

DIAGNOSING CLEFT LIP PATHOLOGY IN 3D ULTRASOUND: A LANDMARKING-BASED APPROACH

*Original*

DIAGNOSING CLEFT LIP PATHOLOGY IN 3D ULTRASOUND: A LANDMARKING-BASED APPROACH / Vezzetti, E., Marcolin, F., Fracastoro, G., Speranza, D.. - In: IMAGE ANALYSIS & STEREOLOGY. - ISSN 1580-3139. - ELETTRONICO. - 35:1(2016), pp. 53-65. [10.5566/ias.1339]

*Availability:*

This version is available at: 11583/2625310 since: 2016-10-20T11:34:45Z

*Publisher:*

international society for Stereology

*Published*

DOI:10.5566/ias.1339

*Terms of use:*

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

*Publisher copyright*

(Article begins on next page)

1 **DIAGNOSING CLEFT LIP PATHOLOGY IN 3D ULTRASOUND:**  
2 **A LANDMARKING-BASED APPROACH**

3  
4 ENRICO VEZZETTI<sup>1</sup>, DOMENICO SPERANZA<sup>2</sup>, FEDERICA MARCOLIN<sup>3,1</sup>, AND GIULIA FRACASTORO<sup>1</sup>  
5

6<sup>1</sup>Department of Management and Production Engineering, Politecnico di Torino, Italy;  
7<sup>2</sup>Dipartimento di Ingegneria Civile e Meccanica, Università degli Studi di Cassino e del  
8Lazio Meridionale, Italy

9e-mails: enrico.vezzetti@polito.it; d.speranza@unicas.it; federica.marcolin@polito.it;

10giulia.fracastoro@studenti.polito.it

11

12

13

14

15ABSTRACT

16

17Aim of this work is to automatically diagnose and formalize prenatal cleft lip with  
18representative key points and identify the type of defect (unilateral, bilateral, right, or  
19left) in three-dimensional ultrasonography (3D US). Differential Geometry has been  
20used as a framework for describing facial shapes and curvatures. Then, descriptors  
21coming from this field are employed for identifying the typical key points of the defect  
22and its dimensions. The descriptive accurateness of these descriptors have allowed us  
23to automatically extract reference points, quantitative distances, labial profiles, and to  
24provide information about facial asymmetry. Eighteen foetal faces, ten of healthy  
25foetuses and eight with different types of cleft lips, have been obtained through a  
26Voluson system and used for testing the algorithm. Cleft lip has been diagnosed and  
27correctly characterized in all cases. Transverse and cranio-caudal length of the cleft  
28have been computed and upper lip profile has been automatically extract to have a  
29visual quantification of the overall labial defect. The asymmetry information obtained  
30is consistent with the defect. This algorithm has been designed to support  
31practitioners in identifying and classifying cleft lips. The gained results have shown  
32that Differential Geometry might be a proper tool for describing faces and for  
33diagnosis.

34

35Keywords: Cleft lip; dysmorphisms; landmarking; syndrome diagnosis; 3D ultrasound.

36

37

38

39INTRODUCTION

40

41 Three-dimensional ultrasound (US) has been introduced more than twenty years  
42ago into clinical practice (Riccabona *et al.*, 1997). Its applications on diagnosis of  
43anomalies and diseases were a direct consequence of its use. In particular, cleft lip  
44and palate (CLP) detection, whose incidence is 1/700 in United States (Tonni and  
45Lituania, 2013), was widely addressed, as they could be difficult to be diagnosed with  
46bi-dimensional US, especially in earlier gestational ages (Hata *et al.*, 1998). In the  
47effort to quantify the performance of routine ultrasonographic screening on an  
48unselected population, the Eurofetus study (Grandjean *et al.*, 1999) shows that CLP  
49has the lowest rates of detection (18%) and it is diagnosed usually later in pregnancy  
50(only 31.6% before 24 weeks). Furthermore, CLP is identified with a lower occurrence  
51by prenatal US when the anomaly is isolated than in the cases where multiple

1

1

2

52anomalies coexist, as frequently noticed during autopsies following termination of  
53pregnancy of fetuses with diagnosed multiple diseases (Luck *et al.*, 1992).  
54Complementarily, 3D, despite some criticisms (Maarse *et al.*, 2010), has been  
55considered more accurate than bi-dimensional data in detecting unaffected lips at less  
56than 24 weeks (Pretorius *et al.*, 1995).

57 In this work we will focus on cleft lip (CL) alone. CL, “both unilateral and  
58bilateral, includes clefts involving the alveolus and hard palate anterior to the incisive  
59foramen, namely the embryological primary palate” (Demircioglu *et al.*, 2008). The  
60tested rates of antenatal detection of CL range 21-30% (Rotten and Levillant, 2004).

61 Cleft lip has been associated with more than one-hundred different  
62chromosomal abnormalities and genetic syndromes (Jones, 1993), and sometimes may  
63be the only sign of a chromosomal anomaly, as trisomy 18 (Carlson, 2000), trisomy 13,  
64or syndromes such as Cornelia de Lange or Smith-Lemli-Opitz (Roelfsema *et al.*, 2007).  
65Thus, an accurate scan searching for other foetal anomalies and a genetic counselling  
66are paramount when a cleft lip is diagnosed. Cleft lip does not go with any palatal  
67abnormality in 15-25% cases (Bäumler *et al.*, 2011, Offerdal *et al.*, 2008). More  
68generally, if we consider CLP as a whole, the incidence of structural anomalies and  
69syndromes accompanying cleft lip and palate ranges between 21% and 38%  
70(Campbell *et al.*, 2005). But it is important to note that, although they often occur with  
71each other, cleft lip and palate abnormalities are “developmentally distinct processes”  
72(Lee *et al.*, 2000). In particular, the embryological origins of lips and alveolus clefts  
73appear to be distinct from those of secondary palate cleft (Campbell *et al.*, 2005).

74 Lee *et al.* (2000) used three-dimensional ultrasonography to support cleft lip  
75and palate detection. CL was identified by an examiner as “a loss of continuity of the  
76orbicularis oris muscle from a coronal or axial view of the lips” (Lee *et al.*, 2000), so  
77the diagnosis was not automatic. Campbell *et al.* (2005) assessed the clinical value of  
78a three-dimensional US technique, the 'reverse face' view, in the prenatal  
79categorization of orofacial clefts including CL. Then, Platt *et al.* (2006) proposed the  
80'flipped face' view to diagnose lip and palate cleftings, relying on 3D US. When a static  
81volume is acquired, it is rotated 90° so that the cut plane is directed in a chin-to-nose  
82plane and scrolled to examine in sequential order different zones, including lips.  
83Mailáth-Pokorny *et al.* (2010) investigated the role of foetal MRI in the antenatal  
84diagnosis of facial clefts, including cleft lip, although no particular detection technique  
85has been employed. Martinez-Ten *et al.* (2012) investigated whether systematic  
86examination of primary and secondary palate supported the detection of face cleftings  
87during first trimester. Gindes *et al.* (2013) studied the potential of three-dimensional  
88US for palate view in fetuses at high risk for CLP. An in-depth palate assessment was  
89made adopting both 2D and 3D US on the axial plane. Then, the outcoming prenatal  
90diagnosis was compared to after-birth findings.

91 Some authors used landmarks as reference points. Johnson *et al.* (2000)  
92assessed the advantages of three-dimensional US in diagnosing cleft lip. The volume  
93data were displayed in two formats: three orthogonal planar images and a three-  
94dimensional rendered image of the foetal facial surface. The planar images were  
95“rotated with the interactive display into a standard anatomic orientation, so that the  
96three planar images corresponded to the frontal, sagittal, and transverse facial planes”  
97(Johnson *et al.*, 2000). The rendered image provided landmarks for the planar images.  
98Roelfsema *et al.* (2007) used 3D US to perform foetal orofacial clefts examination and  
99quantified the craniofacial variability index (CVI) in distinguishing between isolated

100 cleft lip/palate and cleft lip/palate in chromosomal abnormalities or syndromes. Facial  
 101 landmarks such as tragus, nasion, gnathion, glabella, subnasion, and others were  
 102 employed to extract sixteen craniofacial measurements for the evaluation of after-  
 103 birth abnormal/regular orofacial development. Although none of the fetuses  
 104 evaluated in their study was affected by cleft lip, Sepulveda *et al.* (2010) proposed a  
 105 novel sonographic landmark typical of the first trimester, the 'retronasal triangle', to  
 106 be adopted for the early screening of CP. This landmark has been termed this way  
 107 because coronal plane displays three easily identifiable echogenic lines: the two  
 108 maxilla frontal processes and the primary palate. Manganaro *et al.* (2011) studied CLP  
 109 via MRI and ultrasound, although not 3D. Facial landmarks in the zones of forehead,  
 110 occiput, orbits, nose, lips, chin, mandible were identified and analyzed for each fetus.  
 111 Tonni and Lituania (2012) proposed a new three-dimensional sonographic software, the  
 112 OmniView algorithm, and applied it to unilateral CL, bilateral CLP, and isolated CP. They  
 113 showed that 3D imaging of the foetal hard and soft palates by OmniView was  
 114 technically easier than with previously reported 3D techniques. OmniView allowed  
 115 visualization of all anatomical landmarks of the specific targeted zone, i.e. labia,  
 116 primary palate, alveolar ridge, posterior palate, uvula, velum, and tongue.

