

Linear Elastic Properties of the Facial Soft Tissues Using an Aspiration Device: Towards Patient Specific Characterization.

Vincent Luboz, Emmanuel Promayon, Yohan Payan

► To cite this version:

Vincent Luboz, Emmanuel Promayon, Yohan Payan. Linear Elastic Properties of the Facial Soft Tissues Using an Aspiration Device: Towards Patient Specific Characterization.. Annals of Biomedical Engineering, 2014, epub ahead of print. 10.1007/s10439-014-1098-1. hal-01061677

HAL Id: hal-01061677 https://hal.science/hal-01061677v1

Submitted on 8 Sep 2014

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers. L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

1	Linear elastic properties of the facial soft tissues using an aspiration device:					
2	towards patient specific characterization					
3						
4	V. Luboz ¹ , E. Promayon ¹ , Y. Payan ¹ *					
5	¹ UJF-Grenoble1/CNRS/TIMC-IMAG UMR 5525, Grenoble, F-38041, France, {vincent.luboz,					
6	Emmanuel.Promayon, ypayan}@imag.fr;					
7						
8	Abbreviated title: Characterization of soft tissues elastic properties					
9						
10	*Corresponding author:					
11	Yohan Payan					
12	Equipe GMCAO - Laboratoire TIMC-IMAG					
13	Université Joseph Fourier - CNRS UMR 5525					
14	Pavillon Taillefer					
15	Faculté de Médecine - 38706 La Tronche cedex - France					
16	Tel: +33 (0)4 56 52 00 01 - Fax: +33 (0)4 56 52 00 55					
17	email: <u>Yohan.Payan@imag.fr</u>					
18						
19						
20						
21	To appear in Annals of Biomedical Engineering, DOI: 10.1007/s10439-014-1098-1.					

22 Abstract

23 Biomechanical modeling of the facial soft tissue behavior is needed in aesthetic or maxillofacial surgeries where the simulation of the bone displacements cannot accurately predict the 24 25 visible outcome on the patient's face. Because these tissues have different nature and elastic properties across the face, depending on their thickness, and their content in fat or muscle, 26 27 individualizing their mechanical parameters could increase the simulation accuracy. Using a 28 specifically designed aspiration device, the facial soft tissues deformation is measured at four 29 different locations (cheek, cheekbone, forehead, and lower lip) on 16 young subjects. The 30 stiffness is estimated from the deformations generated by a set of negative pressures using an 31 inverse analysis based on a Neo Hookean model. The initial Young's modulus of the cheek, 32 cheekbone, forehead, and lower lip are respectively estimated to be $31.0 \text{ kPa} \pm 4.6, 34.9 \text{ kPa} \pm$ 33 6.6, 17.3 kPa \pm 4.1, and 33.7 kPa \pm 7.3. Significant intra-subject differences in tissue stiffness 34 are highlighted by these estimations. They also show important inter-subject variability for 35 some locations even when mean stiffness values show no statistical difference. This study 36 stresses the importance of using a measurement device capable of evaluating the patient 37 specific tissue stiffness during an intervention.

38

39 Key terms: Soft tissues; Face; Mechanical parameters; Aspiration; Finite element method.

41

42 **1. Introduction**

43

44 In aesthetic and maxillo-facial surgery, most of the interventions are related to the bony structures and aim either at repairing functionalities of the oro-facial structures or 45 46 improving their shape. To predict the final shape of the face after the displacement of the bones, most of the surgeons rely on their experience. Nevertheless, because of anatomical 47 variations in the facial soft tissues, *i.e.*, in the amount of fat between the muscles, the 48 thickness of the skin, or their material parameters, predictions may not always be accurate. 49 50 Several research groups have presented simulators to help in the evaluation of the outcomes of aesthetic and/or maxillo-facial surgeries. For example, Chabanas et al.⁶ presented a Finite 51 52 Element (FE) model of the skull and face used as an atlas which can be deformed to fit the 53 patient's anatomy. In this study, the soft tissues were modeled as a homogeneous, linear 54 elastic material and its material parameters were chosen to fit a clinical case where pre- and post-operative CT scans were available. It led to a Young's modulus of 15 kPa, and a 55 Poisson's ratio v of 0.49. Other finite element models also based on a linear modeling of the 56 soft tissues have been presented in the literature^{3, 12, 14, 22}. In these articles, the mechanical 57 parameters were chosen either by comparing their simulation results with imaging data 58 59 acquired from patients or were values from the soft tissue literature, although not specifically measured on the facial soft tissues. The validation of the predictions given by these simulators 60 61 were therefore complicated by the fact that these mechanical parameters were either only representative of a single patient, or were not directly related to the facial soft tissues, or were 62

extracted from *ex vivo* measurements (and therefore might be different from *in vivo* because of the lack of perfusion and the difference of temperature¹³).

