Additionally, CT data can be shared among research laboratories all over the world, permitting a widespread use of archaeological collections without moving the investigators or the specimens (Abel *et al.*, 2011).

Both MR and CT can be used for special medical applications: virtual endoscopy, surgical planning and medical training. Virtual endoscopy uses the clinical data, primarily CT, visualized in real-time for on-screen simulation of the interior of viscera (eg, virtual bronchoscopy and colonoscopy) and vessels (virtual angioscopy), helping in diagnosis and surgical planning. 3-D visualization can provide simulation of complex surgical procedures, such as organ transplantation (McGhee, 2010).

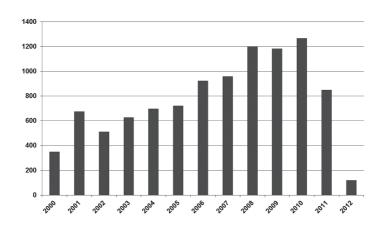


Fig. 1 - Papers with the key words "3D", "face", "human" published between 2000 and 2012 (research performed on May, 16th 2012). The colour version of this figure is available at the JASs website.

Additionally, research can make use of CT archival images, selected from the existing databases in health care units. Indeed, CT scans are usually made to patients for traumas, fractures or neoplasias, but the databases can be screened according to well defined inclusion criteria, selecting only normal individuals. A similar procedure was followed by Wang *et al.* (2011) who assessed the 3D quantitative morphology of the external ear in normal Han Chinese adults.

However, CT has some limitations: apart from cost, the devices expose patients to high amounts of unnecessary radiation. The most recent modifications of CT, namely the conical x-ray approach or cone beam CT (CBCT), now can offer affordable 3D craniofacial reconstructions, with a reduced radiation exposure (Adams *et al.*, 2004; Hwang *et al.*, 2012).

CBCT systems have been developed specifically for the maxillofacial region, and their field of view allows an efficient imaging of the skull including most of the landmarks used in cephalometric analysis, together with a 3D volumetric rendering of the external facial surface (Maal *et al.*, 2008; Moro *et al.*, 2009; Swennen *et al.*, 2009; Fourie *et al.*, 2011a; Bechtold *et al.*, 2012) (Fig. 2).

CT craniofacial scans do not allow determining dental morphology accurately because of artifacts from metallic restorations or orthodontic brackets. The fusion of dental surface images obtained from a 3D measuring device into maxillofacial CT images has been proposed to overcome this problem (Nakasima *et al.*, 2005; Bechtold *et al.*, 2012).

To reduce patient's exposure to X-rays, the European Academy of DentoMaxilloFacial Radiology (EADMFR) recognized an urgent need to set standards for CBCT use, and developed a set of "Basic Principles" using existing EU Directives and Guidelines on Radiation Protection (www.sedentexct.eu/content/basic-principles -use-dental-cone-beam-ct, accessed on August, 10th 2012). These statements recommend that CBCT should not be repeated 'routinely' on a patient without a new risk/benefit assessment having been performed. CBCT examinations must be justified for each patient to demonstrate that the benefits outweigh the risks.

Considering these radioprotection norms, Nakasima *et al.* (2005) proposed to create a standard skeletal and facial model from CT images of subjects of a well-defined ethnic group, and to obtain individual models by fitting the standard model to each patient by using his or her cephalograms and facial photographs. 3D digital dental models can be fused with the individual model, thus obtaining a complete 3D image with a low biological price. Although interesting,

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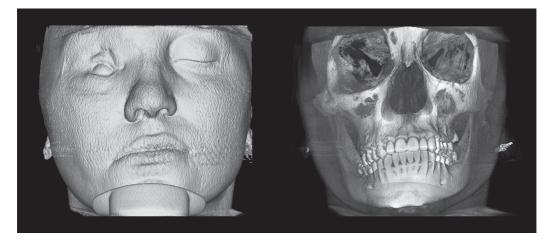


Fig. 2 - Three-dimensional reconstruction of craniofacial hard and soft tissues in a 24 years old woman. The images were obtained with cone beam computerized tomography (White Fox, De Goetzen, Olgiate Olona, Varese, Italy; X-ray tube voltage 105 KV, X-ray tube current 8 mA). A cephalometric, expanded field of view was used (diameter 200 mm, height 170 mm). A: soft tissue reconstruction. A notable facial asymmetry can be observed (the left labial commissura is more cranial than the right one, the right nasal ala is bigger than the left one), together with alterations in the right orbital area. B: hard tissue reconstruction. The occlusal plane is asymmetric, and the right orbital cavity altered. The colour version of this figure is available at the JASs website.

the method would require a set of reference CT scans selected for sex and ethnicity, posing ethical problems for the individuation of the normal individuals to be scanned. Also, the deformations required to modify the 3D scan according to the 2D cephalograms change the skeletal structures with an isotropic model that probably does not actually represent the true shape variations.

Magnetic resonance

Among the other applications, magnetic resonance imaging has recently been used for the 3D assessment of labial dimensions in healthy subjects. In particular, lip thickness was measured, with a good accord between 3D age-related changes and classic histological findings (Iblher *et al.*, 2008; Penna *et al.*, 2009). Unfortunately, the method could not efficaciously record the anatomy of the underlying supporting hard tissues, impeding the assessment of the soft- and hard-tissues relationships. Also, MR should be performed in a supine position, with a significant alteration in the normal relationships between the facial soft tissues, especially in the aged persons (See *et al.*, 2007, 2008). Ferrario *et al.* (2009) introduced a method that fused the 3D stone models of the teeth and of the lips, obtaining 3D virtual reproductions of both mucosal and skin labial surfaces. Labial thickness, vermilion area, volume of the upper and lower lips, and relevant dental positions were measured from the digital reconstructions, thus including a complete assessment of the anatomical region and of its sex- and age-related characteristics (De Menezes *et al.*, 2011; Rosati *et al.*, 2012a).