117 This work introduces a methodology for automatically diagnosing cleft lip and  
 118 assessing specific information about the detected cleft, such as transverse and cranio-  
 119 caudal lengths, upper lip outline, and a quantification of facial asymmetry.

120

121

122

## 123 MATERIALS AND METHODS

124

125 During 2013, 38 3D volumes of 38 fetuses at 22-32 weeks' gestation were  
 126 acquired. Eight of them were fetuses affected by cleft lip. Written informed consent  
 127 was obtained from the parents for publication of clinical details, clinical images, and  
 128 videos. Principles outlined in the Declaration of Helsinki have been followed.

129 Among these acquisitions, 18 were selected and processed for the purposes of  
 130 the study, keeping all the eight faces with cleft lip. The leftover ones were excluded  
 131 due to damages, acquisition inaccuracy, noise, and wrong or unusable fetus's  
 132 position, such as hands on face or similar.

133 The US equipment was a Voluson system (GE Healthcare, Wauwatosa, WI, USA),  
 134 with a RAB 4-8 (real time 4D convex transducer probe). The GE RAB 4-8 has a  
 135 frequency range of 4 to 8 MHz and is used for OB applications (Footprint 63.6 x 37.8  
 136 mm, FOV 70°, V 85°x70°). Table 1 shows data details and respective scan settings.

137

Ultrasound examination											
Volume Ultrasound: GE Voluson e - Transducer: RAB 4-8-RS/OB											
Foetus		Scan Setting									Defect
Name	Week	MI	Fr	TIs	Quality	Th	B(°)	V(°)	Mix	SR	Cleft lip?
Anto	32	0,9	4,2/10,8 cm/51 Hz	0,1	max	30	52	65	40/60	II	no
Bart	32	0,9	3,7/11,0 cm/52 Hz	0,1	max	29	50	65	50/50	II	no
Lisa	32	1,	4,1/9,7 cm/54	0,	max	3	53	65	40/6	II	no

5

3

6

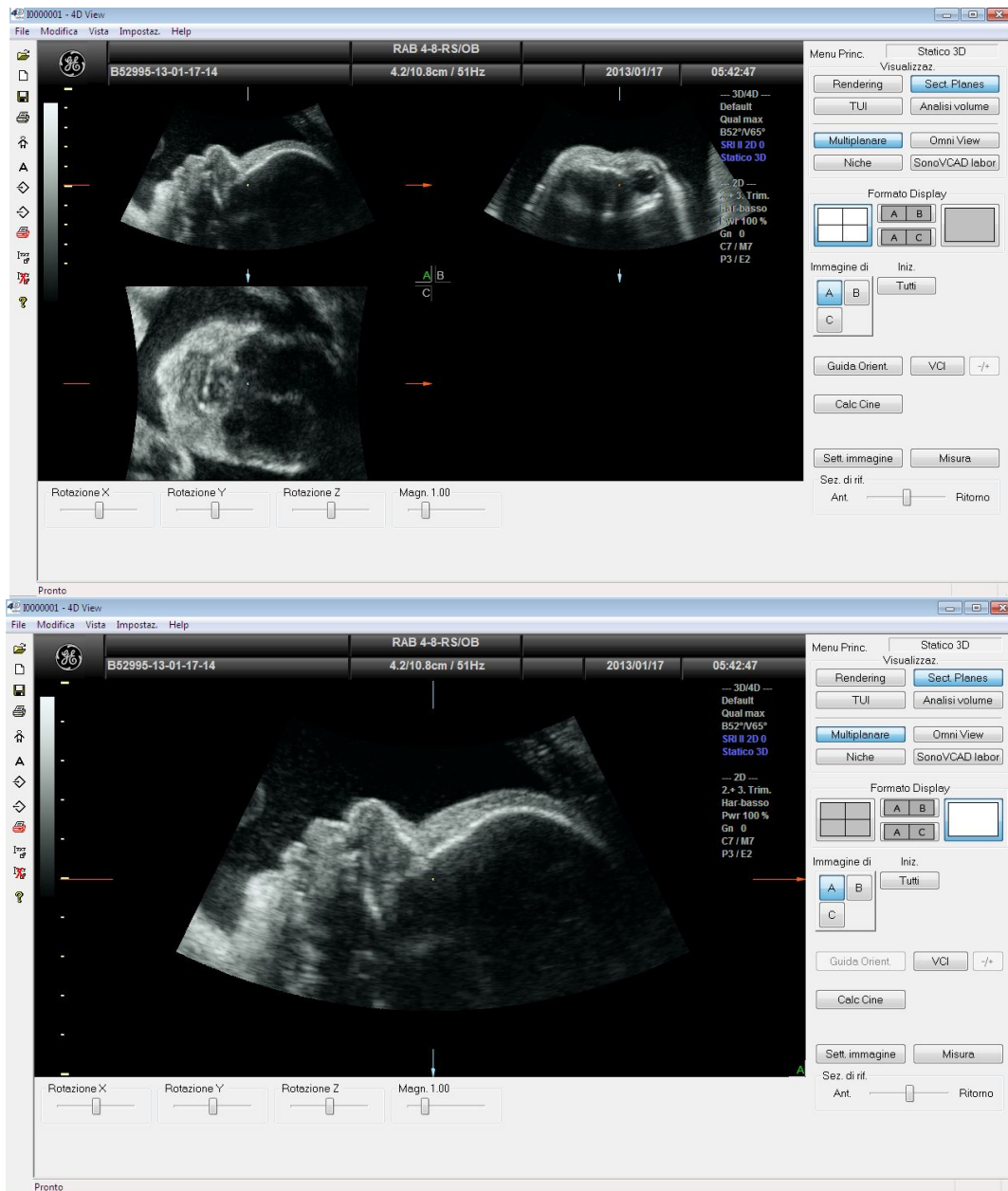
		1	Hz	1		0			0		
Gio	22	1,1	3,6/10,2 cm/58 Hz	0,1	max	30	47	65	40/60	II	no
Gian	22	1,0	3,6/8,1 cm/68 Hz	0,1	high 2	30	46	65	40/60	II	no
Paul	32	1,1	2,8/10,9 cm/49 Hz	0,2	max	30	54	65	40/60	II	no
Pie	32	1,1	1,7/8,1 cm/55 Hz	0,1	max	30	58	65	40/60	II	no
Elena	32	0,9	4,2/10,8 cm/47 Hz	0,1	max	30	56	65	40/60	II	no
Fede	32	0,9	4,4/11,1 cm/51 Hz	0,1	max	30	50	65	40/60	II	no
Simon	32	1,1	3,5/9,6 cm/56 Hz	0,1	max	30	50	65	40/60	II	no
A	32	0,9	4,2/10,8 cm/51 Hz	0,1	max	30	52	65	40/60	II	Unilateral complete
B	32	0,9	3,7/11,0 cm/52 Hz	0,1	max	29	50	65	50/50	II	Unilateral complete
C	32	0,9	4,2/10,8 cm/47 Hz	0,1	max	30	56	65	40/60	II	Bilateral complete
D	32	0,9	4,4/11,1 cm/51 Hz	0,1	max	30	50	65	40/60	II	Bilateral complete
E	22	1,0	3,6/8,1 cm/68 Hz	0,1	high 2	30	46	65	40/60	II	Unilateral incomplete
F	32	1,1	4,1/9,7 cm/54 Hz	0,1	max	30	53	65	40/60	II	Unilateral incomplete
G	32	1,1	2,8/10,9 cm/49 Hz	0,2	max	30	54	65	40/60	II	Unilateral complete
H	32	1,1	3,5/9,6 cm/56 Hz	0,1	max	30	50	65	40/60	II	Unilateral incomplete

138 **Table 1.** Weeks' gestation, scan settings, and eventual cleft lip features for each baby.

139  
140 4D VIEW software allows to see the acquired images on three orthogonal planes: axial,  
141 sagittal, and coronal (Fig. 1, above). The plane chosen for the facial shell modelling is  
142 the midsagittal (Fig. 1, below).

