“Management of sagittal craniosynostosis: morphological comparison of 8 surgical techniques”

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Management of sagittal craniosynostosis: morphological comparison of 8 surgical techniques

Abstract

The aim of this study was to carry out a retrospective multicenter study comparing the morphological outcome of 8 techniques used for the management of sagittal synostosis versus a large cohort of control patients. Computed tomography (CT) images were obtained from children CT-scanned for non-craniosynostosis related events (n=241) and SS patients at pre-operative and post-operative follow-up stages (n=101). No significant difference in morphological outcomes was observed between the techniques considered in this study. However, the majority of techniques showed a tendency for relapse. Further, the more invasive procedures at older ages seem to lead to larger intracranial volume compared to less invasive techniques at younger ages. This study can be a first step towards future multicenter studies, comparing surgical results and offering a possibility for objective benchmarking of outcomes between methods and centers.

Introduction

Sagittal synostosis (SS) is caused by premature fusion of the sagittal suture[1-3]. This condition leads to bi-temporal narrowing and anterio-posterior growth of the skull. Several techniques have been developed for the management of SS.[4-5] These include less invasive surgeries such as spring cranioplasty, usually performed before 6 months of age, to the more invasive approaches such as total vault remodelling, usually performed at the age of about 12 months.[2]

A number of studies have compared the outcomes of different techniques for the management of SS.[6-11] These studies have already highlighted some of the differences between the existing techniques. However, to the best of our knowledge, there is still a lack of multicentre studies comparing a range of approaches versus a strong dataset of normal calvarial growth. The aim of this study was to compare the morphological outcomes of 8 different techniques for the management of SS from 3 European centres against a data set of normal calvarial growth.

Methods

Patient data: Retrospective computed tomography (CT) images were obtained from normal children CT scanned for non-craniosynostosis related conditions (i.e. minor trauma without bone lesions and seizures - control group) from the Necker – Enfants Malades University Hospital in Paris (n=241, from birth to 48 months of age; study №2018RK18). CT data were also collected for SS patients at pre-operative and post-operative follow-up stages from 3 European centres: Necker–Enfants Malades University Hospital in Paris (n=67; 4 techniques; study №2018RK18); Prof. Dr. Stanislaw Popowski Regional Specialized Children's Hospital in Olsztyn (n=16; 2 techniques; study №148/K/16); and Sahlgrenska University Hospital in Gothenburg (n=18; 2 techniques; study №784-11). All data were anonymised and the ethical approvals were authorized by the corresponding institutions local ethical committee.

Surgical techniques: Paris techniques involved: 'H-craniectomy' (1) before and (2) after 6 months of age (H<6 & H>6) according to Renier[12] and corresponding to retro-coronal and pre-lambdoid craniotomies; a 4 cm sagittal strip of bone overlying the superior sagittal sinus, between the bregma and the lambda, was removed and two triangle osteotomies were performed behind the coronal sutures and in front of the lambdoid sutures; (3) the ‘modified H-craniectomy’ (Hm) corresponded to a similar technique with the additional removal of the coronal sutures; (4) total vault remodelling (performed in patients older than 6 months of age) involved a posterior tilt of the forehead with a resection of the inter-bregmatic-lambdoid band and the creation of parietal flaps; retro-lambdoid petalage was also performed (TVR1).

Olsztyn techniques involved: (1) total vault remodelling involving parietal craniotomies with the removal and shortening of the anterior part of the sagittal suture (TVR2); (2) endoscopic approach with parietal craniotomies and removal and shortening of the anterior part of the sagittal suture; this technique operated on children at 3-6 months of age.

Gothenburg techniques involved a midline sagittal craniotomy of the closed suture combined with either 2 or 3 springs that were placed to span the craniotomy. See Fig 1 for the schematic of all reconstructions.

Image processing: CT images were reconstructed in an image processing software (Avizo, Thermo Fisher Scientific, USA). Intracranial volume (ICV) was measured after manual segmentation. Anatomical landmarks were used to measure key morphological parameters. The skull length was determined between the glabella (the part of the forehead above and between the eyebrows) and the opisthocranion (most posterior point of the occipital bone). The skull width was determined between left and right euryons, corresponded to the extremity, on either side, of the greatest transverse diameter of the head. The skull length and width were used to compute the cephalic index (CI - i.e. (the skull width / the skull length) × 100). The skull circumference was measured using the glabella and opisthocranion.

