A 3D head model for 0-2-year-olds using statistical shape modelling as a tool for pediatric craniofacial surgery

Pam Heutinck^{1,4}, Paul Knoops¹, Naiara Rodriguez Florez², Benedetta Biffi³, William Breakey¹, Greg, James¹, Maarten Koudstaal⁴, Silvia Schievano^{1,3}, David Dunaway¹, Owase Jeelani¹, Alessandro Borghi¹

- 1. UCL GOS Institute of Child Health, London, UK; Great Ormond Street Hospital, London, UK
- 2. Universidad de Navarra, TECNUN Escuela de Ingenieros, San Sebastian, Spain
- 3. UCL Institute of Cardiovascular Science, London, UK
- 4. Erasmus MC Hospital, Rotterdam, the Netherlands

ORCID Dr Alessandro Borghi: HTTPS://ORCID.ORG/0000-0002-1514-1979

<u>SUMMARY</u>

The aim of this study is, firstly, to create a population-based 3D head shape model for the 0 to 2-year-old subjects to describe head shape variability within a normal population and, secondly, to test a combined normal and sagittal craniosynostosis (SAG) population model, able to provide surgical outcome assessment.

3D head shapes of patients affected by non-cranial related pathologies, and of SAG patients (pre- and post-op) were extracted either from head CTs or 3D stereophotography scans and processed. Statistical shape modelling (SSM) was used to describe shape variability using two models – a normal population model (MODEL1) and a combined normal and SAG population model (MODEL2). Head shape variability was described via principal components analysis

(PCA) which calculates shape modes describing specific shape features.

MODEL1 (n=65) mode 1 showed statistical correlation (p<0.001) with width (125.8±13.6mm), length (151.3±17.4mm) and height (112.5±11.1mm) whilst mode 2 showed correlation with cranial index (83.5mm±6.3mm, p<0.001). The remaining 9 modes showed more subtle head shape variability MODEL2 (n=159) revealed that post-operative head shape still did not achieve full shape normalization with either spring cranioplasty or total calvarial remodelling. This study proves that SSM has the potential to describe detailed anatomical variations in a

paediatric population

<u>Keywords</u>

Normal head shape, craniosynostosis, statistical shape modelling, spring assisted cranioplasty

INTRODUCTION

Sagittal craniosynostosis (SAG) is the most common type within the single suture cranial synostoses (*Massimi et al.*, 2012; *Cornelissen et al.*, 2016). The most common treatment for craniosynostosis is surgical correction which occurs early in life to prevent the aforementioned complications (*Morris*, 2016). Available surgical procedures include total calvarial remodeling (TCR), subtotal calvarial remodeling or less invasive procedures such as springs assisted cranioplasty (SAC) (*Rodgers et al.*, 2017; *Runyan et al.*, 2020). However, due to the complex anatomy of the skull and the lack of accurate objective normative 3D shape information, sometimes the optimal procedure is difficult to select and satisfactory head shape correction is not achieved.

Normative data of the head anthropometric measurements are available in the literature, which however relay on linear/angular distances and ratios (*Waitzman et al.*, 1992; *Delye et al.*, 2015; *Pindrik et al.*, 2016).

A new method to assess head shape is statistical shape modelling (SSM), that allows to perform statistics on complex 3D anatomical shapes extracted from 3D anatomical images and to describe morphological average and variations within a population (*Pennec*, 2009).

SSM was used by other groups in the past to create 3D morphable models of the face (Booth

et al., 2018; *Tanikawa et al.*, 2019) and head (*Staal et al.*, 2015; *Dai et al.*, 2017). These models describe variations in large populations of normal subjects with the aim of describing shape differences in the healthy population, reconstruct incomplete data by means of model regression and perform subject clustering in terms of genetic variations.

This study aimed to create a population-based 3D head shape model for the 0 to 2-year-old normal population to describe head shape variability within a normal population. Furthermore, we produced a second head shape model by combining the normal population with a SAG population, in order to test its capability to assess surgical procedures.

•

MATERIAL AND METHODS

Ethical approval was obtained for the use of patient image data for research purposes (UK REC 15/ LO/0386 - Research Ethics Committee approval - study n.14DS25). This is a retrospective cohort study.