143

144



145

146

147

148

**Figure 1.** Multiplanar image (above) and midsagittal plane (below).

149

150

151

152

153

154

155

156

157

158

159

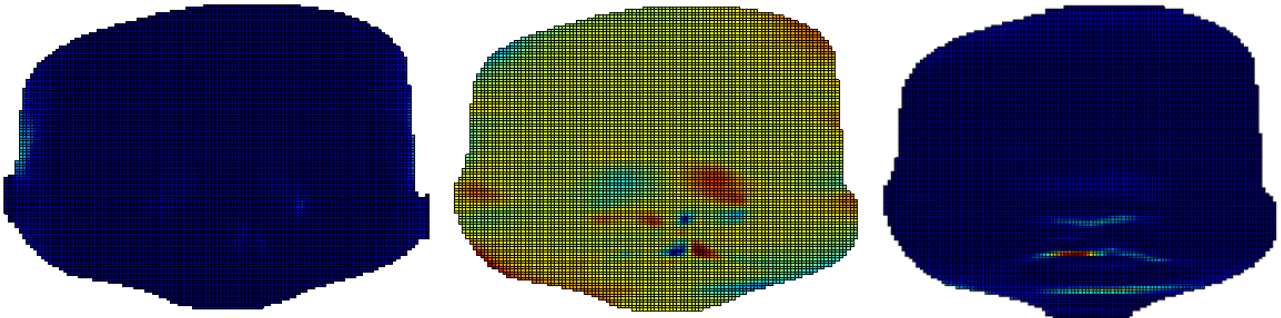
160

Appendix. These descriptors rely on previous work of our research group (Calignano

161and Vezzetti, 2010; Vezzetti *et al.*, 2011-2014). Figures 2-8 show their behaviour on a  
162facial shell with cleft lip.

163

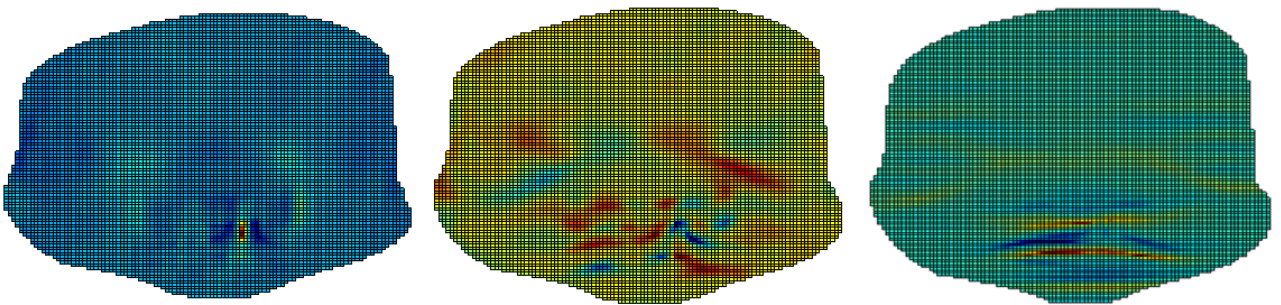
164



165

166

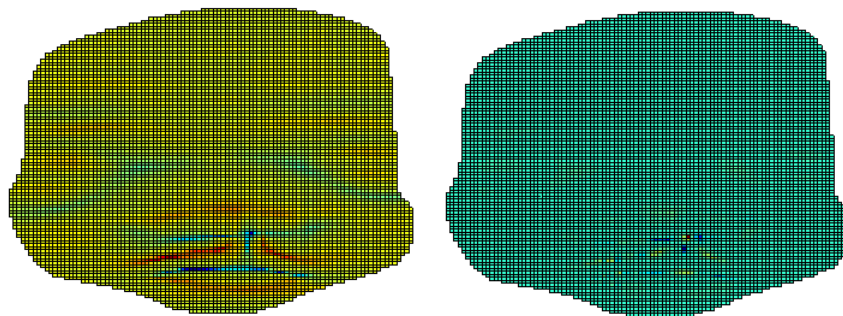
**Figure 2.** The coefficients of the first fundamental form  $E$ ,  $F$  and  $G$ .



167

168

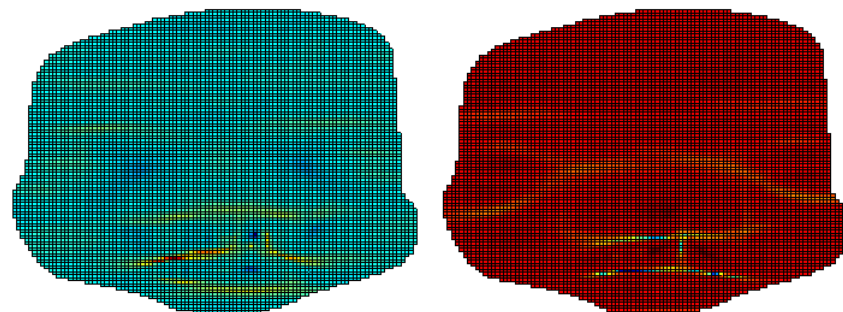
**Figure 3.** The coefficients of the second fundamental form  $e$ ,  $f$  and  $g$ .



169

170

**Figure 4.** The mean and Gaussian curvature  $H$  and  $K$ .



171

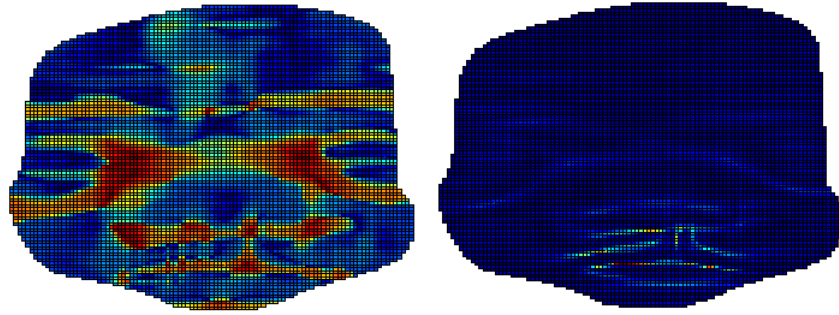
172

173

**Figure 5.** The principal curvatures  $k_1$  and  $k_2$ .

11

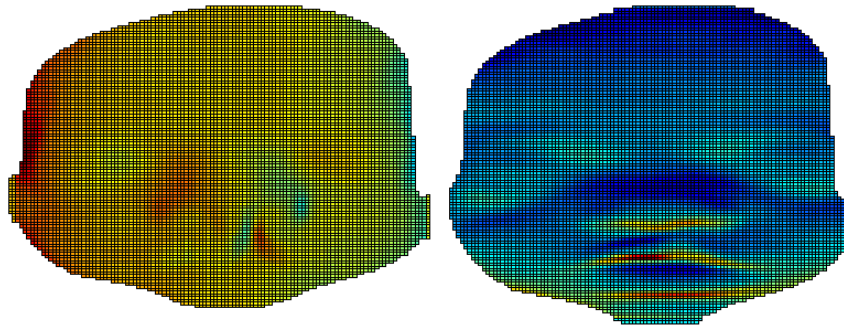
12



174

175

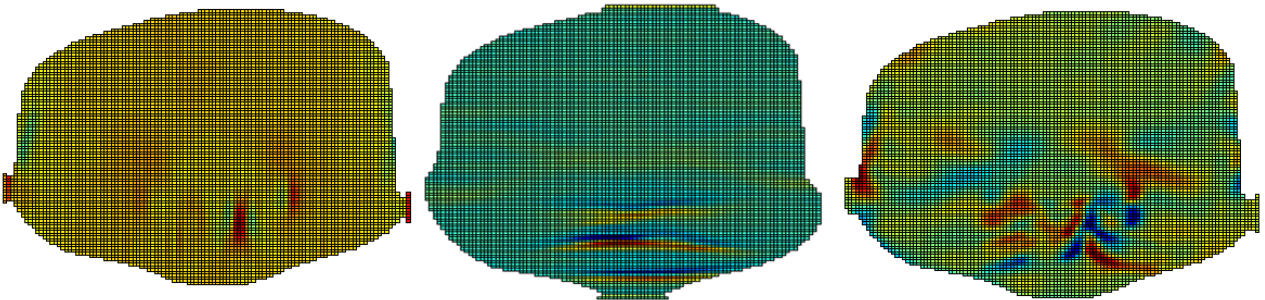
**Figure 6.** The Shape and Curvature Indexes  $S$  and  $C$ .