Statistical analysis: Five linear models were first used to predict the skull length, width, circumference, CI and ICV as functions of age in the control group and for pre-operative SS. A quadratic term and an interaction parameter between the groups and age was used to describe the natural development of the skulls. The model coefficients were compared at 0 using Student tests.

Three linear hierarchical models were used to predict the CI, ICV and circumference as functions of age in the post-operative groups with different techniques in comparison to the control group. A quadratic term and an interaction parameter between each group and age were used. A hierarchical model was used to account for repeated measurements in a single patient and thus non-independent data. A random effect on the intercept was introduced for each individual.

The same approach as above was used to compare outcome measurements of different techniques This significance threshold was defined as $p < 0.05$; a significant parameter had an effect on the relevant variables for each model. Assumptions of normality and homoscedasticity of errors were tested. The statistical analyses were performed on *R 3.6.2*[13] using the *nlme*[14] and *ggplot*[15] packages. Note, the models used in this study estimated various trends. The approach is more robust at points/ages corresponding to actual data while at the points/ages that there were no actual data the predictions (regression curves) should be considered with caution.

Results

Cases: A detailed summary of all cases considered in this study and various measurements carried out is provided in Table 1. Here, the control data and post-operative data were classified under different age groups i.e. under 6 months of age (6M), between 6M and 2 years (Y), between 2Y-5Y and older than 5Y. For several patients, there were multiple follow-up CT images. The Gothenburg patients all had two follow-up CT scans at 6 months post-operation and at 36 months of age while the other two centres' performed post-operative CT scans only when clinically required. Detailed results of all regression analyses are included in the Appendix while the key findings are described here.

Controls: Analysis of the control data highlighted a significant difference between the ICV of the males and females. The males had a larger ICV than the females (+88.07±14.44; $p < 0.001$, Table

A1). This significant difference was due to the differences at 2-5 years of age (1210 ±114.9 vs. 1311±128.3) as the ICV was similar between the two groups (males and females) under 6 months of age (Table 1). However, there was no significant difference between the CI of males and females (p=0.254, Table A1). Also, there seems to be a gradual decrease in the CI from birth to about 4 years of age (p=0.003, Table A1).

Cases vs. controls, pre-operative: The comparison between the pre-operative data and the control data highlighted the typical morphological features of a SS patient e.g. a lower cephalic index (p<0.001 – Fig 2A-C). ICV of all the pre-operative SS were higher than the control data (Table 1). For example, ICV of H<6 (n=21; mix of both male and female) before surgery was 772.4±111.8 (ml), while for the control data (n=54; mix of both male and female), it was 670±151.9 (ml), without statistical age difference between groups (102.4±37.4 vs. 87.2±56.9).

Cases vs. control, post-operative: All surgical techniques improved the calvarial morphology and CI of the SS patients. The endoscopic technique had the highest CI increase from 70.6±4.1 to 79.9±3.2 (by 13% in n=4 - Table 1). However, the comparison between the post-operative data of all considered techniques and the control data highlighted that none of the considered techniques could fully normalise the calvarial morphology. The CI of all techniques was significantly lower than the control data with the exception of the endoscopic technique (perhaps due to the lower number of cases - Fig 3). However, there was not a clear difference between the post-operative ICV measurements from different techniques and the control data (Fig 4). The ICV of control data between 2-5Y of age (n=74 mix of male and female) was 1273.1±132.1 (ml) while ICV of H<6 (n=4), 2 & 3 spring cranioplasty (n=10 & n=8) for the similar age range were 1339.6±177.1 (ml), 1245±166.9 (ml) and 1239±133.8 (ml), respectively (none were significant even considering age and sex match – Table 1).

Comparing the outcomes of different techniques, there was almost no significant difference between them in terms of CI, skull circumference and ICV (Fig A2-A3). The exceptions were: (1) a higher CI (+3.667±1.730, p=0.043) and skull circumference (+71.24 ±14.40, p<0.001) in 2 springs patients compared to H patients at the early post-operative period (< 6 months) but no differences for older children (p=0.058 and p=0.061 respectively) ; (2) a higher skull circumference (+75.25 +/- 19.03, p=0.001) in 3 springs patients compared to H patients at the early post-operative period (< 6 months) but no differences for older children (p=0.381) ; (3) a lower augmentation of the ICV over age compared to the H group in the 2 & 3 springs groups (respectively -5.127±1.287, p=0.001 and -5.882±1.153, p<0.001).