Stereophotogrammetry

Stereophotogrammetry is safe, non-invasive, fast (typical scan time 2 ms), does not require a physical contact between the instrument and the face, and it provides superior quality 'external surface' photographs, coupling a color facial image (texture) with a 3D mesh of the analyzed surface. In stereophotogrammetry a light source illuminates the face, and two or more coordinated cameras (or set of cameras) record the images from different points of view (Fig. 3). The different views/ images of the face are merged into a 3D point cloud to represent the surface of the subject's face. Using a previous calibration of the instrument, a computerized stereoscopic reconstruction of the face is finally produced (Hammond *et al.*, 2008; de Menezes *et al.*, 2010; Heike *et al.*, 2010; Schimmel *et al.*, 2010; Friess, 2012). Two additional three-quarter color pictures are mapped onto the mesh formed by the point cloud to reproduce facial appearance.

The systems can be divided into passive, where the cameras record the black and white (finer resolution) and the color (lower resolution) images of the face that are combined to give a final 3D mesh covered by a color texture, or active. In these last instruments, the face is also lightened by structured light (usually in the infrared field), whose interferences with the facial structures enhance the final 3D reconstruction. Precision (difference between repeated measures of the same item) and repeatability (precision relative to the actual biological difference among subjects) of stereophotogrammetry have been reported to be very satisfactory, even better than caliper measurements (Aldridge et al., 2005; Gwilliam et al., 2006; Ghoddousi et al., 2007; de Menezes et al., 2010; Schimmel et al., 2010; Aynechi et al., 2011; Fourie et al., 2011b).

Previous marking of the landmarks of interest increases the instrument precision, without reducing the information content of the acquired 3D image, a topic already discussed in our previous review (Sforza & Ferrario 2006), but that had received greater attention in the last years (Ghoddousi et al., 2007; de Menezes et al., 2010; Aynechi et al., 2011). Indeed, some landmarks can be efficaciously identified only with palpation of the underlying bone surface, a procedure that cannot be performed on the facial scan. For instance, the error of gonion identification was 2-4 times larger than that of the other facial landmarks. Other landmarks (tragus, menton, orbitale superior) were of difficult identification because the facial region was covered by hair, or because the scan was not optimal (Gwilliam et al., 2006; de Menezes et al., 2010; Heike et al., 2010).

Due to its safety, the fine resolution images and the acquisition time (2 ms), this instrument

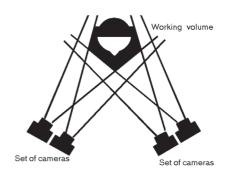


Fig. 3 - Scheme of a stereophotogrammetric device for the analysis of facial soft tissues. Two sets of TV cameras record the facial characteristics from the right and the left sides. The working volume (black area) represents the part of space seen by two or more cameras with nonparallel optical axes. After a calibration procedure, the computer can obtain the metric 3D coordinates of each point of the working volume.

is ideal to collect the 3D data of faces, even in children, babies or disabled persons, where acquisition time is going to be critical. In particular, Mutsvangwa *et al.* (2011) found that stereophotogrammetry can obtain the 3D coordinates of facial landmarks in infants with a high level of precision. The instrument can be used also for the digital analysis and reconstruction of other body regions, like the head and the neck (Dirven *et al.*, 2008; Schaaf *et al.*, 2010).

In a recent review, Heike *et al.* (2010) detailed the main technical issues related to the practical use of stereophotogrammetry, including its physical location, suggestions to reduce image artifacts and maximize facial surface coverage, and hints for the analysis of children and persons with special needs.

Figure 4 shows an example of a 3D scan performed using a stereophotogrammetric instrument.

Laser scanners

Laser scanners are another well-known class of instruments that can be used for surface analysis. The instrument shines a low-intensity laser (below 0.00008 W) on the object and poses no risk to the patient's vision. Digital cameras



Fig. 4 - Three-dimensional reproduction of the facial soft tissues of a normal 20-y old woman obtained by a stereophotogrammetric instrument (three-dimensional image with texture, and polygonal mesh). Areas covered by hairs (eyelashes, head), and areas covered by other structures (lateral part of the face, below the mandibular angle) cannot be completely identified by the system. The colour version of this figure is available at the JASs website.

capture the images (Fig. 5); the depth information is obtained by triangulation geometry (Kau *et al.*, 2006; Ramieri *et al.*, 2006, 2008; Primozic *et al.*, 2009; Friess, 2012; Joe *et al.*, 2012). During data acquisition, either the face or the laser light move to cover the entire surface. For example, the laser scan used by Ramieri *et al.* (2006) moves 360 degrees around the subject, digitizing 512 vertical profiles in approximately 17 s, with a scanning precision of 0.65 mm. Repeated scans of human subjects were reported to result in a mean scanning error of 1.0–1.2 mm and a recording error of 0.3–0.4 mm. Figure 6 shows the 3D facial reconstruction of the same subject imaged in Figure 4 obtained by laser scanning.

Laser scans have been proved to be as precise, if not more so, than the traditional caliper and steel tape method of measurement, providing a more consistent data acquisition process compared with the traditional manual methods. In the experiment reported by Joe *et al.* (2012), 80% of the analyzed facial measurements had lower standard deviations for the digital method than for the traditional manual method. Their main limitation may be the time necessary for a complete facial scan, which is significantly higher than that necessary for stereophotogrammetry (Kovacs *et al.*, 2006; Germec-Cakan *et al.*, 2010; Zhuang *et al.*, 2010a; Fourie *et al.*, 2011b).

In a multicentric study, Kau *et al.* (2010) used both laser scanning and stereophotogrammetric acquisitions, showing that the two instruments can be efficiently used sharing data among laboratories. In contrast, Germec-Cakan *et al.* (2010) compared 3D nasal dimensions obtained by facial impressions (stone casts), laser scanning and stereophotogrammetry, and reported that laser scanning was not sensitive enough to visualize the deeper indentations such as nostrils, while better results were obtained by stereophotogrammetry.