176

177

**Figure 7.** The first derivatives  $D_x$  and  $D_y$ .



178

179

**Figure 8.** The second derivatives  $D_{xx}$ ,  $D_{yy}$  and  $D_{xy}$ .

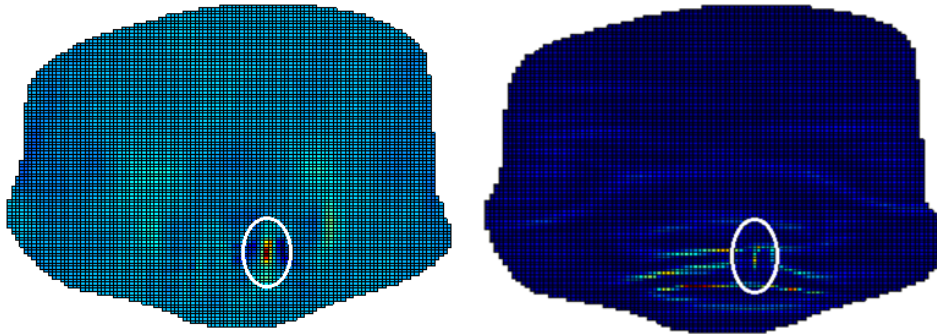
180

181

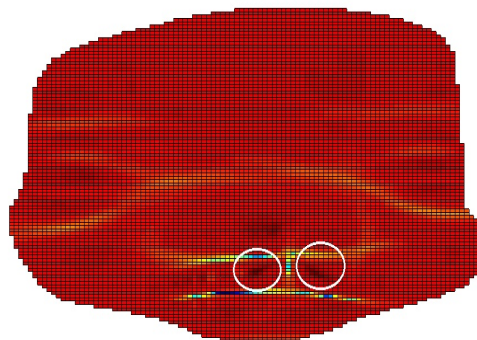
182

## 183 DETECTION OF THE DEFORMITY

184  
185 Cleft lip is a gap/indentation in the upper lip. The proposed algorithm  
186 demonstrates that this defect could be detected via point-by-point mapping  
187 geometrical descriptors on facial depth map. This indentation is characterized by high  
188 numerical values of coefficient  $e$  and of Curvedness Index  $C$  in correspondence to the  
189 zone of interest, as shown in Figure 9. Moreover, the two parts of the lip that are  
190 located beside the indentation are characterized by two maximums of the principal  
191 curvature  $k_2$ , as can be seen in Figure 10.  
192



193  
194 **Figure 9.** The behaviour of the coefficient  $e$  (left) and of the Curvedness Index  $C$  (right) in a foetus with  
195 cleft lip. The circle highlights the area of the gap.

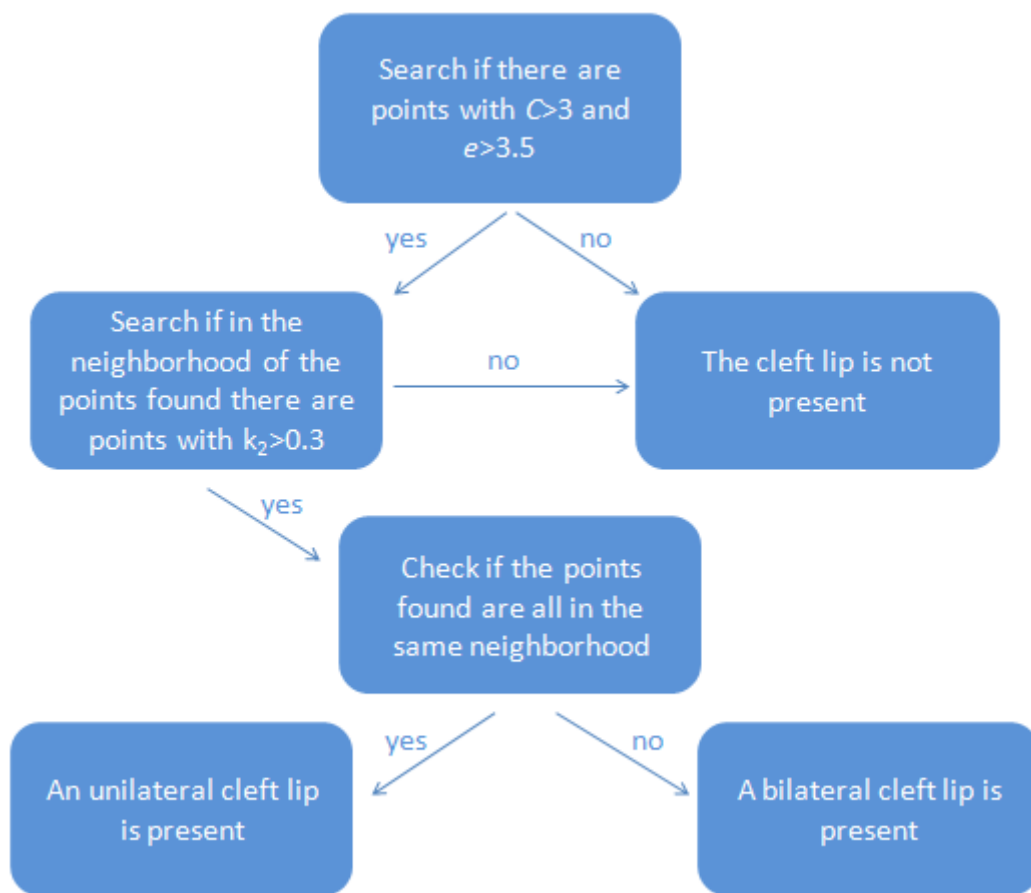


196  
197 **Figure 10.** The behaviour of the principal curvature  $k_2$  in a foetus with cleft lip. The two circles highlight  
198 the areas of the lip beside the gap.  
199

200 The designed algorithm adopts the previous geometrical features to detect  
201 whether the cleft lip is present or not in a foetus's face. Moreover, this algorithm is  
202 able to automatically distinguish between unilateral and bilateral cleft lip. It is  
203 composed by the following steps.

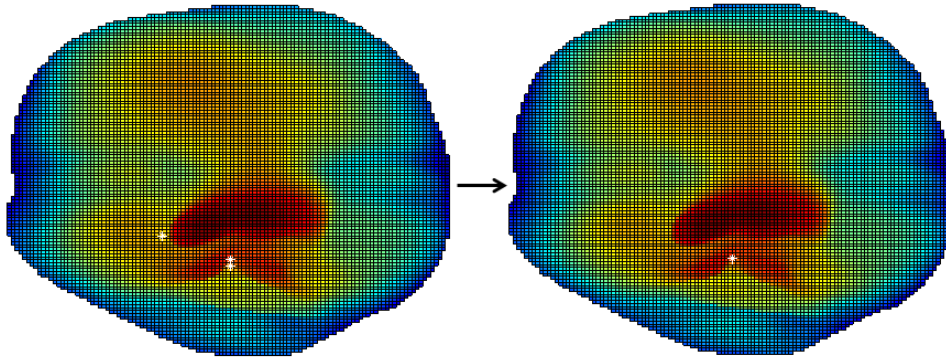
- 204 1. The algorithm searches if there are points whose coefficient  $e$  and Curvedness  
205 Index  $C$  are greater than a threshold value ( $C > 3$  and  $e > 3.5$ ). These are the  
206 geometrical features of the gap in the lip. Thresholds are set via  
207 experimentation.
- 208 2. If the search of the step 1 gives no results, the cleft lip is not present.  
209 Otherwise, another check is performed in order to verify that a cleft lip is really  
210 present. For each point that satisfies the conditions of step 1, the algorithm  
211 searches if in its neighbourhood there are points with a high value of the  
212 principal curvature  $k_2$  ( $k_2 > 0.3$ ). These are the geometrical features of the two  
213 parts of the lip beside the gap. This further condition is needed, as in some

214 cases the points close to the *a/ae* of the nose could have the same geometrical  
 215 features searched in step 1.  
 216 3. If the search of the previous step gives no results, the cleft lip is not present;  
 217 otherwise it is.  
 218 4. In order to verify if it is an unilateral or bilateral cleft lip, the algorithm checks if  
 219 the points that satisfy the condition of step 1 and 2 are all in the same  
 220 neighbourhood or not. If they do not belong to the same neighbourhood, the  
 221 cleft lip is bilateral.  
 222 The steps of the process are explained in the scheme of Figure 11.  
 223 In Figure 12, the points found in step 1 and 2 are shown in a shell with an unilateral  
 224 cleft lip.  
 225 In Figure 13, the points found in step 1 and 2 are shown in a shell with a bilateral  
 226 cleft lip.  
 227

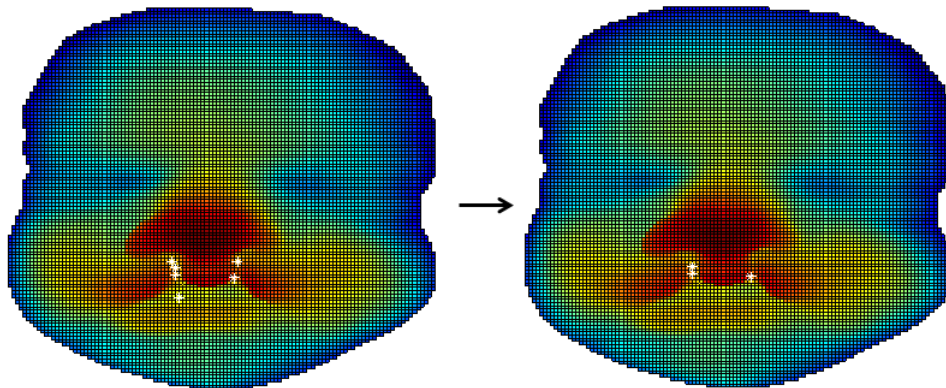


228  
 229

**Figure 11.** Scheme of the process for cleft lip diagnosis.



230  
 231 **Figure 12.** On the left: the points found in the first step of the algorithm. On the right: the points found in  
 232 the second step of the algorithm.