Nonetheless, two observations are worth highlighting:

(1) No difference was observed in the CI of H techniques before and after 6 months of age and the modified H techniques. Comparing TVR1 and TVR2, the latter had a higher CI and ICV (Fig A2&A3). There was also no difference between the 2 and 3 spring cranioplasty in terms of all measured parameters in this study. Also, follow-up showed that the CI of spring cranioplasty was not as stable as other techniques on the long term.

(2) The more invasive treatments at older ages seem to have led to a larger ICV compare to the less invasive techniques at a younger age, in 2-5 years follow up. For example, ICV of H>6 (n=6), TVR1 (n=7) and TVR2 (n=8) at 2-5 years follow up were 1366.5±176.5, 1437.4±119 and 1421.6±117.8 respectively; and ICV of H<6 (n=4), 2 and 3 spring cranioplasty (n=10 and n=8) at the same age range had smaller values: 1339.6±177.1, 1245±166.9 and 1239±133.8 respectively (Table 1).

Discussion

The comparison of the pre- and post-operative data within each technique is indeed reassuring that all techniques improved the pre-operative aesthetic morphology of the SS skull. There was no significant difference in the post-operative CI and ICV in all the techniques considered in this study. The main take-home message of this study, given its limitations, is that no technique has obvious superior morphological results: craniofacial teams should consider using the technique that they are more familiar with. But there seems to be good evidence that more invasive techniques have higher blood loss and associated surgical costs than the less invasive techniques.[11]

This aside two key patterns emerged from this study: First, different techniques seem to have different levels of relapse pending on the age at surgery and on the type of craniotomies. Data presented here suggest that spring cranioplasty has the highest level of relapse, about 4%. This is based on comparing the CI between the 6M-2Y vs. 2Y-5Y data (Table 1). This was similar to the recent findings of van Veelen et al.[16]. The fact that H<6 does not show the same level of relapse suggest that the inherent differences between the two procedures are perhaps the key contributing factor. The two considered TVR approaches also showed a relapse, about 2% drop in CI in 2Y-5Y follow ups. This was not significant but a similar pattern to other TVR studies.[7,9] It is interesting to note that even in the control group there was about a 1.5% drop in CI from 6M-2Y to 2Y-5Y.

Second, the observation that more invasive procedures at older ages seem to lead to a larger ICV in long term follow-ups compared to less invasive techniques at younger ages require further investigation. This seems to be consistent with the study of van Veelen et al.[9] who found that total calvarial remodelling patients (n=36 - operated at an average age of 11.6M) had higher ICV in compare to those who had extended strip craniotomy (n=59 - operated at 4.4M). However, Fischer et al.[10] did not find a significant difference in the post-operative follow-ups between the ICV of Π-plasty (n=39 – operated after 6M of age) and spring cranioplasty (n=64 – operated before 6M of age). It is interesting that based on the data presented here one can also say that open/invasive techniques are leading to higher ICV even comparing to the control group. However, from a biomechanical point of view, a more extensive technique perhaps releases constraints on the growing brain more efficiently than a less extensive technique such as endoscopic craniectomies.[17]

There is a large body of ongoing research to understand the possible neurodevelopmental differences between different techniques related to ICV values.[18-21] It is known that raised ICP and mental impairment are linked but raised ICP and cognitive impairment are both rare in SS.[22,23] An early surgery (<1year of age) has been suggested to lead to a better prognosis for mental and cognitive development in patients with SS.[22,23] While some studies suggest that neurodevelopment in non-syndromic craniosynostosis could be under genetic control[24] functional brain imaging data[26] and biomechanical models[27-29] could contribute to advance our understanding of the interplay between calvarial reconstruction, ICV and brain development.[29]

The key limitations of this study are: (1) while over 370 CT scans were analysed in this study, the number of cases per technique could be increased; in the endoscopic group, there were only four cases but we decided to include these cases for future studies to build on our findings; (2) the control group originated from only one of the included centres and hence the representativity can be an issue; (3) complications[30] were not described here; such data is important to fully illustrate the dis/advantages of different techniques and (4) the routine for capturing follow-up CT varied between centres. The follow-up CT could be performed in all cases or only when needed for a particular reason and that could affect the result.