To improve the evaluation of these FE models, it seems important to be able to 65 determine the material parameters of the facial soft tissues for a specific patient, or at least to 66 give an accurate cartography of the face mechanical properties for an average patient, if 67 possible. In a first attempt to reach this aim, an aspiration device, called the Cutometer 68 (http://www.courage-khazaka.de)^{7, 18}, was used to define several specific parameters such as 69 immediate distension, delayed distension, immediate retraction, or final deformation of the 70 71 face skin. These studies showed that viscoelastic properties are significantly influenced by aging. Unfortunately, in both studies, no clear link can be established between the Cutometer 72 73 specific parameters and the more classical parameters used in mechanical constitutive laws. 74 This device is mainly aimed at helping dermatologists in their need to quantify the elasticity 75 in an aging trend more than for mechanical simulation purpose. Sonographic elastography has proven its ability to estimate the stiffness of soft tissues for maxillo-facial applications². It 76 provides a map of Young moduli for tissues' superficial layers which values can only be used 77 for simulations assuming a small deformations framework. Other studies^{4, 5, 9, 15, 17} tried to 78 mechanically quantify the skin stiffness either by direct measurements or by using inverse 79 methods to match deformations visualized on medical images. Unfortunately the initial 80 81 Young's modulus (i.e., the initial slope of the stress-strain curve) and Poisson's ratio reported in these studies had fairly important ranges. For example, the Young's modulus was estimated 82 by Bickel et al.⁵ to 78 kPa and the Poisson's ratio to 0.47 using a Neo Hookean model. The 83 84 Young's modulus was found to vary between 4 kPa and 18.8 MPa in in vivo and in vitro measurements according to Lapeer et al.¹⁵. Another study¹⁷ also evaluated the initial Young's 85

modulus to 15 kPa using a Mooney Rivlin model (where $C_{10} = 2.5$ kPa). In a previous study⁹, 86 we evaluated the in vitro stiffness of the cheek of a fresh cadaver to 15 kPa. This work was 87 done in the context of a maxillo-facial simulator. The skin initial Young's modulus was 88 evaluated to 22.8 kPa using a Mooney Rivlin model (where $C_{10} = 3.8$ kPa) and measurements 89 on different locations on the face of one subject by Barbarino et al.⁴. In a recent study, a 90 micro-robotic device was used by Flynn et al.⁸ to record the force-displacement response of 91 92 the cheek of five volunteers. Facial skin exhibits a non-linear, anisotropic, and viscoelastic force-displacement response. When modeled using an Ogden FE model, the skin initial 93 Young's modulus was found to be between 15.9 kPa and 89.4 kPa. Flynn et al.⁸ also showed 94 95 variations in stiffness between different locations on the face for one subject. Such a paper 96 stems questions about patient specific variations of the stiffness of the facial soft tissues and 97 the stiffness variation depending on the location for different subjects.

98 In the present paper, we aim at clarifying these patient specific variations in order to 99 improve the planning of different maxillo-facial surgeries using FE model. The objective is to 100 provide a tool to evaluate the facial soft tissue stiffness (characterized here with the Young's 101 modulus) while being compatible with the constraints of the operating room. The goal is to 102 evaluate the *in vivo* initial Young's modulus for the facial soft tissues at four representative 103 locations, namely the cheek, the cheekbone, the forehead, and the lower lip, and for a panel of 104 subjects of different ages and body mass indexes. For the maxillo-facial application, a quasi-105 static framework can be assumed since boundary conditions corresponding to bone 106 displacements are applied and simulated without taking into account the dynamic visco-107 elastic behavior of the soft tissues.

108

111 2.1 Aspiration technique

112

A device characterizing the mechanical behavior of the soft tissues was used to 113 114 determine their initial Young's modulus. This device, called LASTIC (for Light Aspiration 115 device for in vivo Soft TIssue Characterization), is based on the aspiration technique and was first introduced by Schiavone et al.¹⁹ while quantifying the brain behavior²⁰. This technique 116 has also been used by Hollenstein et al.¹¹ for other applications such as the uterus or the liver. 117 It also has been used on various *in vivo* tissues such as the forearm skin and the tongue²¹. In 118 119 its current version, Figure 1, LASTIC is a 33 mm x 34 mm metal cylinder composed of two 120 compartments. The lower one is an airtight chamber, open at the bottom by a 12 mm diameter 121 circular aperture and closed at the top by a glass window. The upper compartment holds the electronic part consisting of a miniature 2 megapixel digital camera and a LED used as a light 122 123 source. The aspiration chamber is connected to a programmable syringe pump that can 124 generate a negative pressure (measured by a manometer) which deforms the tissues on which 125 LASTIC is laid on. This deformation is imaged by the camera via a 45 degree inclined mirror which provides a view of the tissue from the side. The height of the tissue deformation is 126 127 segmented on the recorded image. A basic camera calibration is performed to determine the 128 pixel size. On average, the pixel size is around 0.01 mm. Measuring the deformation height 129 corresponding to several steps of increasing negative pressures can give an estimation of the behavior of the tissues. LASTIC is fully sterilizable and can consequently be used inside the 130 131 sterile fields of operating rooms.