233  
 234 **Figure 13.** On the left: the points found in the first step of the algorithm. On the right: the points found in  
 235 the second step of the algorithm.

236

### 237 LOCALIZATION OF KEY POINTS

238

239 In order to quantify the deformation, four key points are automatically localized:  
 240 the two points of the lip that are beside the cleft and the ending points of the cleft,  
 241 shown in Figure 14.

242



**Figure 14.** The four key points of the cleft lip.

243  
 244  
 245

246 As mentioned above, the principal curvature  $k_2$  has two maximums in the first  
247 two points. The automatic localization algorithm:

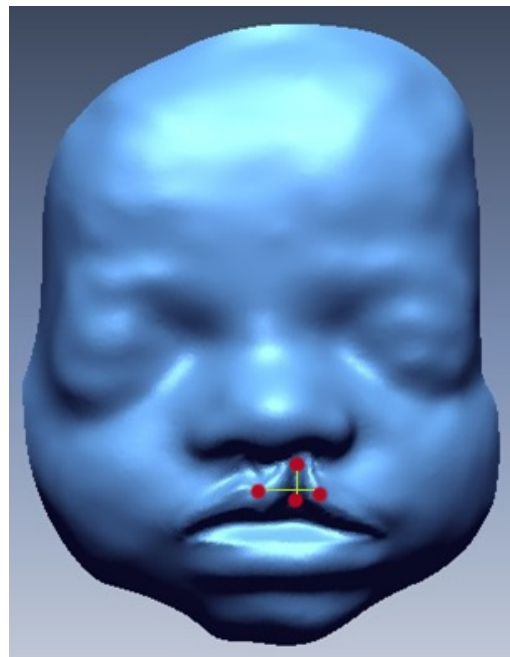
- 248 1. after deformity detection, identifies two regions in the neighbourhood of the  
249 cleft, one on the right side and one on the left side;
- 250 2. in each region, selects the points with  $D_y < 0$ ;
- 251 3. maximizes the principal curvature  $k_2$ .

252 The other two points are located in the gap of the lip. As said above, this area is  
253 characterized by high values of the Curvedness Index  $C$  and of coefficient  $e$ . To extract  
254 these points, firstly the algorithm localizes the centre of the cleft maximizing the  
255 coefficient  $e$ . Then, it analyzes the neighbourhood of this point, moving upwards from  
256 the centre to the high ending point and downwards till the low ending point. The  
257 algorithm, for each  $y$  value, maximizes the coefficient  $e$  in a neighbourhood of the cleft  
258 lip. The ending points are the first two maximums that are lower than a proper  
259 threshold value, established via experimentation.

260  
261  
262 MEASUREMENT OF THE DEFORMATION AND EXTRACTION OF THE UPPER LIP  
263 OUTLINE

264  
265 Transverse diameter of the cleft was evaluated by computing the Euclidean  
266 distance between the first two points extracted; its cranio-caudal length by computing  
267 the Euclidean distance between the last two points extracted. These two distances,  
268 represented in Figure 15, are the most adopted in the estimation of cleft size.

269

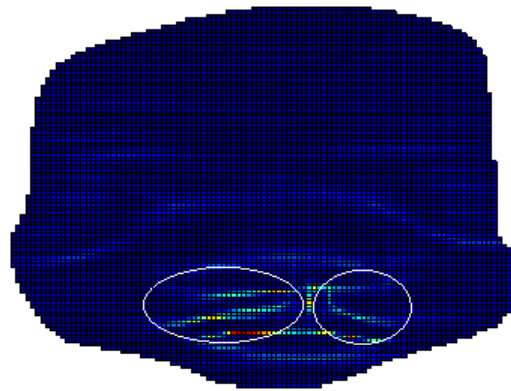


270  
271 **Figure 15.** The transverse (horizontal) and cranio-caudal length (vertical) of the cleft.  
272

273 The outline of the upper lip was also extracted, in order to provide an extra  
274 information about its shape. The Curvedness Index was adopted, as it is one of the  
275 geometrical descriptors that more accurately highlights upper lip surface behaviour. As  
276 shown in Figure 16, the Curvedness Index has a maximum behaviour in  
277 correspondence to the upper lip. To extract the outline, for each  $x$  value in the upper

278lip area, the Curvedness Index is maximized. This way, we obtain a sequence of  
279points, namely a line, in the 3D space that describes the upper lip area.  
280

281



**Figure 16.** The Curvedness Index. The two circles highlight the upper lip area.

282

283

284

285

## 286 EVALUATION OF FACE ASYMMETRY

287

288 Facial asymmetry was also evaluated in the cases of unilateral cleft lip. To  
289 perform this evaluation, the mean of the absolute value of the coefficient  $e$  was  
290 computed in both left and right parts of the mouth. By comparing these two mean  
291 values, we obtain an useful information about the asymmetry of the face. Coefficient  $e$   
292 is chosen and its absolute value is taken, as in correspondence of the cleft lip two  
293 minimums and a maximum are present (as it was previously shown in Figure 8); the  
294 absolute value will avoid that the minimum and maximum behaviour will annul each  
295 other when the mean area is computed.