Patient populations

The radiological imaging database of GOSH was reviewed: patients aged 0-2 years who had received head CT scans for non-craniofacial indications between 2014 and 2017 were recruited (NORM group); similarly, all patients treated in the Craniofacial Unit for scaphocephaly, aged 0-2, and with available scans (either volumetric CT or 3D surface scans)

were recruited (SAG group).

For the NORM group, head CT scans were first reviewed for normality. Each radiology report was assessed and normality was determined by using the following exclusion criteria: scans were excluded if the imaging report contained any notes about abnormal head shape, abnormal head size or any underlying conditions which could potentially affect the head shape such as hydrocephalus, vein of Galan malformation or intraventricular hemorrhage (*Rao et al.*, 2011; *Alvis-Miranda et al.*, 2013; *Kuruvilla*, 2014). Patients having local defects (e.g. dermoid cysts) were included if such defects did not affect the head shape, verified by the radiologic report.

For the SAG group, head scans of non-syndromic, single suture, sagittal synostosis patients were collected: head shape of patients who underwent cranial reshaping were retrieved from CTs as well as from 3D handheld surface scanner (as described by Rodriguez-Florez et al 2017a). SAG patients underwent either SAC or TCR: scans were relative to preoperative (PRE) or post-operative (POST) shapes. Table 1 shows a summary of the populations used for this study.

Data processing

To be able to use SSM the retrieved scans had to be converted to 3D surface meshes. Simpleware Scan IP (Synopsys Inc., Mountain View, America) was used to convert CT scan DICOM files into 3D surfaces. Artifacts were removed, and scans were exported in stereolithography (STL) format. 3D surface scans were exported using the same format. All STL models were similarly processed in Meshmixer (Autodesk Inc., Toronto, Canada) to isolate the region of interest for SSM: each 3D model was cut with a plane encompassing the nasion and the two tragions (figure 1, Tenhagen et al (*Tenhagen et al.*, 2016)), and afterwards aligned on this base plane using Rhinoceros (Robert McNeel & Associates, Seattle, WA, USA).

Data analysis

The following anthropometric measurements were retrieved on each processed 3D model and used for correlation with SSM result output: cranial height and cephalic length, width and index (CI).

To analyze the variability between the 3D surface meshes within one model SSM was carried out with DEFORMETRICA (www.deformetrica.org), a framework for statistical analysis of complex shapes extracted from 3D anatomical images able to determine the population average head shape (called template) and its corresponding variations (*Durrleman et al.*,

2014). Figure 1 shows an overview of the method.

Two different statistical models were created: first, a NORM model (MODEL 1) to assess the head shape variance for healthy children; second, a combined NORM + SAG model (MODEL 2) including PRE and POST scans in order to compare shape differences between normal and

sagittal craniosynostosis cases, but also to assess the effect of both types of surgeries, SAC and TCR.

Principal component analysis (PCA) which describes the shape variance around the template by extracting the deformations required to turn the template shape back to each individual shape (shape vectors)(*Pennec*, 2009), was performed on both models. Each individual model can thus be described by the mean shape and individual shape deformation vectors. Deformation vectors relative to similar feature of the head shape of each model were categorized as variation modes and thus stands for a particular feature in the variation within the population.

Variations between the mean template and the modes of variations were calculated using closest point distance (implemented in VMTK - The Vascular Modeling Toolkit, Bergamo, Italy and MATLAB, MathWorks, Natick, MA, USA) and visualized between -2.7SD (standard deviation) and +2.7SD in Paraview (Kit-ware, Clifton Park, NY, USA) (*Ahrens et al.*, 2005). Age

(0-3, 4-6, 7-12, 13-18 and 19-24 months old) and sex stratification were performed.

Statistical analysis

Mean values and standard deviations were calculated for all anthropometric measurements and for the PCA shape vectors in the normal population and the sagittal synostosis population. Wilcoxon-rank sum test was used to calculate the differences between the data of different age groups within the two different populations. Pearson's *r* correlation was used to assess the relationship between the variation modes and the anthropometric measurements in MODEL1 and MODEL2. Kruskal-Wallis test was employed to determine the differences between the PCA values of the different patient groups within MODEL2. Either t-test or Mann-Whitney test were used to assess difference between pairs of groups, with post-hoc Bonferroni correction. Conventional statistical analysis was performed in Matlab R2018a (MathWorks, Natick MA).