In summary, no significant difference in morphological outcomes was observed between the techniques considered in this study. However, the majority of techniques showed a tendency for relapse for CI and ICV. Further, the more invasive procedures at older ages seem to lead to larger ICV compared to less invasive techniques at younger ages. The outcomes must be interpreted with caution. Instead, the principal value of the present study lies in the unique collaboration between several centers and in the large control dataset.

Acknowledgments

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Figures and table captions

Table 1: Summary of cases and data analysed in this study. Note: CT=computed tomography; NA= not applicable; M=month; Y=year.

Fig 1: Illustrations of the difference reconstructions from their respective groups. Showing areas of defects (Black), cranial bone (Yellow) and placement of springs (Grey).

Fig 2: Comparing pre-operative sagittal synostosis cases (red) versus normal skulls (blue) in terms of cephalic index, skull circumference and intracranial volume. Note at the points/ages that there were no actual data the predictions (regression curves) should be considered with caution.

Fig 3: Comparing post-operative cephalic indexes versus normal skulls.

Fig 4: Comparing post-operative intracranial volumes versus normal skulls.

Fig 1

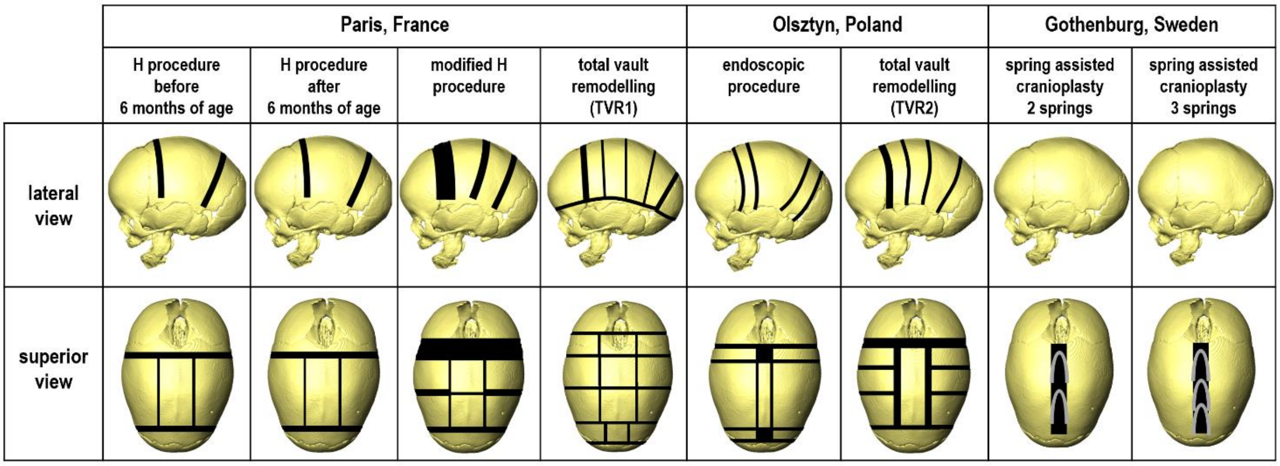

Paris, France
Olsztyn, Poland
Gothenburg, Sweden
H procedure before 6 months of age
H procedure after 6 months of age
modified H procedure
total vault remodelling (TVR1)
endoscopic procedure
total vault remodelling (TVR2)
spring assisted cranioplasty 2 springs
spring assisted cranioplasty 3 springs
lateral view
superior view