296

297

298

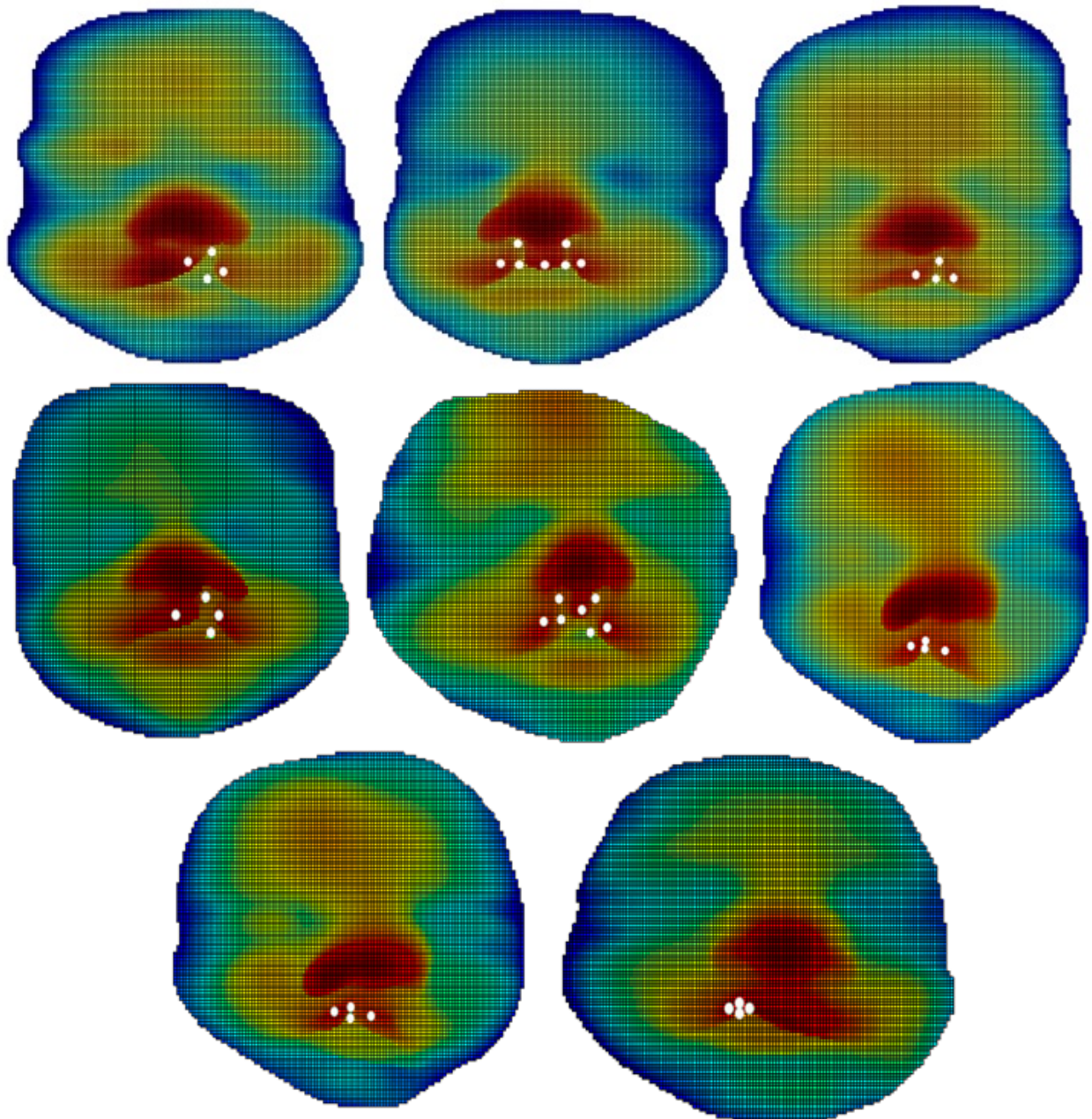
## 299 RESULTS AND DISCUSSION

300

301 The algorithm for the diagnosis of cleft lip was tested on the eighteen  
302 ultrasounds (eight with cleft lip and ten without). In all these cases, the algorithm  
303 correctly detected the presence/absence of the cleft and, in the two shells with  
304 bilateral cleft lip, the algorithm detected both the clefts.

305 In the eight ultrasounds with cleft lip, the four key points were localized. In  
306 Figure 17 the resulting four key points are shown for each shell.

307



**Figure 17.** The resulting four key points for each shell with cleft lip.

308  
 309  
 310  
 311 After having localized the four key points, transverse and the cranio-caudal length are  
 312 computed. In Table 2, the values of these distances for each shell are shown. The unit  
 313 of measurement is the millimetre. As can be seen, the shells that present the lowest  
 314 cranio-caudal length are the ones with an incomplete cleft.

315  
 316

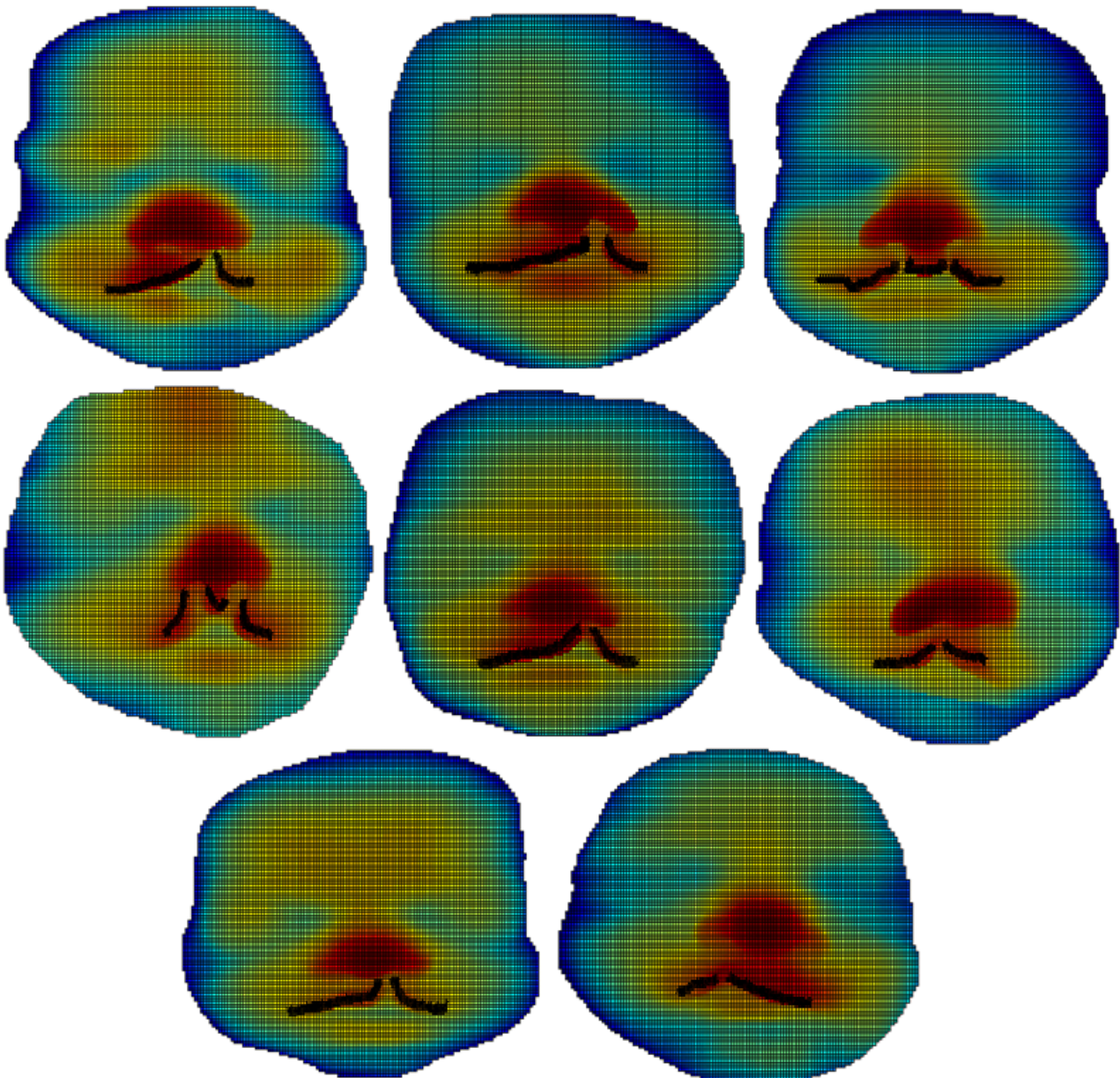
<b>A</b>	7.19	6.78
<b>B</b>	8.31	9.59
<b>C (left cleft)</b>	15.08	7.00
<b>C (right cleft)</b>	12.04	7.06
<b>D (left cleft)</b>	12.65	6.09
<b>D (right cleft)</b>	10.01	12.34

<b>E</b>	6.69	1.81
<b>F</b>	6.67	1.64
<b>G</b>	6.19	4.34
<b>H</b>	3.17	0.62

317 **Table 2.** Computed distances for each shell.

318 For each shell with cleft lip, upper lip outline was extracted. Results are shown in  
319 Figure 18.

320



321

322

323

**Figure 18.** The resulting upper lip outline for each shell with cleft lip.

324 We computed facial asymmetry in the six shells with unilateral cleft lip and on the ten  
325 shells without cleft lip; the evaluation was not performed on the two shells with  
326 bilateral cleft lip. The results are shown in Table 3 (shells with unilateral cleft lip) and 4  
327 (shells without cleft lip).

328

<b>A</b>	1.08	0.41	0.68
<b>B</b>	1.34	0.4	0.94
<b>E</b>	1.10	0.36	0.74
<b>F</b>	0.82	0.60	0.22
<b>G</b>	1.09	0.33	0.76
<b>H</b>	0.44	0.28	0.16

329 **Table 3.** Results of asymmetry evaluation for shells with unilateral cleft lip.

<b>Anto</b>	0.28	0.33	0.05
<b>Bart</b>	0.30	0.48	0.18
<b>Elena</b>	0.16	0.27	0.11
<b>Fede</b>	0.33	0.30	0.03
<b>Gian</b>	0.22	0.33	0.11
<b>Gio</b>	0.16	0.24	0.08
<b>Lisa</b>	0.36	0.21	0.14
<b>Paul</b>	0.17	0.22	0.05
<b>Pie</b>	0.15	0.20	0.05
<b>Simon</b>	0.18	0.25	0.07

330 **Table 4.** Results of asymmetry evaluation for shells without cleft lip.

331 As can be seen in Tables 3 and 4, the difference between the two sides of the  
332face is usually higher in the shells with cleft lip. The mean difference value is 0.58 mm  
333in shells with cleft lip instead it is 0.09 mm in shells without cleft lip, i.e. about six  
334times smaller. The shell with cleft lip with the lowest difference value is H, where an  
335incomplete cleft lip is present. Probably in this case the asymmetry was not high  
336because the cleft lip was not accentuated, as can be verified in Table 2, where the  
337shell H has the lowest cranio-caudal length. Also, the other shell with a low difference  
338value, namely shell E, presents an incomplete cleft lip. Instead, in the shells without  
339cleft lip the difference between the two face sides is usually low, with values ranging  
340between 0.05 and 0.18 millimetres. The highest values (Bart and Lisa) are probably  
341due to the quality of the ultrasound.