RESULTS

Model 1 (normal head shape model)

In total, 65 CT scans from 65 healthy head cases between 0 and 24 months old were included in the database (60% male subjects, table 2). Most common indications for CT were follow up

after trauma, suspected craniosynostosis or suspected abnormal intracranial appearances.

Mean values and standard deviations for head width, height, length and CI are reported in

Table 3. When stratifying the patients by gender, we found no significant difference for the anthropometric measurements between the two groups.

The 65 normal head CT scans were found suitable for statistic shape modelling to create an average model (template) of normal head shape. The template of the normal model is shown in figure 2A. 11 variation modes were calculated and accounted for 90% of population variability. As expected, mean anthropometric measurements of the NORM population showed good agreement (difference <0.45%) with the equivalent anthropometric measurements of the template (Table 3). Shape Mode 1, accounting for 67% of variability, correlated strongly with cranial width (r = 0.75, p<0.001, figure 3A), height (r = 0.84, p<0.001, figure 3B) and length (r = 0.84, p<0.001, figure 3C) as well as patient age (r = 0.76, p<0.001, figure 3D), indicating that Mode 1 mainly captures size. Shape Mode 2, accounting for 7% of variability, correlated with CI (r = -0.72, p<0.001, figure 3E). The remaining 9 modes (16% of variability) did not show significant correlations with the anthropometric measurements, but described subtler 3D local shape variations, currently not captured by conventional linear measurements. Color maps visualized the variation within the population for Mode 1 (figure 2B) and Mode 2 (figure 2C) between -2.7 SD and 2.7 SD. In figure 4 four patients from the normal population are depicted, having respectively minimum and maximum value of mode 1 and minimum and maximum value of mode 2. This highlights the clinical correlation between individual patient shape mode value and anatomical presentation: smaller to larger heads present with increasing values of mode 1; furthermore, patients with a more brachicephalic head shape present low values of mode 2 while patients with a more scaphocephalic head shape present high values of mode 2.

Model 2 (combined head shape model)

Ninety-four 3D head surface/CT scans of patients with sagittal synostosis were processed along with the NORM group in Deformetrica to create a combined SSM. 58 of these 94 patients underwent SAC (5). 54 scans were acquired pre-operatively (29 head CT scans, 25 3D surface scans), and 23 scans post-operatively (all 3D surface scans). Mean pre-operative age was 5.2 \pm 3.2 months, and post-operative 9.8 \pm 1.7 months. Sixteen patients underwent TCR (*Sharma et al.*, 2018). Thirteen scans were pre-operative and 4 post-operative. Mean age preoperatively was 16.6 \pm 4.9 months, and post-operatively 22.1 \pm 1.7 months. Pre and Postoperative cephalic width, length, height and CI are reported in Table 4. For Model 2, 159 scans were used in total, combining NORM and SAG cases (PRE and POST).

The first 10 shape modes represented 91% of the whole population variability. To show the clinical impact of using this method to analyze shape variation differences in an population we used mode 1 and 2 to assess differences between the 5 subgroups (NORM, SAC PRE, SAC POST, TCR PRE and TCR POST). Kruskal-Wallis test showed statistical difference among all MODEL 2 sub-groups (p<0.05) for modes 1 and 2. Mode 1, which was related to size, showed statistical difference between NORM and SAC POST (p<0.005) and NORM and TCR PRE (p<0.005) as well as between SAC PRE and SAC POST (p<0.005) and SAC PRE and TCR PRE (p<0.005). Mode 2 described variation in shape related to cranial index, highlighting statistical differences between NORM and SAC PRE, SAC POST, TCR PRE (p<0.005). SAC PRE was statistically different from SAC POST (p<0.005) and SAC POST was different from TCR PRE (p<0.005).

Principal component 2D plot (figure 5) showed clustering of the different groups (figure 6) with SAC POST and TCR POST approaching the normal population but remaining distinct.

DISCUSSION

This study describes a SSM methodology to assess and describe the anatomical and geometrical variations in a pediatric population, to an extent which cannot be captured using conventional bi-dimensional anthropometric measurements. This novel method provides an accurate 3D description the pediatric head, which can be used to assess head shape and help quantifying the effect of corrective surgery. The main innovation in this study is the use of SSM as a tool for modeling the average normal head shape in a 0-24 month old pediatric population.