Fig 2

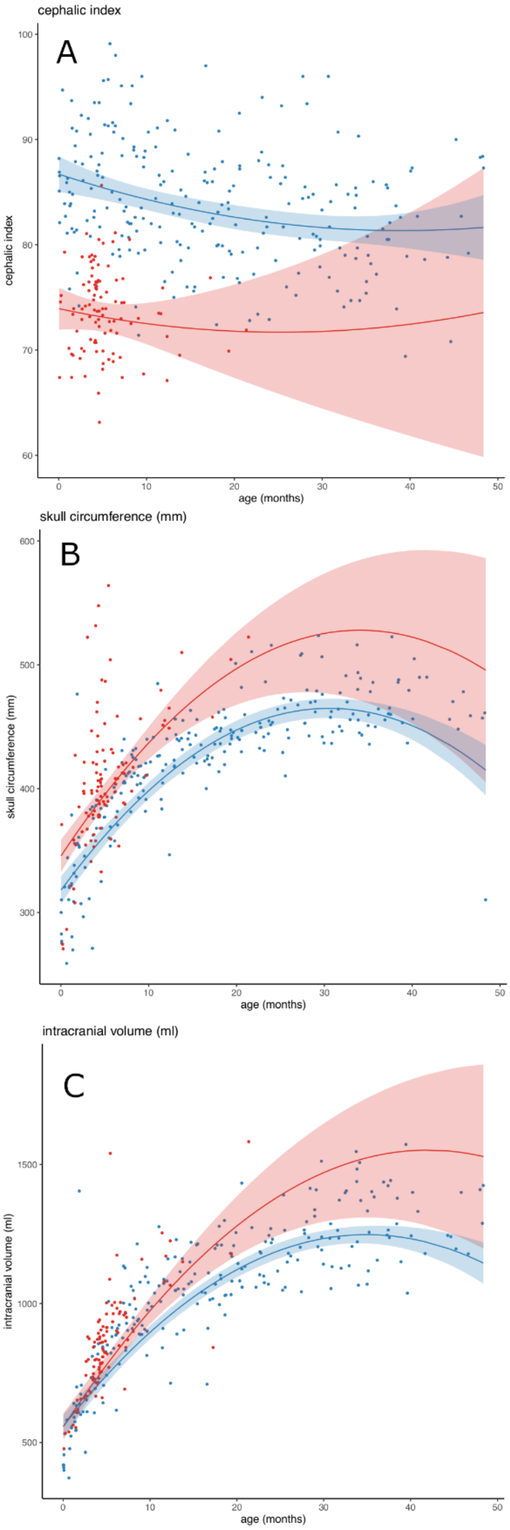