342

343

344

### 345 CONCLUSIONS

346

347 This work presents a new algorithm for diagnosing cleft lip on 3D ultrasound.  
348The proposed algorithm was developed with Matlab® and tested on eighteen fetuses'  
349faces (eight with cleft lip and ten healthy). The algorithm automatically states whether  
350the defect is present or not, classifies it (unilateral, bilateral, right, left), extracts four  
351key points, transverse and cranio-caudal length of the cleft, and upper lip outline, and  
352provides information on the facial asymmetry. The defect has been correctly  
353diagnosed and classified for all the fetuses.

354 Differential Geometry provided us with a set of descriptors leading this research  
355activity. The result is that these descriptors are suitable to describe facial shape and  
356curvedness, allowing an accurate extraction of the interested facial features.

357

31

32

358  
359  
360

## 361ACKNOWLEDGEMENT

362

363The authors declare that they have no conflicts of interest to disclose.

364

365

366

367

## 368REFERENCES

369

370 Bäumler M, Faure JM, Bigorre M, Bäumler-Patris C, Boulot P, Demattei C, Captier  
371G (2011). Accuracy of prenatal three-dimensional ultrasound in the diagnosis of cleft  
372hard palate when cleft lip is present. *Ultrasound Obstet Gynecol* 38:440-444.

373 Calignano F, Vezzetti E (2010). Soft tissue diagnosis in maxillofacial surgery: a  
374preliminary study on three-dimensional face geometrical features-based analysis.  
375*Aesthetic plastic surgery* 34(2):200-11.

376 Campbell S, Lees C, Moscoso G, Hall P (2005). Ultrasound antenatal diagnosis of  
377cleft palate by a new technique: the 3D 'reverse face' view. *Ultrasound Obstet Gynecol*  
37825:12-18.

379 Carlson DE (2000). Opinion — The ultrasound evaluation of cleft lip and  
380palate—a clear winner for 3D. *Ultrasound Obstet Gynecol* 16:299-301.

381 Demircioglu M, Kangesu L, Ismail A, Lake E, Hughes J, Wright S, Sommerlad BC  
382(2008). Increasing accuracy of antenatal ultrasound diagnosis of cleft lip with or  
383without cleft palate, in cases referred to the North Thames London Region. *Ultrasound*  
384*Obstet Gynecol* 31:647-51.

385 Gindes I, Weissmann-Brenner A, Zajicek M, Weisz B, Shrim A, Geffen KT, Mendes  
386D, Kuint J, Berkenstadt M, Achiron R (2013). Three-dimensional ultrasound  
387demonstration of the fetal palate in high-risk patients: the accuracy of prenatal  
388visualization. *Prenatal Diagnosis* 33:436-41.

389 Grandjean H, Larroque D, Levi S (1999). The performance of routine  
390ultrasonographic screening of pregnancies in the Eurofetus Study. *Am J Obstet*  
391*Gynecol* 181(2):446-54.

392 Hata T, Yonehara T, Aoki S, Manabe A, Hata K, Miyazaki K (1998). Three-  
393Dimensional Sonographic Visualization of the Fetal Face. *American Journal of*  
394*Roentgenology* 170(February):481-3.

395 Luck CA (1992). Value of routine ultrasound scanning at 19 weeks: a four year  
396study of 8849 deliveries. *BMJ* 304(6840):1474-8.

397 Johnson DD, Pretorius DH, Budorick NE, Jones MC, Lou KV, James GM, Nelson TR  
398(2000). Fetal Lip and Primary Palate: Three-dimensional versus Two-dimensional US.  
399*Radiology* 217(1):236-9.

400 Jones MC (1993). Facial clefting. Etiology and developmental pathogenesis. *Clin*  
401*Plast Surg* 20(4):599-606.

402 Lee W, Kirk JS, Shaheen KW, Romero R, Hodges AN, Comstock CH (2000). Fetal  
403cleft lip and palate detection by three-dimensional ultrasonography. *Ultrasound Obstet*  
404*Gynecol* 16:314-20.

405 Maarse W, Bergé SJ, Pistorius L, Van Barneveld T, Kon M, Breugem C, Mink van  
406der Molen AB (2010). Diagnostic accuracy of transabdominal ultrasound in detecting  
407prenatal cleft lip and palate: a systematic review. *Ultrasound Obstet Gynecol* 35:495-  
408502.

409 Mailáth-Pokorny M, Worda C, Krampfl-Bettelheim E, Watzinger F, Brugger PC,  
410 Prayers D (2010). What does magnetic resonance imaging add to the prenatal  
411 ultrasound diagnosis of facial clefts?. *Ultrasound Obstet Gynecol* 36:445-51.

412 Manganaro L, Tomei A, Fierro F, Di Maurizio M, Sollazzo P, Sergi ME, Vinci V,  
413 Bernardo S, Irimia D, Cascone P, Marini M (2011). Fetal MRI as a complement to US in  
414 the evaluation of cleft lip and palate. *Radiol med* 116:1134-48.

415 Martinez-Ten P, Adiego B, Illescas T, Bermejo C, Wong AE, Sepulveda W (2012).  
416 First-trimester diagnosis of cleft lip and palate using three-dimensional ultrasound.  
417 *Ultrasound Obstet Gynecol* 40:40-6.

418 Mittermayer C, Lee A (2003). Picture of the Month — Three-dimensional  
419 ultrasonographic imaging of cleft lip: the winners are the parents. *Ultrasound in*  
420 *Obstetrics and Gynecology* 21:628-9.

421 Offerdal K, Jebens N, Syvertsen T, Blaas HG, Johansen OJ, Eik-Nes SH (2008).  
422 Prenatal ultrasound detection of facial clefts: a prospective study of 49,314 deliveries  
423 in a non-selected population in Norway. *Ultrasound Obstet Gynecol* 31(6):639-46.

424 Platt LD, DeVore GR, Pretorius DH (2006). Improving Cleft Palate/Cleft Lip  
425 Antenatal Diagnosis by 3-Dimensional Sonography — The “Flipped Face” View. *J*  
426 *Ultrasound Med* 25:1423-30.

427 Pretorius DH, House M, Nelson TR, Hollenbach KA (1995). Evaluation of Normal  
428 and Abnormal Lips in Fetuses: Comparison Between Three- and Two-Dimensional  
429 Sonography. *American Journal of Roentgenology* 165(5):1233-7.

430 Riccabona M, Pretorius DH, Nelson TR, Johnson D, Budorick NE (1997). Three-  
431 Dimensional Ultrasound: Display Modalities in Obstetrics. *J Clin Ultrasound* 25(4):157-  
432 67.

433 Roelfsema NM, Hop WCJ, Van Adrichem LNA, Wladimiroff JW (2007). Craniofacial  
434 variability index determined by three-dimensional ultrasound in isolated vs. syndromal  
435 fetal cleft lip/palate. *Ultrasound Obstet Gynecol* 29:265-70.

436 Rotten D, Levallant JM (2004). Two- and three-dimensional sonographic  
437 assessment of the fetal face. 1. A systematic analysis of the normal face. *Ultrasound*  
438 *Obstet Gynecol* 23:224-31.

439 Sepulveda W, Wong AE, Martinez-Ten P, Perez-Pedregosa J (2010). Retronasal  
440 triangle: a sonographic landmark for the screening of cleft palate in the first trimester.  
441 *Ultrasound Obstet Gynecol* 35:7-13.

442 Tonni G, Lituania M (2012). OmniView Algorithm — A Novel 3-Dimensional  
443 Sonographic Technique in the Study of the Fetal Hard and Soft Palates. *J Ultrasound*  
444 *Med* 31:313-8.

445 Tonni G, Lituania M (2013). Arthrogryposis multiplex congenita-like syndrome  
446 associated with median cleft lip and palates: First prenatally detected case. *Congenital*  
447 *Anomalies* 53:13-40.

448 Vezzetti E, Marcolin F (2012). 3D human face description: landmarks measures  
449 and geometrical features. *Image and Vision Computing* 30(10):698-712.

450 Vezzetti E, Marcolin F (2012). Geometrical descriptors for human face  
451 morphological analysis and recognition. *Robotics and Autonomous Systems* 60(6):928-  
452 39.

453 Vezzetti E, Marcolin F (2012). Geometry-based 3D face morphology analysis:  
454 soft-tissue landmark formalization. *Multimedia Tools and Applications* 68(3):895-929.