The tissue measurements are then processed through an inverse analysis to estimate the tissue mechanical behavior. This analysis consists of matching the measured deformation/pressure curve to a pre-computed library of displacement heights determined by a FE Analysis of the aspiration experiment using a Neo-Hookean constitutive law¹. Such a material is fairly stable and shows a behavior similar to the one simulated by Yeoh or Mooney-Rivlin materials at strains levels observed for such aspiration experiments. The Neo-Hookean equation is written as:

where I_1 is the first invariant of the left Cauchy-Green deformation tensor, C_{10} is a material parameter, J is the determinant of the deformation gradient F, D is a material incompressibility parameter (with D=(1-2v)/C₁₀), and W is the strain energy. As in Chabanas et al.⁶, the skin is assumed to be nearly incompressible and a Poisson's ratio v of 0.49 was chosen. Note that, for small extensions (*i.e.*, in the linear elastic domain when I₁ is close to 3) the initial Young's modulus, *i.e.*, the initial slope of the stress-strain curve, can be approximated by E = 6C₁₀.

The facial soft tissues are modeled by a thick circular slice while LASTIC is described 147 by a rigid hollow cylinder (Figure 2). Taking advantage of the axisymmetric geometry of our 148 149 model, the mechanical study is reduced to a two-dimensional structural analysis. The sample 150 is meshed with approximately 2,000 linear quad elements. The mesh is refined in the 151 neighborhood of the aspirated region, where highest deformation occurs, in order to increase the accuracy of the computed solution. The interface between LASTIC and the sample is 152 153 specifically meshed with contact elements in order to ensure that the aspirated skin tissue 154 slides without friction inside the LASTIC hole.

Given the different thicknesses of the studied facial tissues, an estimation of their 155 156 variation was performed on a CT scan of a head (courtesy of subject #4). It presented a thickness of 5 to 6 mm for the forehead skin and of 15 mm or more for the tissues of the lip, 157 158 cheek and cheekbone. To take this variation into account, two different axisymmetric models were used: one with a tissue thickness of 5 mm and one with a thickness of 15 mm (Figure 2). 159 160 There was no need to create a model for each location over 15 mm because the maximal 161 negative pressure created by LASTIC does not influence layers over 13 mm, see Figure 2. On 162 the other hand, for the model with a tissue thickness of 5 mm, the maximal negative pressure 163 created by LASTIC leads to a deformation of the tissues that is influenced by the tissue thickness. In this case, the maximum deformation measured in the tissues is around 13 %164 165 (assuming that we do not consider the specific region of contacts between the tissues and the LASTIC cylinder). For a tissue thickness of 15 mm, the maximum deformation is 17 %. 166 167 These two values show that the material deformations are not too large; using a Neo Hookean 168 model (thus neglecting the non-linearity due to very large deformations) is therefore relevant 169 here.

The pre-computed library of displacements was generated using a wide range of C_{10} and applied negative pressure for the two different thicknesses. Matching the measurements with the corresponding library (the 5 mm model for the forehead and the 15 mm model for the lip, cheek, and cheekbone), using a least-square minimization method, leads to an estimation of the C_{10} value corresponding to the tissue stiffness. This minimization is performed in less than a second.

- The device has been validated in Luboz et al.¹⁶ on several types of samples including
 silicone rubbers, with stiffness ranging from 10 kPa to 90 kPa, and compared to tensile tests.
 - 8

This validation showed that LASTIC overestimates the stiffness by 16 % on average with a standard deviation of 9.5 %. This overestimation is mainly due to errors generated during the acquisition, namely due to the manometer precision and the camera calibration, which decreases the precision of the image segmentation to evaluate the tissue deformation.

182

- 183 2.2 Cartography of the face stiffness
- 184

185 To be able to improve the planning of the outcome of an aesthetic or maxillo-facial surgery, it is necessary to estimate the stiffness of the facial soft tissues in several places. Four 186 187 locations with presumably different tissue thicknesses and different amounts of fat and muscle 188 were consequently chosen: the cheek, the cheekbone, the forehead, and the lower lip. To 189 study the possible variations between subjects, the stiffness estimation was performed on a 190 group of 16 healthy subjects, eight males and eight females, of different ages and body mass indexes (mean age = 29.2 ± 6.3 , mean BMI = 21.5 ± 2.1). Subjects gave their informed consent 191 192 to the experimental procedure as required by the Helsinki declaration (1964) and the local Ethics Committee (study agreement CERNI n°2013-11-19-30). LASTIC was used to estimate 193 194 the stiffness of the soft tissues at these four locations for these 16 subjects, see Figure 3. Five measurements were performed for each location. In order to prevent the experimenter from 195 196 applying too much pressure on the subject's skin with LASTIC and therefore creating a 197 discomfort and a possible bias in the measurement, each subject was asked to place and to 198 maintain LASTIC him/herself. The experimenter helped the subjects to reposition LASTIC as 199 closely as possible to the previous location. The range of negative pressures applied at each

location varied for each subject. The initial negative pressure was 0 kPa while the maximal
negative pressure was up to 7.3 kPa (= 73 mbar), depending on the subject and location.

To avoid any leaks at the interface between LASTIC and the tissues, a water wet gauze compress was used to wipe the skin before each measurement. This set up left a slight amount of water facilitating the suction and reducing the viscosity. Furthermore, LASTIC was very slightly pressed on the tissue by the subjects to ensure that the bottom compartment entire surface lies on the skin. The first three measured values were not used during the minimization process in order to compensate the initial load applied by the positioning of LASTIC, which could be observed as a bump on the video screen.