Handheld laser scanners combine optical scanning of the face and electromagnetic detection of the position of the instrument, which is manually swept over the object by the operator, paralleling a kind of spray painting, They are

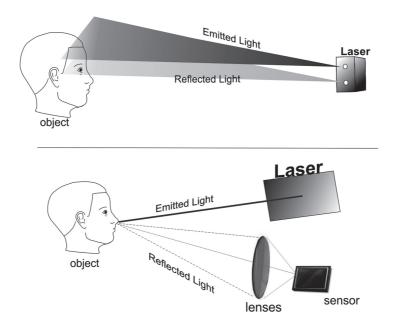


Fig. 5 - Principle of a laser triangulation. The laser dot, the camera and the laser emitter form a triangle, the distance between the camera and laser emitter is known, as well as the angle of the emitted laser. The angle of the camera can be determined through laser dot in the camera's field of view determining the principle of triangulation. The colour version of this figure is available at the JASs website.

portable, and allow a sufficiently fast and accurate digitization of the face (Harrison *et al.*, 2004; Hennessy *et al.*, 2005; Schwenzer-Zimmerer *et al.*, 2008; Sforza *et al.*, 2011c, 2012b, 2012d). They can be a practical solution for laboratories or clinical facilities with a reduced budget, or in countries where the patients cannot easily reach the health care units. The principal limitation is the time required for a scan, with the possibility of motion artifacts.

An additional use of handheld laser scanners may be the digitization of objects, and in particular of stone casts of dental arches and palate. In this case, there is no risk of motion artifacts, and the main limitation is the presence of shadowy areas that may be not completely imaged by the instrument. Technology offers dedicated instruments, that are usually employed in dentistry for the design and manufacturing of single or multiple teeth prostheses, where a laser scan is automatically swept around the object (or the object is moved inside the laser light). Unfortunately, these instruments cannot be used for soft tissue data collection, and monetary limitations have prompted the researchers to alternative solutions. For instance, Sforza *et al.* (2012a) successfully used a stereophotogrammetric unit to digitize the palatal casts of children with cleft lip and palate.

Video scanners and photography: a low cost alternative?

Among the disadvantages of stereophotogrammetric systems and laser scans there are their cost and their dimensions. Low-cost photographic alternatives have therefore been devised in several medical fields, especially for small, private clinical practices, where a first screening of



Fig. 6 - Three-dimensional reproduction of the facial soft tissues of a normal 20-y old woman obtained by laser scanning (three-dimensional polygonal mesh, and homogenous surface rendering). Areas covered by hairs (eyelashes, head) cannot be completely identified by the system. The colour version of this figure is available at the JASs website.

the facial appearance is made, followed if necessary by more complex and complete analyses.

A recent introduction in the market is the video scanner. This instrument is similar to a video camera which captures images up to 16 frames per second producing 3D images. These frames are automatically aligned in real-time, which makes scanning easy and fast. The digital cameras capture the images and the depth information is obtained using triangulation geometry. The advantages of these video scanners are their portability, relative fast acquisition time, colored texture and good scan resolution (3D point precision, up to 0.1 mm). Indeed, they do not require markers or calibration, and use a flash bulb as light source (no laser). The cost (around US\$13,000) is inferior compared with laser scanners (price range: US\$25,000 to US\$55,000) and stereophotogrammetry systems (price range: US\$30,000 to US\$140,000). Otherwise, the main limitation may be the reduced texture resolution (1.3 Mpixel), which may impede a precise identification of dots/ landmarks used in three-dimensional facial anthropometry (Weinberg *et al.*, 2004; De Menezes *et al.*, 2010).

In several clinical applications a 2D profile view can be sufficient for diagnosis and followup, leaving 3D assessments only to selected patients (Dimaggio et al., 2007; Tollefson & Sykes 2007; Abed et al., 2009; de Menezes et al., 2009; Deli et al., 2010; Han et al., 2010). In these applications, a set of separate 2D facial photographs is taken under standardized conditions, the images are calibrated and merged, and commercial software allows to perform quantitative measurements in the three dimensions. The method has been found to be sufficiently precise and repeatable for clinical application but with some errors in the labial, orbital and auricular areas (de Menezes et al., 2009). Indeed, discrepancies in facial structures lower than 1.5 mm cannot be usually appreciated by the naked eye, thus defining some kind of precision threshold for clinical use (Fourie et al., 2011; Lubbers et al., 2012). While landmark digitization was found to have an acceptable precision, errors due

to subject and camera relocation for multiple photographs were large, up to 5.3 mm for distances and 5.6 degrees for angles (de Menezes *et al.*, 2009). For reduction in measurement error due to head movements among separate poses, photographs may be obtained simultaneously with the use of three cameras, as described by Deli *et al.* (2011), but this would increase the monetary cost of the analysis.

Nonetheless, photographs continue to be widely used in clinical settings (Han *et al.*, 2010), even if they often do not include appropriate scales. Driessen *et al.* (2011) devised a technique for calibrating photographs that have no scale or grid included, starting from iris diameter, which has been found to be of stable dimension from the age of 5 years. For facial structures placed outside the coronal plane of the iris, a linear correction factor can be calculated to compensate for the different distances from the camera. The method makes it possible to perform life-size measurements in a frontal view photograph.

Tools, applications and fields of use

Fusion of images from different sources

While CT scans offer a detailed image of the skeletal surfaces and volumes, 3D facial images obtained by an optical method can provide additional information about color and surface texture, as well as higher resolution of soft-tissue surfaces (Kovacs *et al.*, 2006; Cevidanes *et al.*, 2010; Hammond & Suttie, 2012). The two methods may therefore be combined, providing a more complete assessment of the patients.