In the past, SSM has been used to assess the shape of the aortic arch in relation to its function, to relate surgical parameters to outcome in head shape, for surgical planning by analyzing individual head shapes of craniosynostosis patients, for quantifying the effect of corrective surgery for trigonocephaly by illustrating the average effects of surgery and to plan midface defect reconstruction (*Mendoza et al.*, 2014; *Bruse et al.*, 2016; *Rodriguez-Florez et al.*, 2017a; *Rodriguez-Florez et al.*, 2017b; *Fuessinger et al.*, 2019). By translating such methodology to the description of the pediatric calvarium, we were able to show the benefits of SSM, i.e. the fact that both global and local variations are displayed simultaneously, in contrast to

anthropometric measurements, which only capture global head shape features. SSM also allows visual appreciation of the variation within a population. In MODEL1, 11 modes of variations described 90% of the variation of the population with Mode 1 and 2 accounting for 74% of inter-individual variability. Mode 3 to 11 did not show any significant correlation with the measurements but described more local features of the head shape. Such information can provide important directions and outcome measurements for the surgical treatment of patients affected by craniosynostosis.

In the present work, SSM was also used to assess the effect of surgical correction of nonsyndromic craniosynostosis by assessing the differences between the NORM and the SAG group. CI is clinically used to assess sagittal synostosis correction; however it does not describe more subtle and localized features such as frontal bossing, occipital bulleting, biparietal narrowing and a low posterior vertex (*Wilbrand et al.*, 2011). Mode 2 of the combined model showed significant differences between the NORM, SAC PRE, SAC POST and CTR PRE groups. Differences in Mode 2 show that shape is modified post-intervention but still not fully normalized. This is in accordance with other studies in the literature stating that sagittal craniosynostosis correction alters the head shape of the patients but does not always achieve full normalization (Liaw et al., 2019). A recent study used PCA to evaluate the use of spring for the treatment of sagittal synostosis by analyzing the variation of linear measurements in a SAC population (Satanin et al., 2019). TCR Post only counted four subjects hence no statistical difference was achieved, however visual inspection shows that Mode 2 values for TCR POST group are lower than NORM, hence showing this mode depicts differences in these two populations. The reason behind the small number of patients in this group was double: in GOSH TCR patients only receive CT scan postoperatively in case of complications; furthermore, most of the patients who underwent postoperative imaging were older than 2 year of age and were therefore excluded from the current study. Clustering shows improvement for both the SAG and TCR populations but no full overlap of these populations with the NORM group. Further research is necessary to specify the differences and to understand the specific limitations of the procedures to be able to improve them.

This study could be expanded to create a larger database of normal head shapes, which could be used as reference for surgery: CT imaging provides a good contrast between bone and soft tissue and constitute the ideal candidate for producing head shapes. Although small, our cohort well depicts the general pediatric population. The mean values of the normal anthropometric measurements taken on the NORM group showed good agreement (< 0.45% difference) with earlier published values of normal head shape (*Waitzman et al.*, 1992); similarly, the anthropometric measurements of the pre-operative sagittal synostosis patients were close to those reported in the literature for a similar population (<7% difference for SAC PRE, <2% difference for TCR PRE) (*Thomas et al.*, 2015). The difficulty in gathering a large pediatric population in the age range considered lies in the need of imaging, such as CT scans, which require exposure to ionizing radiation. Recent studies have shown that 3D stereophotography represents a promising method of collecting reproducible data relative to head shape and craniometrics as well as anthropometric measurements (*Pindrik et al.*, 2016).

CONCLUSION

Statistical shape modelling (SSM) is an innovative way to calculate subtle normal head shape data which cannot be captured with the current normal data available. By combining the normal 3D head model with affected 3D head scans pre-operative and post-operative differences can be assessed. Future developments will address the comparison of different techniques in view of maximizing aesthetic outcomes in the treatment of scaphocephaly.