For each location, five measurements were made repeatedly: the first measurement was performed successively on the cheek, the cheekbone, the forehead, and the lower lip; then, the second measurement was performed successively on the cheek, the cheekbone, the forehead, and the lower lip, etc... until the fifth measurements was performed the same way. This repetitive cycle allowed the tissue of each location to relax between each measurement. A single measurement took about three minutes which means that overall, each subject's 20 measurements were performed in about one hour.

During all the measurements, the subjects were asked to stay as relaxed as possible in order to keep the activations of the underlying muscles of the face as low as possible and consequently to reduce the impact of tissue anisotropy and initial tension on the measurements.

220

221 **3. Results**

222

223 The stiffnesses of the facial soft tissues (characterized here with the initial Young's 224 modulus) measured with LASTIC on 16 healthy voluntary subjects at four locations, as well as the sex, age and BMI of each subject, are shown in Table 1. The cheek, cheekbone, 225 226 forehead, and lower lip mean stiffnesses of each subject, as well as the standard deviation resulting from the five measurements at each location, are given in the four last columns. The 227 228 overall subjects' mean stiffness for each of the four locations is also given on the bottom row. 229 The corresponding initial Young's modulus are $E_c = 31.0$ kPa ± 4.6 for the cheek, $E_{cb} = 34.9$ kPa \pm 6.6 for the cheekbone, E_f = 17.3 kPa \pm 4.1 for the forehead, and E_l = 33.7 kPa \pm 7.3 for 230 231 the lower lip. Neither tissue stiffening nor softening is observed for the repeated 232 measurements; we therefore assume that there is probably little influence of the pre 233 conditioning.

The complete measurements are given in the supplementary material. Figure 4 presents a Whisker box plot showing the mean, minimal and maximal initial Young's modulus (in kPa) for the cheek, cheekbone, forehead and lower lip. The result of the bilateral paired Welch's T-test between the forehead and the three other locations is also presented. This test is an adaptation of the Student's t-test intended for use with two samples having possibly unequal variances²³.

Table 2 shows the results of a bilateral paired Welch's T-test between each measurement location. The p-value resulting from this test demonstrates that the difference between the mean stiffness of the forehead E_f and the cheek E_c (p=2.5E-5) is statistically significant (p<=0.05). This is also significant for the difference between E_f and E_l (p=7E-6) and for E_f and E_{cb} (p=1E-6). On the other hand, there are no statistical differences between E_c and E_l , between E_c and E_{ch} , and between E_l and E_{ch} .

It is to be noted that the evaluated mean stiffnesses do not show any dependence neither with the age, BMI or sex.

Nevertheless, subject to subject differences can be observed for each location even if 248 249 there is no overall statistical difference. It is the case for example for the cheekbone and lower lip stiffness of subjects #5 and #15: $E_{cb}(5) = 22.1$ kPa and $E_{l}(5) = 33.3$ kPa 250 while 251 $E_{cb}(15) = 35.1$ kPa and $E_{l}(15) = 22.3$ kPa. Another example of the disparity can be seen 252 between subjects #10 and #12 for the cheek and lower lip stiffness: $E_c(10) = 37.1$ kPa and 253 $E_1(10) = 28.0$ kPa while $E_c(12) = 31.6$ kPa and $E_1(12) = 45.7$ kPa. These two subjects have 254 completely different stiffness values compared to the mean stiffness E₁ for the lower lip (it can be observed that $E_1(10) = E_1 \times 83$ % while $E_1(12) = E_1 \times 135$ %.), see Figure 5, and for the check 255 256 while overall there is no statistical difference between these two locations (p=0.424). For all these values, the standard deviations for the five measurements used to obtain these mean 257 258 values are relatively low (between 4.0 and 7.9 kPa).

259

260 **4. Discussion**

261

The stiffness values presented in Table 1 and Figure 4 and outlined in the previous paragraph show fairly important variations between subjects, even if there is no statistical difference over the whole subject pool. The cheek stiffness measured on all the 16 subjects fall within the range given by Flynn et al.⁸ (which is based on cheek measurements on five volunteers): from 15.9 kPa to 89.4 kPa.

As shown in Table 2, the stiffnesses of the forehead and the cheek, of the forehead and the lower lip, and of the forehead and the cheekbone are statistically different. It can be

explained by the smaller tissue thickness (and different boundary conditions) for the forehead as compared to the cheek, the lower lip, and the cheekbone. Precisely measuring tissue thicknesses at different locations (with MRI or US imaging) should help in understanding more deeply these differences Measuring and estimating variations in tissue types or muscles activations should also provide some clues to explain the observed differences.