The fusion can be made using landmarks or surface-based methods that are currently provided by some software tools, but the soft-tissue structures may be not stable enough as references, thus including an unknown amount of error (Cevidanes *et al.*, 2010). Modifications in the activity of facial muscles (especially around the eyes, the nose, the mouth), together with alterations in head and neck position, were found to provoke significant errors in facial reconstruction. The combined images should therefore be controlled to avoid deformation and misalignment.

One step towards a possible solution of the problem is the definition of a good set of fiducial landmarks, that is points imaged with both techniques that act as reference for the subsequent superimposition of the digital images (Baik & Kim, 2010; Gupta et al., 2010; Rosati et al., 2010). These landmarks should be sufficiently distant one from the other to allow the individuation of a reference plane for image registration and surface matching. Boulanger et al. (2009) matched CBCT and stereophotogrammetric scans using a set of titanium targets. Together with the use of fiducial points, surface matching between homologous areas of couples of 3D facial images has been found to be effective, with average deviations between repeated scans lower than 1 mm (Maal et al., 2010). A combined use of fiducial landmarks (manual selection and initial matching) and of facial areas that were not modified by the treatment (manual selection and automatic fine matching) is usually employed for longitudinal investigations (Baik & Kim, 2010).

A more recent and refined method is the "anthropometric mask", where the classic set of anthropometric landmarks is expanded in a spatially dense way using around 10,000 quasi landmarks (Claes *et al.*, 2012a,c). Superimpositions using this new tool appear to produce more biologically plausible results. Maal *et al.* (2008) devised a method to fuse 3D facial images obtained using stereophotogrammetry (textured) and CBCT (untextured). After an initial positioning of the two surfaces by indicating fiducial landmarks on both of them, the manual exclusion of regions with large registration errors allows the automatic transfer of texture from textured surface to untextured surface using non-rigid registration.

Kochel *et al.* (2010) combined two-dimensional lateral head radiographs with 3D stereophotogrammetric facial images, finding a set of significant correlations between hard and soft tissue angles and distances. Incrapera *et al.* (2010) assessed pre- and post-treatment records, discovering a good accord between 3D and 2D modifications at selected soft-tissue landmarks.

In an attempt to couple the benefits of surface stereophotogrammetric images and digital images of the dental arches, Rangel *et al.* (2008) and Rosati *et al.* (2010) devised and tested a fusion protocol that integrated a digital dental cast into a 3D facial picture. According to the average distance between the matched areas (anterior teeth, incisors, canines and first premolars) obtained in a group of patients, the method was reported to be reliable, without systematic errors and with reduced random errors (technical error of measurement less than 1 mm, relative error of the mean up to 1.2%).

Because the fusion between the 3D face and the digital casts must use the anterior teeth as the reference, any displacement or inclination of the digital dental arch would add a position error in the posterior region, which is of difficult assessment and quantification (Rosati *et al.*, 2012b).

Bechtold et al. (2012) proposed the use of a dental face bow connected to an extra-oral reference frame: an individual dental splint allowed a repeatable positioning of the reference frame permitting a good fusion of the facial and dental images. Unfortunately, the face bow increases the vertical dimension of the lower part of the face, creating image modifications and skin artifacts (Heike et al., 2010). Also, the method needs 10 separate steps to provide the final integration of the dental arches inside the stereophotogrammetric facial scan, and each step can increase the error. Overall, the authors reported a good precision in vertical distances, while the sagittal measurements revealed more deviations (Bechtold et al., 2012).

Automatic landmark identification

Together with the technological developments for image recording, research focused on mathematical, geometrical and statistical tools that allow to extract the largest possible amount of information from the 3D facial reconstructions. One of the most promising fields is the automatic extraction of landmark coordinates. Currently, landmark assessment is a lengthy process that requires expert operators, and that may hinder a widespread use of 3D scans. The reliability of the data depends strongly on the operator's experience, because landmarks are usually located within relatively large and curved areas, rather than in correspondence of discrete points (Gwilliam *et al.*, 2006; Kovacs *et al.*, 2006; de Menezes *et al.*, 2010; Calignano & Vezzetti, 2011; Claes *et al.*, 2012a). Previous marking of the landmarks on the patient's skin reduces both the measurement error and the time required for image analysis, but even this process requires expertise and effort, and it may not be feasible for all subjects (Mutsvangwa *et al.*, 2011).

Considering that each facial scan provides a 3D mesh of known coordinates, we can assess the invariant geometric characteristics of the mesh, such as curvatures, and combine them with anatomical knowledge to find the required set of landmarks and selected facial structures, namely, the eyes, nose, and mouth. Common geometric shapes such as peak, ridge, pit, and ravine are defined from a mathematical point of view, and coupled to the anatomical landmarks on hard and soft tissues (Gupta et al., 2010; Deo & Sen, 2010; Calignano & Vezzetti, 2011; Fang & Fang, 2011; Arca et al., 2012). Identification of the midsagittal plane and facial midline is obtained from the symmetry of a set of primary landmarks. From facial midline, associated landmarks can be recognized by using local identification algorithms (Deo & Sen, 2010; Fang & Fang, 2011). 3D facial and head scans can also be virtually sectioned along selected anatomical planes, thus allowing a direct assessment of different faces or the longitudinal analysis of growth, aging or treatment effects. In particular, the use of multisectional spline curves gives a global morphological evaluation of the soft tissues, and it seems to be the most efficient solution for maxillofacial surgical assessments (Ramieri et al., 2008; Deo & Sen, 2010; Vezzetti et al., 2010).

Using model-base segmentation techniques, Chakravarty *et al.* (2011) obtained an automatic identification of facial landmarks in magnetic resonance images of adolescents. The method requires landmarks identification only on the model of the face, with subsequent customization of their position on each individual face.

Individual identification

Individual identification and/or classification have a large number of commercial, security, forensic and medical applications (Aeria *et al.*, 2010; Smeets *et al.*, 2010; Arca *et al.*, 2012). The necessity to identify faces from pictures obtained by video surveillance systems prompted to devise new mathematical and geometric methods that may match 3D facial images obtained from different sources, or 3D images with 2D photographs, and automatically identify the best correspondences (Cadoni *et al.*, 2010; Smeets *et al.*, 2010; Arca *et al.*, 2012).