ACKNOWLEDGEMENTS AND CONFLICT OF INTEREST STATEMENT

The work has been funded by Great Ormond Street Hospital for Children Charity (grant number 12SG15) as well as the NIHR British Research Council Advanced Therapies for Structural Malformations and Tissue Damage pump-prime funding call (grant n. 17DS18), the Engineering and Physical Sciences Research Council (EP/N02124X/1) and the European Research Council (ERC-2017-StG-757923). This report incorporates independent research from the National Institute for Health Research Biomedical Research Centre Funding Scheme. The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research or the Department of Health.

<u>Ethical approval</u>: Ethical approval was obtained for the use of patient image data for research purposes (UK REC 15/ LO/0386 - Research Ethics Committee approval - study n.14DS25).

Declaration of Interest: Mr Owase Jeelani acts as consultant for KLS Martin.

<u>Author Contributions</u>: All authors have made substantial contributions to the conception and design of the study and analysis and interpretation of data; all authors have contributed to drafting or revising the article and have provided final approval of the version submitted.

REFERENCES

Ahrens J, Geveci B, Law C: ParaView: An End-User Tool for Large Data Visualization. In: Hansen C, Johnson C (ed.), The Visualization Handbook. Amsterdam: Elservier, 717-731, 2005.

Alvis-Miranda HR, Milena Castellar-Leones S, Alcala-Cerra G, Rafael Moscote-Salazar L: Cerebral sinus venous thrombosis. J Neurosci Rural Pract 4:427-438, 2013.

Booth J, Roussos A, Ponniah A, Dunaway D, Zafeiriou S: Large Scale 3D Morphable Models. Int J of Comput Vis 126:233-254, 2018.

Bruse JL, McLeod K, Biglino G, Ntsinjana HN, Capelli C, Hsia TY, Sermesant M, Pennec X, Taylor AM, Schievano S: A statistical shape modelling framework to extract 3D shape biomarkers from medical imaging data: assessing arch morphology of repaired coarctation of the aorta. BMC Med Imaging 16:40, 2016.

Cornelissen M, Ottelander B, Rizopoulos D, van der Hulst R, Mink van der Molen A, van der Horst C, Delye H, van Veelen ML, Bonsel G, Mathijssen I: Increase of prevalence of craniosynostosis. J Craniomaxillofac Surg 44:1273-1279, 2016.

Dai H, Pears N, Smith W, Duncan C: A 3D Morphable Model of Craniofacial Shape and Texture Variation. Int J Comput Vis 128: 547-571, 2020.

Delye H, Clijmans T, Mommaerts MY, Sloten JV, Goffin J: Creating a normative database of agespecific 3D geometrical data, bone density, and bone thickness of the developing skull: a pilot study. J Neurosurg Pediatr 16:687-702, 2015.

Durrleman S, Prastawa M, Charon N, Korenberg JR, Joshi S, Gerig G, Trouve A: Morphometry of anatomical shape complexes with dense deformations and sparse parameters. Neuroimage 101:35-49, 2014.

Fuessinger MA, Schwarz S, Neubauer J, Cornelius CP, Gass M, Poxleitner P, Zimmerer R, Metzger MC, Schlager S: Virtual reconstruction of bilateral midfacial defects by using statistical shape modeling. J Craniomaxillofac Surg 47:1054-1059, 2019.

Kuruvilla LC: Benign enlargement of sub-arachnoid spaces in infancy. J Pediatr Neurosci 9:129-131, 2014.

Liaw WXZ, Parr WCH, Peltz TS, Varey A, Hunt J, Gianoutsos M, Marucci DD, Walsh W: Quantification of Head Shape and Cranioplasty Outcomes: Six-compartment Volume Method Applied to Sagittal Synostosis. Plast Reconstr Surg Glob Open 7:e2171, 2019.

Massimi L, Caldarelli M, Tamburrini G, Paternoster G, Di Rocco C: Isolated sagittal craniosynostosis: definition, classification, and surgical indications. Childs Nerv Syst 28:1311-1317, 2012.

Mendoza CS, Safdar N, Okada K, Myers E, Rogers GF, Linguraru MG: Personalized assessment of craniosynostosis via statistical shape modeling. Med Image Anal 18:635-646, 2014.

Morris LM: Nonsyndromic Craniosynostosis and Deformational Head Shape Disorders. Facial Plast Surg Clin North Am 24:517-530, 2016.