274 A first estimation of facial tissue stiffness can nonetheless be given with our LASTIC 275 measurements. For a given location, the inter-subject variability can be estimated by the 276 standard deviation $sd(E_i/E)$, where E_i is the normalized Young moduli of subject i and E is the 277 average Young modulus of all E_i. The inter-subject variability sd(E_i/E) is equal to 27 %, 29 278 %, 29 %, and 27 %, respectively for the forehead, cheek, lower lip, and cheekbone. For a 279 given location, the intra-subject variability can be estimated by the average standard deviation 280 mean(sd($E_{i,i}/E_i$)), where $E_{i,j}$ is the resulting measured Young modulus for the measurement j 281 of subject i. The intra-subject variability mean(sd(E_{i,j}/E_i)) is equal to 22 %, 16 %, 21 %, 19 %, 282 respectively for the forehead, cheek, lower lip, and cheekbone. This shows that for a given 283 location, the intra-subject variability (i.e., the standard deviation per subject) is smaller than 284 the inter-subject variability (i.e., the standard deviation per location). Consequently the small 285 variation of position due to the repositioning of the device between two measurements for the 286 same location has less effect on the estimation than the change of stiffness from a subject to 287 another. Furthermore, we could question the fact that muscle activation could play a role in 288 the estimation of the stiffness since two locations include muscles that can be voluntarily 289 activated (i.e., lip and forehead) while the other two include muscles that are more difficult to 290 activate voluntarily (i.e., cheek and cheekbone). The lower lip and forehead have indeed 291 higher inter-subject variability than the cheek and cheekbone. Finally, it is important to note

that the maximal difference between location variability being 6 % (between forehead and cheek), these variations could also be explained by a change of device positioning, or a measurement error (see our previous work¹⁵ for an estimation of LASTIC errors).

The stiffness differences pointed out in the last part of the results section illustrate the 295 fact that even if there is no statistical difference over the whole subject pool between some 296 297 locations, for example between cheekbone and lower lip, there are fairly important variations 298 of the stiffness between subjects. For example, it would be inaccurate to take the mean value E_{cb} = 34.9 kPa for the cheekbone for subjects #4 and #13 while the measured stiffness values 299 300 were evaluated to $E_{cb}(4) = 50.7$ kPa and $E_{cb}(13) = 51.6$ kPa, which would correspond to an 301 underestimation of 30%. The same observation can be made for the stiffness of the lower lip 302 in subject #8: the mean value $E_1 = 33.7$ kPa while the subject's stiffness value was estimated 303 to $E_1(8) = 17.9$ kPa; this would lead to an over-estimation of 88%. It therefore seems essential 304 in the context of FE model for surgical planning to take these inter-subject variations into 305 account.

306 Two types of limitations should be considered for this study: the first one concerns the 307 experimental set up, and the second one concerns the mechanical set up. The experimental set 308 up has four main limitations: the fact that muscle activation is not recorded during the experiments, the assumption that the facial soft tissues are homogeneous, the assumption that 309 310 those tissues exhibit a linear stress-strain response, and the low variation of the subject pool in 311 terms of age and BMI. The main limitation is relative to muscle activation. Even though 312 subjects were asked to be as relaxed as possible, we cannot guarantee that their muscles were 313 not activated at all, which would consequently have biased the measurements by stiffening the 314 tissues. Because this activation could not be measured without using invasive EMG sensors, it is likely that the measurements with high standard deviation are the consequence ofinvoluntary muscle activation.

317 Assuming that the facial soft tissues are homogeneous is also erroneous: they are 318 composed of several layers of skin (including epidermis, dermis and hypodermis), muscles 319 and fat and can be more than a centimeter thick. Given the level of aspiration generated by 320 our LASTIC device (never higher than 7.3 kPa and a maximum tissue bump of about 5.1 mm, 321 with a maximal pre-load of 3.2 mm, leading to an actual deformation directly due to the 322 suction of 1.9 mm), the obtained characterization is mainly limited to the superficial layers of 323 the facial tissue (epidermis and dermis), few millimeters below the skin at most. Assuming 324 that these tissues are homogeneous consequently results in a non-completely accurate 325 stiffness estimation. The stiffness estimation could be improved by considering a 326 heterogeneous model with several layers of tissues with different mechanical properties. For 327 instance, a two layer model including a thin superficial layer for the skin and a thicker one for 328 the underlying tissues could be considered as a better approximation of the face tissues. 329 Measuring the facial soft tissue stiffness in their full thickness would also need a higher level 330 of negative pressure, which would probably have been refused by the Ethics Committee 331 because of the risk for generating pain or damaging the tissues.

Assuming that the facial soft tissues exhibit a linear stress-strain response is also inaccurate for large deformations: because of their heterogeneity, the tissues mainly have a nonlinear response⁹. Estimating the Young's modulus corresponding to a Neo Hookean constitutive law is consequently accurate only for the initial low strain stiffness. Using a more complex constitutive law, such as one derived from a Mooney Rivlin or Ogden formulation, would probably improve the accuracy of the stiffness estimation with LASTIC.

338 Finally, despite some individual differences, the relatively small variations of the 339 stiffness measured on our group of subjects can be explained by its low variance in age and in BMI. The subjects being all young or relatively young (between 23 and 44) their skin is likely 340 341 to be in good shape and fairly elastic. As for the subject's BMI, it ranges between 16.8 and 26, 342 and only four subjects are outside the standard deviation range [19.4; 23.6]. Most of the 343 subjects therefore have probably a small amount of fat tissues under their face skin. The 344 studied group is consequently not extremely representative of the world population neither in 345 age nor in BMI.