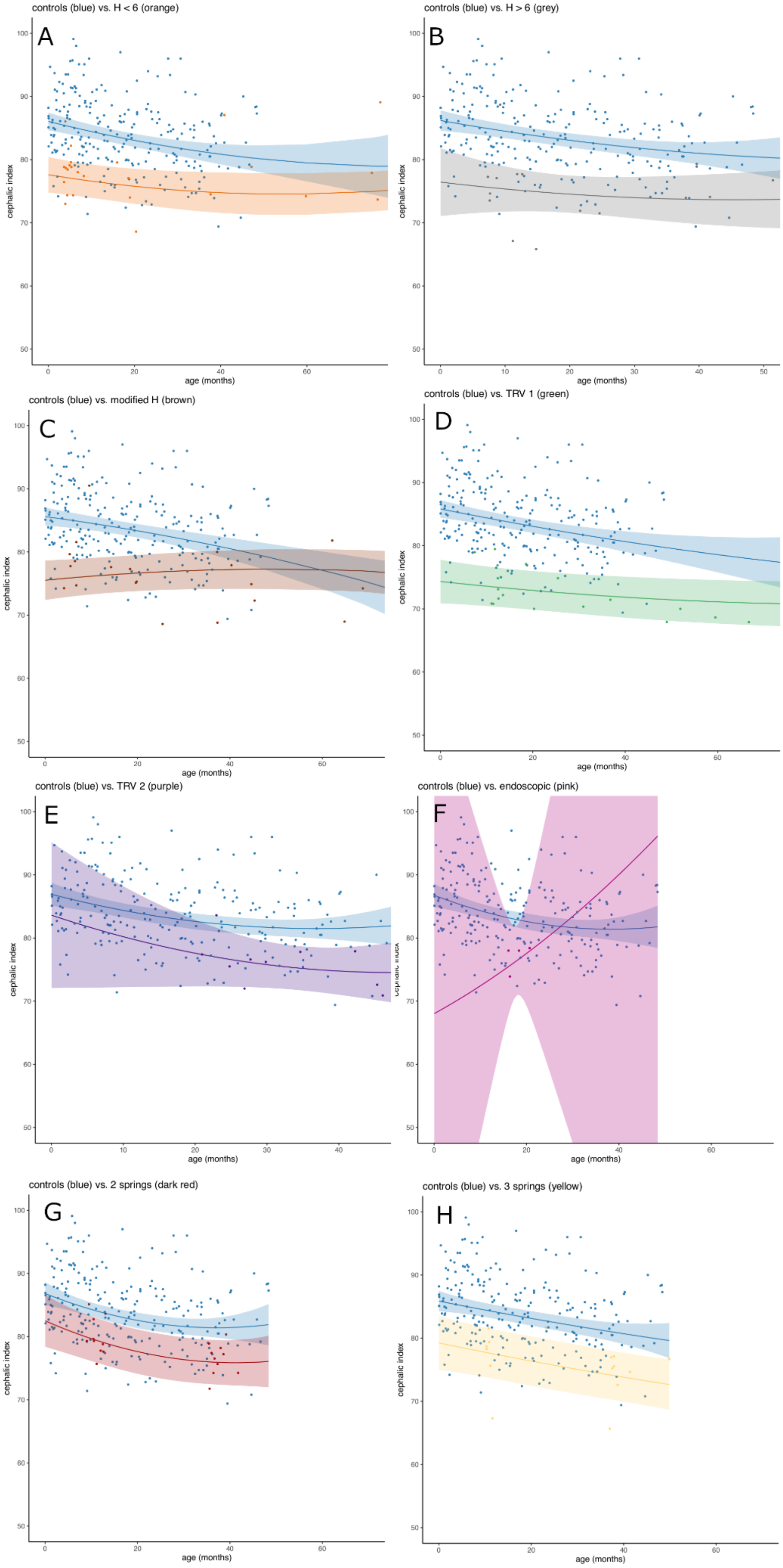