In the last two decades, the problem of face recognition has been widely investigated, and research permitted to produce algorithms that perform as well as or better than humans on controlled, high-resolution images, that is frontal face, without occlusion, with uniform background and homogeneous illumination. In these conditions, from 2002 to 2006, the error rate dropped by an order of magnitude (Arca et al., 2012). The best results, in terms of correct identification, are obtained by 3D images. Indeed, the use of 2D views is unsatisfactory, and identification/ verification was found to be unreliable unless both profile and full-face images were included in an analysis (Davis et al., 2010), or exactly the same view was reproduced (Buck et al., 2011).

A typical method extracts invariant features from the 3D face template, and the salient characteristics obtained from the two images to be compared are used to determine their similarity. At first the images are corrected and aligned because of different points of view between the test and reference images, fiducial points or landmarks are extracted (around the eyes, mouth, nose), and then numerical data providing a vector description of the facial representation are obtained. A score of similarity between the two faces is computed (Arca *et al.*, 2012). A successful method of 3D shape-based recognition should also deal with facial expressions (Smeets *et al.*, 2010).

To the scope, stereophotogrammetry is currently employed to define large data bases of normal faces, thus permitting the analysis of face shape variation and the development of statistical tools for a successful personal identification (Aeria *et al.*, 2010; Cadoni *et al.*, 2010; Evison *et al.*, 2010; Gor *et al.*, 2010; Mallett *et al.*, 2010; Fang *et al.*, 2011; Ritz-Timme *et al.*, 2011).

The acquisition of statistically adequate population data banks may provide useful information for the reconstruction of biological profiles of unidentified individuals, particularly concerning ethnic affiliation, and possibly also for personal identification (Ritz-Timme *et al.*, 2011). These new data will enhance the potentials of the current anthropological databases, where single measurements (linear distances, angles, areas and volumes) are listed according to sex, age, ethnic origin, but without a global geometric morphometric framework (Sawyer *et al.*, 2009b; Sforza *et al.*, 2009a,b, 2010b, 2012c; Dong *et al.*, 2010; Ji *et al.*, 2010; Wang *et al.*, 2011).

Practical applications in the forensic field are the age estimation of an individual, artificial aging of facial records of missing children, information for facial reconstruction from skeletal remains (De Greef et al., 2006; Cattaneo et al., 2009; Claes et al., 2010; Wilkinson, 2010; Ritz-Timme et al., 2011; Hwang et al., 2012; Lee et al., 2012). The detection of facial dimensions that remain stable over time (or that have reduced age-related variations) may help in personal identification even years after the actual crime or the disappearance of the subject (Mallett et al., 2010). In contrast, those characteristics that show the largest age-related variations may be used for the estimation of the age of both living and dead persons, using direct measurements as well as 2D or 3D virtual records. The same data may enter into simulations of facial growth and aging, helping in personal identification. Facial reconstructions and artificial facial aging need data collected from living people of well identified ethnic groups, and from the widest possible age span, supplying information that help in simulating the modifications of facial features during normal growth and aging (Sforza et al., 2009b).

The assessment of facial dimensions and ratios also find application in the fight against pedopornography, where it may be necessary to age subjects represented in photographs and videos (Cattaneo *et al.*, 2009). In these subjects, often make-up and shaving are performed to deceive the viewer, and morphological and metrical analyses of their faces have been recently proposed and found to offer a better relation with chronological age than sexual characteristics (Cattaneo *et al.*, 2012). Within European people, the best results were found when country-specific reference samples were used (Cattaneo *et al.*, 2012).

One of the first steps in personal identification is the recognition of the ethnic group. For instance, interethnic variability in facial proportions has been investigated, finding that the height of the forehead had the greatest variations, coupled with pronounced differences in the measurements of the eyes, nose, and mouth (Fang et al., 2011). These measurements may therefore be efficaciously used to differentiate among the facial images of people belonging to different ethnic groups. A recent investigation by Ritz-Timme et al. (2011) compared the faces of young adult men from Germany, Italy and Lithuania, and found that almost all measurements and indices, except labial width and intercanthal-mouth index, showed significant differences between the three populations.

Facial muscles motion

The influence of facial muscles motion on facial morphology has been investigated by Maal et al. (2010, 2011), who found that intentional laughing increased the mean registration error between repeated 3D facial images by 300-400%. Involuntary facial muscle movements were analyzed by Lübbers et al. (2012), who found a mean error of 0.32 mm in adult healthy subjects. Including the technical error of the instrument, the mean global error was 0.41 mm (range 0-3.3 mm). This range of involuntary facial movements may pose some problems in the eye, mouth and nose regions, and clearly exceeds the 1.5 mm threshold for soft tissues (Lubbers et al., 2012). Stereophotogrammetric instruments and laser scanners are presently used also for the detection and quantification of facial motion in three dimensions, but both methods require a sufficiently large non-moveable part of the face (typically the forehead), thus restricting the kind of analysable movements and necessitating carefully controlled experimental conditions (Mehta *et al.*, 2008; Sawyer *et al.*, 2009a; Popat *et al.*, 2010; Verzè *et al.*, 2011a,b).

Facial modifications may also pose problems for automatic individual identification and recognition (see below), and a possible solution was proposed by Aeria *et al.* (2010) by mathematically decomposing the effects of facial motion.

Navigation systems in surgery

When we wrote our previous review (Sforza & Ferrario, 2006), contact methods for facial anthropometry (electromagnetic and electromechanic digitizers) were still commonly used, and optical instruments (laser scanners and stereophotogrammetric digitizers) had a limited diffusion. In the subsequent years, the tendency reversed, and the current use of contact digitizers for living subjects is reserved to particular clinical settings or to new applications.