Three main limitations can be listed concerning the mechanical set up: the low level of negative pressure generated by LASTIC, the initial load that may have been applied on the soft tissues, and the possible inaccuracy or non-reproducibility of the position of the measurements on each subject.

As stated above, the level of aspiration generated by LASTIC is never higher than 7.3 kPa which therefore limits the estimation of the stiffness to only superficial tissues. Using higher negative pressures could help to quantify deeper tissues but could also injure the subject; this was consequently not performed in our study.

Another source of inaccuracy in the stiffness estimation is due to the fact that the initial load applied on the soft tissues at the beginning of each measurement (to avoid any leaks) is not simulated in the FE model nor used for the inverse analysis. Removing the first three measured values seems a reasonable approximation as it is assumed that the pressure compensates the initial load and the consequent deformation of the tissues¹⁵. The initial load is always kept below the precision threshold of the manometer by checking the measured pressure on the manometer and the camera image. The degree of this initial pressure applied

by the subjects is controlled during and after the experiments. This initial load creates an initial deformation of the tissues and a light aspiration has consequently no influence on them. Once the pressure is strong enough to aspirate the tissues, the tissue deformation is visible on the camera image. This threshold was reached around the third pressure step. Nevertheless, this compensation is not accurate and might lead to a deviation of the stiffness value.

The inaccuracy of the location of the measurements for each subject could also be responsible for increasing the resulting variance. The experimenter visually estimates the positioning error to a maximum of 5 mm; we therefore assume that this has a minimal effect on the stiffness evaluation.

370

371 **5.** Conclusion

372

373 A map of the stiffness of the facial soft tissues is presented in this paper as measured 374 by LASTIC, a device based on the aspiration technique. Using an inverse analysis with a FE 375 Neo Hookean behavior, it provides an estimation of the stiffness of the tissues at four locations: the cheek, the cheekbone, the forehead and the lower lip. On average, the stiffness 376 377 coefficient of the soft tissues composing the cheek, the cheekbone, the forehead, and the lower lip are respectively estimated to be 31.0 kPa, 34.9 kPa, 17.3 kPa, and 33.7 kPa. 378 379 Considering all measurements, it seems difficult to obtain and use values describing an 380 average patient. With statistical differences between the forehead and the cheek (p=2.5E-5), 381 between the forehead and the lower lip (p=7E-6) and between the forehead and the cheekbone (p=1E-6), this study shows that the tissue thickness as well as the amount and nature of fat 382 tissues and muscles below the skin probably play a role in the stiffness. Although no 383

384 dependences can be exhibited between the mean tissue stiffnesses and neither the age, the 385 BMI nor the sex of the subjects, this study gives an interesting first insight in the variation of the stiffness between subjects at different locations on the human face. The inter-subject 386 387 variations appearing in our measurements are pointing out that in vivo patient specific measurements are essential to accurately model the facial soft tissues and that an average 388 389 stiffness value is not adequate for a patient specific model. Specifically designed small 390 aspiration devices are a convenient and practical way for doing so. As LASTIC can be 391 sterilized, it could be used routinely during clinical practice in order to assess rapidly the 392 patient specific tissue stiffness during the planning of aesthetic or maxillo-facial surgeries.

393 Future works will aim at correcting the limitations of this study. Firstly, the range of 394 the population tested with LASTIC should be broaden by measuring the stiffness of the 395 tissues on younger and older subjects and with a larger variation in BMI. Secondly, the 396 accuracy and reproducibility of the device positioning during the measurements could also be 397 improved, for instance by marking precisely onto the skin the aspiration locations. Increasing 398 the level of negative pressure that LASTIC can generate in order to quantify the stiffness of 399 deeper tissues is also possible but can only be done after evaluating the risk of damaging the 400 skin. Quantifying the properties of the different skin layers and underlying tissues could also be implemented by using different sizes of orifice for the suction similarly to the work of 401 Hendricks et al.¹⁰. Another improvement to be addressed is the fact that following only the 402 403 deformation of one point at the top of the tissue aspired dome is not enough to evaluate soft 404 tissues' anisotropy. We therefore plan to segment the whole deformation dome from the 405 acquired images and to measure its possible asymmetries which could lead to study the 406 tissues' anisotropy. Lastly, monitoring the muscle activation might be possible using surface

EMG, even though it might be difficult to avoid the electrodes placed close to LASTIC, thusinterfering with the aspiration device.

409

410 Acknowledgments

411 Competing interests: None.

412 Funding: This work was supported by French state funds managed by the ANR within the

413 Investissements d'Avenir programme (Labex CAMI) under reference ANR-11-LABX-0004.

414 Ethical approval: This study was conducted according to the principles expressed in the

415 Declaration of Helsinki and all participants gave their written informed consent. Ethical

approval was given by the CERNI committee under the reference 2013-11-19-30.

417 We would like to thank Jacques Ohayon (TIMC-IMAG) for his contribution to this work and

418 especially his help to design LASTIC and the process to estimate the stiffness modulus.

419

420 **References**

421 1. Ansys. Theory Reference. Ansys manual, release 5.6, 1999.

422 2. Ariji, Y., M. Nakayama, W. Nishiyama, and E. Ariji. Applications of sonographic
423 elastography to the oral and maxillofacial region. Journal of Radiology & Radiation
424 Therapy, 2(2): 1049-57, 2014.