cephalic index
A
cephalic index
100
90
80
70
60
0
10
20
30
40
50
age (months)
skull circumference (mm)
B
skull circumference (mm)
600
500
400
300
0
10
20
30
40
50
age (months)
intracranial volume (ml)
C
intracranial volume (ml)
1500
1000
500
0
10
20
30
40
50
age (months)

Fig 3



controls (blue) vs. H < 6 (orange)

controls (blue) vs. H > 6 (grey)

controls (blue) vs. modified H (brown)

controls (blue) vs. TRV 1 (green)

controls (blue) vs. TRV 2 (purple)

controls (blue) vs. endoscopic (pink)

controls (blue) vs. 2 springs (dark red)

controls (blue) vs. 3 springs (yellow)

Fig 4

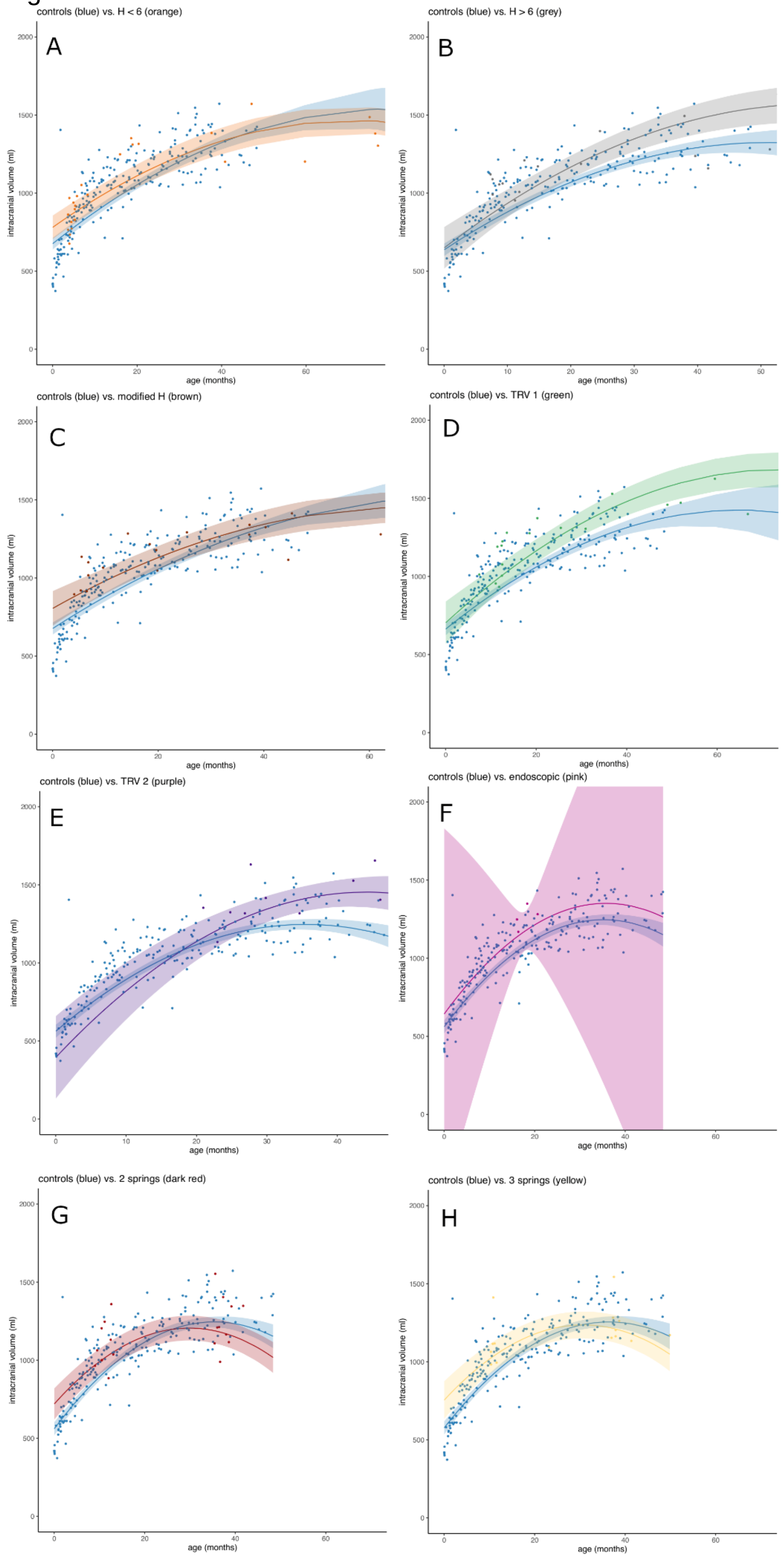

controls (blue) vs. H < 6 (orange)
A
controls (blue) vs. H > 6 (grey)
B
controls (blue) vs. modified H (brown)
C
controls (blue) vs. TRV 1 (green)
D
controls (blue) vs. TRV 2 (purple)
E
controls (blue) vs. endoscopic (pink)
F
controls (blue) vs. 2 springs (dark red)
G
controls (blue) vs. 3 springs (yellow)
H
intracranial volume (ml)
2000
1500
1000
500
0
age (months)
0
10
20
30
40
50
60

Table 1: Summary of cases and data analysed in this study. Note: CT=computed tomography; NA= not applicable; M=month; Y=year.