One promising use of contact instruments is as navigation systems for image guided surgery. Head surgery is becoming more and more reliant on computerized facilities to measure the positions of the patient and surgical tools. Together with optical tracking technologies working in the infrared field, in the recent past electromagnetic tracking systems have shown an increase in their use in medical applications (Seeberger et al., 2012). The system is made by tracking bodies that are attached rigidly to the patient and the surgical tools respectively. While optical tracking devices need a free line of sight that may not be feasible within a surgical unit, the drawbacks of electromagnetic tracking are the requirement of cables attached to the electromagnetic tracking sensors and the possible ferromagnetic interferences that can compromise tracking precision (Sforza & Ferrario, 2006; Seeberger et al., 2012).

Geographical groups and human biology

Sample of 3D faces can help to formulate a normative database for different populations. Using a laser scan and a stereophotogrammetric camera capture system, Kau *et al.* (2010) analyzed five population groups from Europe (Hungary, Wales, Slovenia), Africa (Egypt) and North America (Texas, USA). Facial images were overlaid and superimposed, and a dedicated mathematical algorithm was performed to generate a composite facial average (one male and one female) for each group. Facial morphological differences were greatest between the Egyptian subjects and the other groups, with distinct differences in the nasal, malar, labial and chin regions. The European and North American groups were more similar, but differences in the maxillary and mandibular anteroposterior relationships were seen, with a relatively larger mandibular protrusion in Slovenian women

compared to Welsh or Texas women, and a relatively larger maxillary protrusion in Hungarian men compared with Texas men. The method allows to identify the position of

the different facial features in the various populations and ethnicities, thus producing populationspecific norms that may help the orthodontists and the maxillofacial surgeons in diagnosis and treatment planning (Kau *et al.*, 2010).

In the fields of bioarchaeology, evolution, and ecology, geometric morphometrics based mainly on 3D co-ordinates represents a new approach in the evaluation of variability (Pellegrini et al., 2011). One kind of these applications in human biology is related with anthropological determination of population affinity or ancestry (Baynam et al., 2011; Claes et al., 2012c) and determination of sex (Claes et al., 2012c; Garvin & Ruff, 2012; Shearer et al., 2012). Bigoni et al. (2010) analyzed the sexual dimorphism of crania from the Central European population and verified whether sex could be determined using shape characteristics of the cranium. Using an electromechanic digitizer, the authors analyzed 139 adult crania of known age and sex from the Central European population. They found significant sexual dimorphism in five selected regions of cranium: the midsagittal curve, the upper face, the orbital, nasal, and palatal regions. 3D morphometry proved to be a suitable tool for determining sexual dimorphism of cranium shape; the method could be used in comparisons

of various geographically or chronologically distant populations.

Esthetic indices

One of the applications of facial measurements is the definition of esthetic indices, in the quest of mathematical definitions of facial beauty and attractiveness. A detailed analysis of the current views on this topic is beyond the scopes of the present review. Nonetheless, it has to be underlined that physical appearance is one of the factors influencing social acceptance and emotional well-being, with a major role played by facial esthetics (Tollefson & Sykes, 2007; Kochel et al., 2010; Smeets et al., 2010). An attractive face is associated with perceptions of beauty, healthiness, fitness, mixed with feelings of social achievement, intelligence, richness, and happiness. In the general feeling, a beautiful face becomes the key to the success, and several investigators have tried to measure those specific facial dimensions and ratios that characterize faces considered attractive by the general public or by selected juries. Measurements are best obtained in three dimensions (Tollefson & Sykes, 2007; Sforza et al., 2007, 2008, 2009d, 2010c; Kochel et al., 2010; Bottino et al., 2012).

Craniofacial abnormalities

Several human syndromes are characterized by a distinctive set of craniofacial abnormalities, and their objective analysis could help the clinician (in particular the less expert one) facing with dysmorphic patients. Classic facial anthropometry has been widely used to the scope (Allanson *et al.*, 2011; Sforza & Ferrario, 2006), but optical instruments make the procedure less demanding for the patients, thus providing a quantitative support that may assist in the diagnosis of borderline patients or gene carriers (Kau *et al.*, 2006; Dellavia *et al.*, 2008, 2010; Sforza *et al.*, 2009c, 2011a,b, 2012b; Boehringer *et al.*, 2011).

Additionally, 3D surface (laser scan, stereophotogrammetry) or volumetric (CT, MR) data permit a better analysis of the facial configuration than that provided by a set of inter-landmark distances. For instance, facial asymmetry is best appreciated using a 3D approach: current developments in mathematical tools, especially in geometric morphometrics, allow to consider the object symmetry of the human face, separating the effect of selected landmarks to the total facial asymmetry, and assessing also the asymmetry of shape curves (Bock & Bowman, 2006; Sforza *et al.*, 2010c; Damstra *et al.*, 2011; Claes *et al.*, 2011, 2012b,c).

One of the most recent field of application is the biological analysis of statistical outliers, that is of those abnormal/unusual morphologies that can derive from congenital or acquired malformations, traumas or surgery. In these instances, common methods fail to provide a correct representation and quantification of the altered morphology, and dedicated algorithms are necessary (Claes *et al.*, 2012b; Walters *et al.*, 2013).

Fetal alcohol syndrome (FAS) is recognized as a major public health concern worldwide, being a leading identifiable and preventable cause of mental retardation and neurological deficit in the Western world. It affects all racial and ethnic groups. Classification of subjects as having FAS is usually made considering growth retardation, some specific facial anomalies, and central nervous system developmental problems. 3D facial analysis by stereophotogrammetry may allow a more efficient detection of affected children that may be imaged on-site without the need of specialized neurologists and screened off line (Douglas & Mutsvangwa 2010; Mutsvangwa et al., 2011). In particular, the quantitative evaluation of 3D facial characteristics showed accuracy over 95% at 5 years of age, and around 80% at 12 years of age, supporting the notion that FAS facial anomalies diminish with age (Mutsvangwa et al., 2010).