Pennec X: Statistical Computing on Manifolds: From Riemannian Geometry to Computational Anatomy. In: Nielsen F (ed.) Emerging Trends in Visual Computing ETVC 2008. Lecture Notes in Computer Science. Berlin, Heidelberg: Springer-Verlag, 347-386, 2009.

Pindrik J, Molenda J, Uribe-Cardenas R, Dorafshar AH, Ahn ES: Normative ranges of anthropometric cranial indices and metopic suture closure during infancy. J Neurosurg Pediatr 25:667-673, 2016. Rao V, N Mathuriya S: Pediatric aneurysms and vein of Galen malformations. J Pediatr Neurosci 6:S109-17, 2011.

Rodgers W, Glass GE, Schievano S, Borghi A, Rodriguez-Florez N, Tahim A, Angullia F, Breakey W, Knoops P, Tenhagen M, O'Hara J, Ponniah A, James G, Dunaway DJ, Jeelani NUO: Spring-Assisted Cranioplasty for the Correction of Nonsyndromic Scaphocephaly: A Quantitative Analysis of 100 Consecutive Cases. Plast Reconstr Surg 140:125-134, 2017.

Rodriguez-Florez N, Bruse JL, Borghi A, Vercruysse H, Ong J, James G, Pennec X, Dunaway DJ, Jeelani NUO, Schievano S: Statistical shape modelling to aid surgical planning: associations between surgical

parameters and head shapes following spring-assisted cranioplasty. Int J Comput Assist Radiol Surg 12:1739-1749, 2017b.

Rodriguez-Florez N, Goktekin OK, Bruse JL, Borghi A, Angullia F, Knoops PG, Tenhagen M, O'Hara JL, Koudstaal MJ, Schievano S, Jeelani NU, James G, Dunaway DJ: Quantifying the effect of corrective surgery for trigonocephaly: A non-invasive, non-ionizing method using three-dimensional handheld scanning and statistical shape modelling. J Craniomaxillofac Surg 45:387-394, 2017a.

Runyan CM, Gabrick KS, Park JG, Massary D, Hemal K, Owens ES, Thompson JT, 2nd, Couture D, David LR: Long-Term Outcomes of Spring-Assisted Surgery for Sagittal Craniosynostosis. Plast Reconstr Surg 146:833-841, 2020.

Satanin L, Teterin I, Evteev A, Sakharov A, Kölby L, Lemeneva N, Roginsky V: Introduction of springassisted cranioplasty for scaphocephaly in Russia: first cases evaluated using detailed craniometry and principal component analysis. J Plast Surg Hand Surg 53:173-179, 2019.

Sharma JD, O'Hara JL, Borghi A, Rodriguez-Florez N, Breakey W, Ong J, Jeelani NO, Dunaway DJ, James G: Results Following Adoption of a Modified Melbourne Technique of Total Scaphocephaly Correction. J Craniofac Surg 29:1117-1122, 2018.

Staal FC, Ponniah AJ, Angullia F, Ruff C, Koudstaal MJ, Dunaway D: Describing Crouzon and Pfeiffer syndrome based on principal component analysis. J Craniomaxillofac Surg 43:528-536, 2015.

Tanikawa C, Akcam MO, Takada K: Quantifying faces three-dimensionally in orthodontic practice. J Craniomaxillofac Surg 47:867-875, 2019.

Tenhagen M, Bruse JL, Rodriguez-Florez N, Angullia F, Borghi A, Koudstaal MJ, Schievano S, Jeelani O, Dunaway D: Three-Dimensional Handheld Scanning to Quantify Head-Shape Changes in Spring-Assisted Surgery for Sagittal Craniosynostosis. J Craniofac Surg 27:2117-2123, 2016.

Thomas GP, Johnson D, Byren JC, Jayamohan J, Magdum SA, Richards PG, Wall SA: Long-term morphological outcomes in nonsyndromic sagittal craniosynostosis: a comparison of 2 techniques. J Craniofac Surg 26:19-25, 2015.

Waitzman AA, Posnick JC, Armstrong DC, Pron GE: Craniofacial skeletal measurements based on computed tomography: Part II. Normal values and growth trends. Cleft Palate Craniofac J 29:118-128, 1992.

Wilbrand JF, Wilbrand M, Pons-Kuehnemann J, Blecher JC, Christophis P, Howaldt HP, Schaaf H: Value and reliability of anthropometric measurements of cranial deformity in early childhood. J Craniomaxillofac Surg 39:24-29, 2011.