425 3. Barbarino, G.G., M. Jabareen, J. Trzewik, A. Nkengne, G. Stamatas, and E. Mazza.

- 426 Development and validation of a three-dimensional finite element model of the face. J
- 427 Biomech Eng, 131(4):041006-11, 2009.

428 4. Barbarino G.G., M. Jabareen, and E. Mazza. Experimental and numerical study on the
429 mechanical behavior of the superficial layers of the face. Skin Res Technol. Nov;17(4):434430 44, 2011.

- 431 5. Bickel B., P. Kaufmann, M. Skouras, B. Thomaszewski, D. Bradley, T. Beeler, P. Jackson,
- 432 S. Marschner, W. Matusik, and M. Gross. Physical Face Cloning. ACM Transactions on
- 433 Graphics, SIGGRAPH, vol. 31, no. 4, pp. 118:1-118:10, 2012.
- 6. Chabanas M., Y. Payan, C. Marécaux, P. Swider, and F. Boutault. Comparison of linear
 and non-linear soft tissue models with post-operative CT scan in maxillofacial surgery.
 Lecture Notes in Computer Science, 2004, vol. 3078, pp. 19-27.
- 7. Cua A. B., K. P. Wilhelm, and H. I. Maibach. Elastic properties of human skin: relation to
 age, sex, and anatomical region. Archives of Dermatological Research, Volume 282, Issue 5,
- 439 pp 283-288, 1990.
- 8. Flynn C., A. Taberner, P. Nielsen, and S. Fels. Simulating the three-dimensional
 deformation of in vivo facial skin. Journal of the Mechanical Behavior of Biomedical
 Materials. 28, 484-494, 2013.
- 9. Gerard J.M., J. Ohayon, V. Luboz, P. Perrier, and Y. Payan. Non linear elastic properties of
 the lingual and facial tissues assessed by indentation technique. Application to the
 biomechanics of speech production, Medical Engineering & Physics. 27 (10):884-892, 2005.
- 446 10. Hendriks F.M., D. Brokken, C.W.J. Oomens, D.L. Bader, and F.P.T. Baaijens. The
- 447 relative contributions of different skin layers to the mechanical behavior of human skin in
- 448 vivo using suction experiments. Medical Engineering & Physics. 28: 259–266, 2006
- 449 11. Hollenstein M., M. Bajka, B. Röhrnbauer, S. Badir, and E. Mazza. Measuring the In Vivo
- 450 Behavior of Soft Tissue and Organs Using the Aspiration Device. Soft Tissue Biomechanical

- Modeling for Computer Assisted Surgery, Studies in Mechanobiology, Tissue Engineeringand Biomaterials, 11:201-228, 2012.
- 453 12. Keeve E., S. Girod, R. Kikinis, and B. Girod. Deformable Modeling of Facial Tissue for
- 454 Craniofacial Surgery Simulation. Journal of Computer Aided Surgery 3, 228–238,1998.
- 455 13. Kerdok A.E., M.P. Ottensmeyer, and R.D. Howe. Effects of perfusion on the viscoelastic
- 456 characteristics of liver. J Biomech. 39(12):2221-31, 2006.
- 457 14. Koch R., S. Roth, M. Gross, A. Zimmermann, H. Sailer. A framework for facial surgery
- 458 simulation. Technical Report 326, ETH Zurich, 1999.
- 459 15. Lapeer R.J., P.D. Gasson, and V. Karri. A hyperelastic finite-element model of human
- skin for interactive real-time surgical simulation. IEEE Trans Biomed Eng. 58(4):1013-22,
- 461 2011.
- 462 16. Luboz V., E. Promayon, G. Chagnon, T. Alonso, D. Favier, C. Barthod, and Y. Payan.
- 463 Validation of a Light Aspiration device for in vivo Soft TIssue Characterization (LASTIC).
- 464 Soft Tissue Biomechanical Modeling for Computer Assisted Surgery, Springer, 243-256,
 465 2012.
- 466 17. Nazari M.A., P. Perrier, M. Chabanas, and Y. Payan. Shaping by stiffening: a modeling
 467 study for lips. Motor Control. Jan;15(1):141-68, 2011.
- 18. Ryu H.S., Y.H. Joo, S.O. Kim, K.C. Park, S.W. Youn. Influence of age and regional
 differences on skin elasticity as measured by the Cutometer. Skin Res Technol. 14(3):354-8,
 2008.
- 471 19. Schiavone P., E. Promayon, and Y. Payan. LASTIC: a Light Aspiration device for in vivo
- 472 Soft TIssue Characterization. Lecture Notes in Computer Science, 5958:1-10, 2010.