Quantitative assessment of facial phenotype may provide information to discover the root causes of diseases with an unclear genetic background, like cleft lip with or without cleft palate (Boehringer *et al.*, 2011; Hammond & Suttie, 2012). For instance, Weinberg *et al.* (2009) found that the faces of unaffected parents from multiplex cleft families displayed several shape differences compared with the general population, with midface retrusion, reduced upper facial height, increased lower facial height, and excess interorbital width. More recently, Boehringer *et al.* (2011) found a link between facial traits and single nucleotide polymorphisms associated with oral clefts, opening new perspectives for a better understanding of the genetic bases of human facial morphology.

Another set of disorders with an unknown origin are autism spectrum disorders (ASDs), including autistic disorder, Asperger's syndrome and pervasive development disorder (not otherwise specified). The disorders affect as many as 1 in 166 individuals and are characterized by significant impairments in social interaction and communication, as well as inappropriately focused behavior and restricted interests. The heterogeneity of ASDs in phenotype and etiology limits attempts to identify causes, pathogenesis, and develop effective treatments. A specific phenotype within ASDs would help to focus molecular research and uncover genetic causes and developmental mechanisms (Hammond et al., 2008; Aldridge et al., 2011). Recent investigations detected significant facial asymmetry in boys with ASD, mostly localized in the supraand periorbital regions anterior to the frontal pole of the right brain hemisphere. A similar pattern of facial asymmetry was found in the unaffected mothers of children with ASD. This facial asymmetry is paralleled by right dominant asymmetry of the frontal poles of boys with ASD. Both a direct effect of brain growth on facial asymmetry, and the simultaneous action on face and brain growth by genetic factors, may explain the findings, underlying the need for coordinated face and brain studies on ASD patients and their relatives (Hammond et al., 2008). Also, distinctive facial alterations have been found to correlate with particular clinical and behavioral traits, opening the way for future molecular and genetic studies (Aldridge et al., 2011).

Indeed, the face and the brain develop in strict coordination, and abnormalities or differences in facial morphology can be indicative of underlying brain pathology (Hammond *et al.*, 2008; Douglas & Mutsvangwa, 2010; Mutsvangwa *et al.*, 2010; Aldridge *et al.*, 2011; Hammond & Sutie, 2011). The combined use of stereophotogrammetry and of geometric morphometrics allows a better understanding of genetic disorders like trisomy 21. A recent study performed in patients with trisomy 21 and in their non-affected siblings supported the idea that the genes altered in this disease differentially affect developing facial structures rather than causing a generalized disruption to development as previously suggested (Starbuck *et al.*, 2011).

Plastic and reconstructive surgery necessitates of detailed images of the facial areas to be corrected, and often several procedures need to be combined and repeated during the life of a patient, asking for instruments that do not use invasive or dangerous procedures. Facial alterations in cleft lip and palate patients are a typical example, with orthopedic, surgical and orthodontic interventions starting at birth and continuing until young adulthood (Bock & Bowman, 2006; Schwenzer-Zimmerer et al., 2008; van Loon et al., 2010; Simanca et al., 2011; Sforza et al., 2012a; Zreaqat et al., 2012). The use of methods and instruments that limit any additional burden to the patients is mandatory: repeated soft tissue assessments are best performed by instruments that do not increase the radiation exposure of the children.

Orthodontic and orthognatic surgery patients usually do not need the extensive treatments as provided to dysmorphic patients, but considering their number and their age, the use of diagnostic instruments with a reduced biological impact is auspicial. The dimensions and shape of their facial soft-tissue structures are largely dependent from their skeleton and dental arches, and a detailed analysis of the cutaneous and muscular covering may inform about the underlying modifications induced by treatment. The use of notinvasive 3D surface analyzers may increment the existing data base, especially for young children. Indeed, orthodontic treatment in the deciduous dentition is usually indicated in cases of pronounced skeletal dysgnathia, which has a tendency to progress. The clinician do need normal reference values for a correct treatment planning that respects the growth potentials of the children (Ramieri et al., 2008; Dellavia et al., 2008, 2010; Primozic et al., 2009; Tartaglia et al., 2009; Baik & Kim, 2010; Moller et al., 2012).

Facial aging

In Western society the number of aged persons is increasing, both as a percentage of the total population and as absolute value. The assessment of the normal patterns of facial aging is a current matter of interest, where both the modifications in facial dimensions and the variations in facial motion are being considered. For instance, as recently reviewed by Rosati et al. (2012a), with age there is a decreasing display of maxillary incisors coupled with a concomitant increase in exposure of mandibular anterior teeth: increments in upper lip length, decrements in the muscular ability to perform a smiling task, and thinning of upper lip muscles can all contribute to these modifications (See et al., 2007; Van der Geld et al., 2008; Desai et al., 2009; Penna et al., 2009; De Menezes et al., 2011).

Current investigations underline the importance of four-dimensional image acquisition to evaluate dentolabial relationships, adding the effect of motion (time dimension) to the 3D assessment of facial structures (Sforza *et al.*, 2010b,d; Trotman, 2011; Verzè *et al.*, 2011a,b).

Facial reconstruction

In the field of facial reconstruction, reference values for both sexes from selected ethnic groups and ages are necessary. 3D facial images can be usefully employed with the current 3D computerized methods, finding applications in the forensic and archaeological fields (Claes et al., 2010; Wilkinson, 2010; Papagrigorakis et al., 2011; Friess, 2012; Hwang et al., 2012). Lee et al. (2012) proved the efficacy of facial reconstructions made starting from CBCT 3D facial scans of living subjects. On average, the deviation errors between the reconstructed and target faces were less than 2.5 mm in more than 65% of facial surface, with mean errors of 0.42 mm. CBCT scans can also be used to measure the thickness of facial soft tissues, providing new data sets for facial reconstructions. Considering that the subjects are scanned in an upright position, these instruments are likely to perform better than conventional CT, where the subjects are supine (Claes et al., 2010). Indeed, most of the

current data have been obtained from cadavers, but tissue shrinkage, skin compression and head position relative to the gravity vector should be taken into consideration (Hwang *et al.*, 2012). Ultrasound scans, another currently used method for the measurement of soft tissue thickness, do not perform as well as CBCT because no additional data (thickness in correspondence of new sets of landmarks) can be obtained once the subject has been dismissed (De Greef *et al.*, 2006; Sforza & Ferrario, 2006).