				Age	Total scans
Patient group	Sub-group	Sex	Total	(months)	
				Mean (SD)	
NORM	-	Male	38	9.81 (6.88)	65
		Female	27		
SAG	SAC PRE	Male	46	5.22 (3.69)	54
		Female	8		
	SAC POST	Male	21	9.54 (1.34)	23
		Female	2		
	TCR PRE	Male	9	16.6 (4.93)	13
		Female	4		
	TCR POST	Male	4	22.1 (1.73)	4
		Female	-		

Table 1 Populations used for this study

Age	Female	Male	Total
(months)			
0-3	7	8	15
4-6	7	5	12
7-12	4	10	14
13-18	6	8	14
19-24	3	7	10

 Table 2 Patients numbers showing age and gender distribution of the normal patient database

Age (months)	Width (SD)	Length (SD)	Height (SD)	Cranial Index
				(%)
0-3	108.3 (11.5)	128.6 (14.9)	96.6 (11.1)	84.5 (5.6)
4-6	124.2 (8.7)	149.1 (7.8)	111.7 (8.0)	83.4 (6.0)
7-12	127.4 (10.4)	152.1 (10.4)	114.6 (4.6)	83.9 (6.8)
13-18	132.3 (5.1)	163.8 (10.6)	117.0 (3.6)	81.1 (6.8)
19-24	140.2 (6.9)	167.6 (7.7)	123.5 (4.9)	83.8 (6.4)
Overall population	125.8(13.6)	151.3(17.4)	112.5(11.1)	83.5(6.3)
Average				
Template computed	125.4	150.7	112.0	83.53
by SSM				

 Table 3 Mean values and standard deviations (SD) for normal anthropometric measurements

(mm)

	Mean Mean		Mean Height	Mean CI (%)
Patients	Width (SD)	Length (SD)	(SD)	(SD)
SAG PRE	116.2 (8.5)	164.6 (11.9)	104.1 (8.0)	70.8 (4.5)
SAG POST	129.8 (9.9)	177.3 (11.4)	119.8 (7.4)	73.3 (3.5)
TCR PRE	127.5 (4.9)	188.1 (9.3)	118.0 (3.6)	67.9 (3.7)
TCR POST	135.0 (9.3)	178.3 (4.8)	120.0 (7.9)	75.7 (4.0)

Table 4 Anthropometric mean measurements and standard deviation of the SAG PRE, SAG

POST, TCR PRE and TCR POST groups (mm).

FIGURE CAPTIONS

Figure 1 Statistical Shape Method (SSM) applied to the NORM population for the analysis of shape variations (MODEL 1): each patient head shape is retrieved through segmentation of CT or extraction of head shape from 3D scan ("Reconstruction"), it is similarly processed and fed into Deformetrica, which computes template ("SSM"); PCA is used to post-process the data ("Post-Processing") which is then visually ("Visual Results") analysed. Individual patient dimensions, morphometric indices and demographic information are correlated with shape vectors ("Numerical Results").

Figure 2: Visualization of the MODEL 1 average head template (A); visualization of the variation within the NORM population at -2.7 SD and 2.7 SD for Mode 1 (B) and Mode 2 (C)

Figure 3 A-D) Correlation between the principal components from Mode 1 with cranial width (A, r = 0.75, p<0.001), length (B, r = 0.84, p<0.001), height (C, r = 0.84, p<0.001) and age (D, r=0.76, p<0.001). E) Correlation between the principal components from Mode 2 with cranial

Index (r=-0,72, p<0.001). Black square show patients with maximum and minimum mode values, shown in figure 4.

Figure 4: Example of four patients from the normal population: on the top two rows, the patients having minimum and maximum values of mode 1 (highlighted with black squares in figure 3 A,B,C and D); on the bottom two rows, the patients having maximum and minimum values of mode 2 (highlighted with black squares in figure 3E);

Figure 5: Dot plots showing Mode 1 and Mode 2 shape vectors for the different populations. Statistical differences highlighted with * (p<0.005)

Figure 6 Plot of PCA Mode 1 and Mode 2 for the different populations analysed. The graphs shows clustering of the different groups.