455 Vezzetti E, Marcolin F (2014). 3D Landmarking in Multiexpression Face Analysis:  
456 A Preliminary Study on Eyebrows and Mouth. *Aesthetic Plastic Surgery* 38(4):796-811.

457 Vezzetti E, Calignano F, Moos S (2010). Computer-aided morphological analysis  
458for maxillo-facial diagnostic: a preliminary study. *Journal of Plastic, Reconstructive &*  
459*Aesthetic Surgery* 63(2):218-26.

460 Vezzetti E, Marcolin F, Fracastoro G (2014). 3D face recognition: An automatic  
461strategy based on geometrical descriptors and landmarks. *Robotics and Autonomous*  
462*Systems* 62(12):1768-76.

463 Vezzetti E, Marcolin F, Stola V (2013). 3D Human Face Soft Tissues Landmarking  
464Method: An Advanced Approach. *Computers in Industry* 64(9):1326-54.

465 Vezzetti E, Moos S, Marcolin F (2011). Three-Dimensional Human Face Analysis:  
466Soft Tissue Morphometry. *Proceedings of the InterSymp 2011*. Baden-Baden, Germany.

467 Vezzetti E, Moos S, Marcolin F, Stola V (2012). A pose-independent method for  
4683D face landmark formalization. *Computer Methods and Programs in Biomedicine*  
469198(3):1078-96.

470 Vezzetti E, Speranza D, Marcolin F, Fracastoro G (2014). Exploiting 3D  
471Ultrasound for Fetal Diagnosis Purpose through Facial Landmarking. *Image Analysis &*  
472*Stereology* 33(3):167-88.

473

474

475APPENDIX

476

477The First and Second Fundamental Forms are used to measure distance on surfaces  
478and are defined by

479

$$480 \quad Edu^2 + 2Fdudv + Gdv^2, \quad (1)$$

481

$$482 \quad ed u^2 + 2fdudv + gd v^2, \quad (2)$$

483

484respectively, where  $E, F, G, e, f$  and  $g$  are their Coefficients. Curvatures are used to  
485measure how a regular surface  $x$  bends in  $R^3$ . If  $D$  is the differential and  $N$  is the

486normal plane of a surface, then the determinant of  $DN$  is the product

487  $(-k_1)(-k_2) = k_1k_2$  of the Principal Curvatures, and the trace of  $DN$  is the negative

488  $-(k_1+k_2)$  of the sum of Principal Curvatures. In point  $P$ , the determinant of  $DN_P$  is

489the *Gaussian Curvature*  $K$  of  $x$  at  $P$ . The negative of half of the trace of  $DN$  is called the

490*Mean Curvature*  $H$  of  $x$  at  $P$ . In terms of the principal curvatures can be written

491

$$492 \quad K = k_1k_2, \quad (3)$$

493

$$494 \quad H = \frac{k_1+k_2}{2}.$$

$$495 \quad (4)$$

496

497Some definitions of these descriptors are given. These are the forms implemented in  
498the algorithm:

499  
500  $E=1+h_x^2$  , (5)

501  
502  $F=h_x h_y$  , (6)

503  
504  $G=1+h_y^2$  , (7)

505  
506  $e = \frac{h_{xx}}{\sqrt{1+h_x^2+h_y^2}}$  ,  
507 (8)

508  
509  $f = \frac{-h_{xy}}{\sqrt{1+h_x^2+h_y^2}}$  ,  
510 (9)

511  
512  $g = \frac{-h_{yy}}{\sqrt{1+h_x^2+h_y^2}}$  ,  
513 (10)

514  
515  $K = \frac{h_{xx} h_{yy} - h_{xy}^2}{(1+h_x^2+h_y^2)^2}$  ,  
516 (11)

517  
518  $H = \frac{(1+h_x^2)h_{yy} - 2h_x h_y h_{xy} + (1+h_y^2)h_{xx}}{(1+h_x^2+h_y^2)^{3/2}}$  ,  
519 (12)

520  
521  $k_1 = H + \sqrt{H^2 - K}$  ,  
522 (13)

523  
524  $k_2 = H - \sqrt{H^2 - K}$  ,  
525 (14)

526  
 527 where  $h$  is a differentiable function  $z=h(x,y)$ . It is, therefore, convenient to have at  
 528 hand formulas for the relevant concepts in this case. To obtain such formulas let us  
 529 parametrize the surface by

530  
 531  $x(u,v)=(u,v,h(u,v))$ ,  $(u,v) \in U$ ,  
 532 (15)

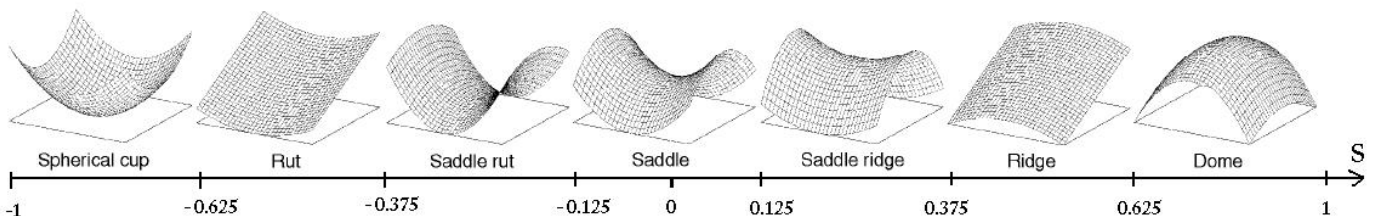
533  
 534 where  $u = x, v = y$ .

535  
 536 The most used descriptors are surely the Shape and Curvedness Indexes  $S$  and  $C$ ,  
 537 introduced by Koenderink *et al.*<sup>1</sup>:

538  
 539  $S = \frac{-2}{\pi} \arctan \frac{k_1+k_2}{k_1-k_2}$ ,  $S \in [-1,1]$ ,  $k_1 \geq k_2$ ,  
 540 (16)

541  
 542  $C = \sqrt{\frac{k_1^2+k_2^2}{2}}$ .  
 543 (17)

544  
 545 For the role they play in the work, a little digression about their significance is needed.  
 546 Their meaning is shown in Figures 19-21 and in Table 5.



547  
 548 **Figure 19.** Illustration of Shape Index scale divided into seven categories. Different  
 549 subintervals of its range  $[-1,1]$  correspond to seven geometric surfaces.

550

Class	S	Type	H	K
cup/pit	$[-1,-0.625)$	elliptical convex	+	+
rut/valley	$[-0.625,-0.375)$	cylindrical convex	+	0
saddle rut/saddle valley	$[-0.375,-0.125)$	hyperbolic convex	+	-
saddle	$[-0.125,0.125)$	hyperbolic symmetric	0	-
saddle ridge	$[0.125,0.375)$	hyperbolic concave	-	-
ridge	$[0.375,0.625)$	cylindrical concave	-	0
dome/peak	$[0.625,1)$	elliptical concave	-	+

**Table 5.** Topographic classes.

551  
 552

431 Koenderink, J.J. and van Doorn, A.J., 1992. Surface shape and curvature scales.  
 44 Image and Vision Computing 10(8), 557-564.

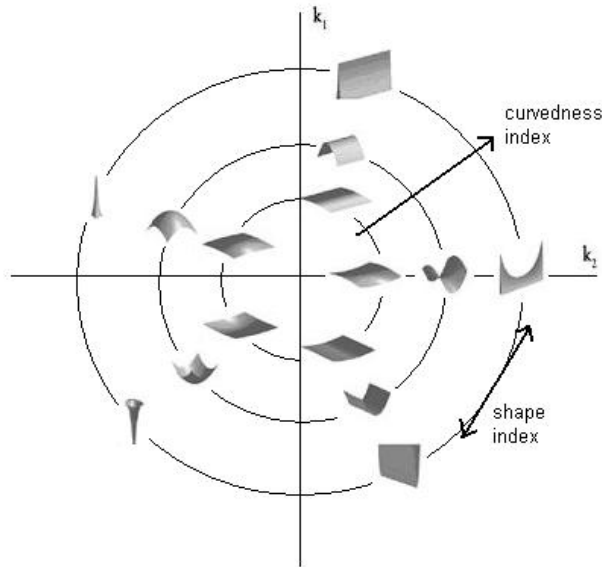


553

554

555

**Figure 20.** Curvedness Index scale, whose range is  $(-\infty, \infty)$ .



556

557

558

559

560

561

**Figure 21.** Indexes  $(S,C)$  are viewed as polar coordinates in the  $(k_1, k_2)$  -plane, with planar points mapped to the origin. The effects on surface structure from variations in the curvedness (radial coordinate) and Shape Index (angular coordinate) parameters of curvature, and the relation of these components to the principal curvatures ( $k_1$  and  $k_2$ ). The degree of curvature increases radially from the centre.