Manufacturing of objects and prostheses

The definition of normal facial dimensions, and of their variations in the various human groups (for sex, age, ethnic origin, body dimensions, but even according to the practiced job), is also necessary for a successful manufacturing of safety objects, like headgears, respirators, or other kinds of personal protective equipment (Zhuang et al., 2010a,b; Fang & Fang, 2011; Joe et al., 2012;). According to Joe et al. (2012), an estimated 5 million U.S. workers are legally required to use respiratory protective equipment while working. 3D facial scans, obtained using either non-invasive optical instruments, or radiographic tomograms, supply the base for off-line calculations and simulations. The same system can be used for the construction of individualized ortheses and prostheses, as well as for surgical guides for dental implantology, maxillofacial and orthognatic surgery (Kimoto & Garrett, 2007; Dirven et al., 2008; Maal et al., 2008; Swennen et al., 2009; Schaaf et al., 2010; Aboul-Hosn Centenero & Hernandez-Alfaro, 2012; Fourie et al., 2012).

Archaeology

Using 3D geometrical, textural, and physical reconstruction, historians and archaeologists can record archaeological excavation data (Sisk, 2010) or develop efficient intelligent algorithms to aid them to reconstruct incomplete 3D puzzles of ancient sculptural groups. Helped by a commercial laser scanner, Merchán *et al.* (2011) digitized and reconstructed multi-piece classical sculptures of a famous iconographic reference during

the Roman Empire called "Aeneas Group". The automated reconstruction of fragmented objects by matching the fragments is currently an active area of research in archaeology, paleontology and art restoration. This study led to some applications that historian and archaeologist colleagues found both useful and with a potential for facilitating the dissemination of historical knowledge. Indeed, measuring the statue freely and precisely lets historians factor out subjective perceptions, and better understand the artist's use of perspective and composition (Merchán *et al.*, 2011).

Ethical issues, data sharing and privacy

Digital technology developed in the last years are changing the use and spread of information, such as the ability to communicate, access information, exchange and store it. Nowadays, biological science and research are more reliant on digital technology and digital data, from images acquisition, measurement of digital samples, and statistical analyses to the virtual reconstruction techniques (Kullmer, 2008). Together with these changes, ethical dilemmas about privacy and data sharing have also being discussed.

Digital information offers new possibility of sharing data or interchange study specimens, opening a wide and inter-disciplinary debate. At present, no general consensus or agreement on how to deal with the data sharing or integration of information in anthropological research has been attained. Among the various topics under discussion, there are both technical (how to develop standard formats for databases, how to create accessible Data Storage Centers) and ethical problems (how to maintain the ownership of the specimens, how to control the widespread copies of digital data, the incorrect uses and abuses of digital tools) (Elton & Cardini, 2008; Kullmer, 2008; Sumner & Riddle, 2009).

Besides, ethics include moral choices made by individuals in relation to the rest of the community, standards of acceptable behavior, and rules governing members of a profession. The broad issues relating to electronic information systems include control of and access to information, privacy and misuse of data, and international considerations. New ethical and legal decisions are necessary to balance the needs and rights of everyone (Lynch, 2000).

When working with subjects' image, with instruments that can record and reproduce the face or external body surface, the privacy issue becomes of primary importance. Among the others, the European Union data privacy directive regulates the processing of personal data; the recommendation includes the standard fair-practice requirements to inform subjects, seek informed express consent, allow data-subject access and rectification of data, and the like. The scientific research is provided for by law and constitutes a necessary measure for public health reasons, but

it can never forget personal rights (European Commission, 1995, 2012).

Concluding remark

Researchers and clinicians can rely on a wide set of instruments for the 3D analysis of human facial morphology in healthy subjects and in patients. We believe that a key point is the choice of the most suitable analytical tools, which should combine mathematically rigorous methods and biological significance. Detailed quantitative and qualitative information about the facial tissues of a given subject, also combining and fusing digital data obtained from various image analyzers, can be made available. A better and faster diagnosis can be offered, together with longitudinal assessments.

Info on the web

Instruments*

www.fastscan3d.com Portable laser scan

www.3dMD.com Stereophotogrammetric face scanner

www.genextech.com Stereophotogrammetric face scanner

www.3d-shape.com/produkte/face_e.php Stereophotogrammetric face scanner

www.canfieldsci.com/ Stereophotogrammetric face scanner

www5.konicaminolta.eu/measuring-instruments/ products/3d-measurement.html Laser scanner

www.artec3d.com/3d_scanners/artec-eva Scanner/ video scanner

www.whitefox-conebeam.com/spip. php?rubrique9 *CBCT scanner*

Facial muscles: description and function*

www.ivy-rose.co.uk/HumanBody/Muscles/ FacialMuscles.php www.artnatomia.net/uk/index.html http://face-and-emotion.com/dataface/ expression/expression.jsp

Geometric morphometrics*

http://life.bio.sunysb.edu/morph/

Human identification, forensic and medical art*

www.lifesci.dundee.ac.uk/cahid/ www.labanof.unimi.it/

Ethical issues*

www.colorado.edu/geography/gcraft/notes/ ethics/ethics_f.html Margaret Lynch, The Geographer's Craft Project, Department of Geography, The University of Colorado at Boulder

http://eur-lex.europa.eu/LexUriServ/LexUriServ. do?uri=CELEX:52012PC0011:EN:NOT

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*accessed on 20th May 2013

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