- 20. Schiavone P., F. Chassat, T. Boudou, E. Promayon, F. Valvidia, and Y. Payan. In Vivo
- 474 Measurement of Human Brain Elasticity Using a Light Aspira-tion Device. Medical Image475 Analysis, 13:673-678, 2009.
- 476 21. Schiavone P., T. Boudou, E. Promayon, P. Perrier & Y. Payan. A light sterilizable pipette
- 477 device for the in vivo estimation of human soft tissues constitutive laws. Proceedings of the
- 478 30th Annual International Conference of the IEEE Engineering in Medicine and Biology
- 479 Society, IEEE EMBS 2008, 4298-4301, 2008.
- 480 22. Zachow S., E. Gladiline, H. Hege, and P. Deuflhard. Finite element simulation for soft
- 481 tissue prediction. In Lemke, H., al., eds.: Computer Assisted Radiology and Surgery,
- 482 CARS'00, Elsevier 23–28, 2000.
- 483 23. Welch B. L. The generalization of "Student's" problem when several different population
- 484 variances are involved. Biometrika 34 (1–2): 28–35, 1947.

487 Figure 1 Luboz











Subjec				Cheekbone		
t # /	age	BMI (kg.m ⁻	Cheek E _c (i)	$E_{cb}(i) \pm std$	Forehead E _f (i)	Lower lip E _l (i)
sex	(years)	²)	± std (kPa)	(kPa)	± std (kPa)	± std (kPa)
1 / M	44	22.0	21.3±3.7	21.5±2.1	10.6±1.6	19.1±3.4
2 / M	35	21.2	20.7±4.5	23.1±3.4	9.9±2.4	20.1±4.1
3 / F	26	20.7	23.4±7.4	29.0±11.8	16.0±2.7	46.1±12.7
4 / F	35	22.8	48.5±9.9	50.7±5.0	24.2±7.4	41.2±7.2
5 / F	26	19.2	21.1±5.0	22.1±2.5	10.5±2.9	33.3±8.2
6 / M	23	21.1	28.9±3.3	32.1±2.8	13.0±2.9	27.1±7.2
7 / F	24	20.3	34.5±4.6	39.3±13.8	30.2±7.9	36.5±7.9
8 / M	23	21.9	19.5±2.3	27.3±6.6	11.7±3.5	17.9±4.6
9 / M	39	26.0	31.2±4.0	41.4±5.8	18.9±3.8	39.8±11.4
10 / F	24	16.8	37.1±4.9	39.3±10.9	19.5±5.1	28.0±5.9
11/ M	27	25.1	29.1±3.3	39.1±10.1	22.8±1.8	38.0±11.9
12 / M	27	19.9	31.6±4.0	30.5±8.1	24.8±6.6	45.7±7.9
13 / M	27	22.1	43.1±±2.6	51.6±±7.5	15.9±4.1	42±12.8
14 / F	32	21.5	44.5±3.7	42.4±3.7	21.9±7.5	39.1±3.8
15 / F	32	21.2	29.5±3.3	35.1±1.0	15.6±2.9	22.3±1.0
16 / F	24	22.3	32.4±7.0	33.7±11.0	11.5±2.9	43.4± 6.3
Mean	29.3±6.		$E_c =$	E _{cb} =		
± std	3	21.5±2.1	31.0±4.6	34.9±6.6	$E_{f} = 17.3 \pm 4.1$	$E_1 = 33.7 \pm 7.3$

501 Table 2 Luboz

	Cheek E _c	Lower lip E ₁	Cheekbone E _{cb}
Forehead E _f	0.000025	0.000007	0.000001
Cheek E _c		0.424	0.238
Lower lip E ₁			0.733

502 Captions:

511

503 Figure 1 – Cross section of LASTIC's two compartments. The lower part is the aspiration 504 chamber with the mirror and the upper part contains the camera that images the deformation. Figure 2 – The two different Finite Element models used to create the precomputed library 505 506 of displacement heights / pressure curves, for a tissue thickness of (a) 5 mm (forehead), and (b) 15 mm or more (lip, cheek, cheekbone). The Von Mises strains are plotted on both sides, 507 508 showing maximum deformations (of (a) 15 % and (b) 26 %) near the interface with LASTIC 509 because of the contact. But the measured displacement height is at the top of the deformation 510 dome.

forehead, and the lower lip. The subjects are asked to position and hold LASTIC themselves
under supervision of the experimenter. From the LASTIC measurements, the stiffness of the
facial soft tissues at the different location can be estimated.

Figure 3 – The measurements are done at four locations: the cheek, the cheekbone, the

Figure 4 – Whisker box plot showing for each location: mean, minimal and maximal initial
Young's modulus (in kPa). The result of the bilateral paired Welch's T-test between the
forehead and the three other locations is also presented.

Figure 5 – Variation of the initial Young's modulus E_l (lower lip) for subjects #10 and #12 (averaged for the five measurements), compared to the mean initial Young's modulus for all subjects. The mean stiffness computed by the inverse analysis using a Neo Hookean approximation is also plotted (continuous lines). Measurement points are also plotted. $E_l(10)$ $= E_l \times 0.83$ and $E_l(12) = E_l \times 1.35$.

- 523 Table 1 Age, body mass index (BMI), sex (M for Male and F for Female), initial Young's
- 524 modulus E (in kPa) and standard deviation (std) of each subject i for the facial soft tissues at
- *four locations: cheek* (E_c) *, cheekbone* (E_{cb}) *, forehead* (E_f) *, and lower lip* (E_l) *.*
- *Table 2 P-value for each possible pair of locations where the stiffness is estimated.*