control	number of CT	age range	mean age (days)	mean length (mm)	mean width (mm)	mean cephalic index	mean circumference (mm)	mean intracranial volume (ml)
	27 (female)	<6M	93.3±57	124.1±9.9	107±9.9	86.3±5.7	344.9±35.3	670.5±142.6
	52(female)	6M-2Y	460.8±158.8	148.6±9.8	123.1±7.1	83.1±5.7	428±29.1	1027.9±135.7
	28(female)	2Y-5Y	973.1±167.7	159.7±6	130.6±4.9	81.9±3.9	454.9±18.3	1210.6±114.9
	0	>5Y	NA	NA	NA	NA	NA	NA
	27 (male)	<6M	81±57.2	122.5±10.3	106.9±11.9	87.1±5.2	342.9±44.2	669.5±163.3
	61 (male)	6M-2Y	400.9±156.4	149.4±8.5	125.6±6.2	84.2±5.4	433.7±23.2	1094±115.7
	46 (male)	2Y-5Y	1021.7±180.7	164.4±6.9	135.3±7.9	82.5±6.3	473.8±21.7	1311.2±128.3
	0	>5Y	NA	NA	NA	NA	NA	NA
H<6								
	21 (18 males)	pre	102.4±37.4	140.6±8.3	104.2±6.8	74.2±2.8	375.7±35.3	772.4±111.8
	12	<6 M	137.3±21.7	141.3±7.5	110.5±4.1	78.3±3.6	392.8±24	846.6±97.5
	6	6M-2Y	444.8±174.9	160.6±10.3	121.4±5.6	75.8±4	458.6±36.8	1211.1±152.6
	4	2Y-5Y	1389.8±293	171.7±10.5	134.8±4.4	78.7±6	473.5±15.9	1339.6±177.1
	6	>5Y	2785.7±671.4	174.3±7.1	136.2±5.3	78.4±5.7	490.2±17.8	1421.5±68.3
H>6								
	14 (11 males)	pre	194.1±75.2	149.8±9.5	110.4±6.9	73.9±4.9	399.6±32.7	928.1±127.3
	NA	<6 M	NA	NA	NA	NA	NA	NA
	10	6M-2Y	338.1±131.9	157.5±6.5	118.3±7.9	75.1±6.4	446.9±42.6	1084.4±87.1
	6	2Y-5Y	1239.5±307.2	171.4±8.5	129.6±7.9	75.6±3	488.1±20.2	1366.5±176.5
	1	>5Y	2995	191.7	142.7	74.4	528.5	1574.2
H modified								
	17 (13 males)	pre	105.1±66.7	139.5±11.3	102.1±9.6	73.3±5.1	369.1±45.7	761.6±188.6
	3	<6 M	149.3±22.9	145.5±5.6	112.6±5.2	77.2±2.7	395.7±36.2	983.9±132.2
	8	6M-2Y	381.4±180.3	154.4±8.4	121.4±5	78.8±5.2	446.6±18.2	1103.4±118.8
	6	2Y-5Y	1151.3±216.9	169.5±7.9	124.7±3.6	73.8±4.7	495.1±21.7	1294.4±99.3
	6	>5Y	2509±615.6	176.8±6.6	133.5±7.5	75.5±5	492.8±27	1439.1±130.8
TVR1								
	15 (13 males)	pre	325.4±284.8	156.9±12.2	113±8.3	72.1±3.3	427.9±47.3	1016.1±212.9
	NA	<6 M	NA	NA	NA	NA	NA	NA
	11	6M-2Y	392.5±105.4	163.1±9.2	121.4±4.9	74.2±3.4	462±35.4	1138.5±148.7
	7	2Y-5Y	1309.3±378.9	183.7±12.5	131.8±6.5	71.9±4.3	505.2±59.9	1437.4±119
	5	>5Y	2500.8±534.2	186.2±9.2	135.3±5.2	72.8±4.6	533.8±59.5	1615.7±280.9
TVR2								
	12 (11 males)	pre	278.8±270.2	154.3±14	113.5±11.7	73.6±3.6	448.8±57.6	1019.9±257.1
	NA	<6 M	NA	NA	NA	NA	NA	NA
	3	6M-2Y	580.3±76.6	163.8±1.7	125.4±5.1	76.6±2.4	460±24.3	1268.1±92.5
	8	2Y-5Y	1130.1±299.2	177.7±6.8	132.8±5.2	74.8±2.7	524.7±44.8	1421.6±117.8
	1	>5Y	1919	179.4	140.8	78.5	508.0	1393.7
endo								
	4 (4 males)	pre	115±58.9	146.3±15.4	103±8.3	70.6±4.1	392.6±29.8	840.5±244.7
	NA	<6 M	NA	NA	NA	NA	NA	NA
	3	6M-2Y	574.3±105	159.7±4.6	127.5±1.5	79.9±3.2	446±14.5	1244±107.9
	1	2Y-5Y	831	179.6	137.6	76.6	485	1629.9
	NA	>5Y	NA	NA	NA	NA	NA	NA
2 springs								
	10 (8 males)	pre	139.5±40.5	148.5±6.1	114.3±5.7	76.9±2.7	455.3±68	800.9±102.1
	NA	<6 M	NA	NA	NA	NA	NA	NA

	10	6M-2Y	334.4±41.1	162.6±8	129.9±5.1	80±3	480.7±28.3	1089.2±145
	10	2Y-5Y	1131.3±63.9	176.9±9.3	135.1±5.4	76.4±2.5	512.5±35.5	1245±166.9
	NA	>5Y	NA	NA	NA	NA	NA	NA
3 springs								
	8 (4 males)	pre	129.3±23.1	150.5±9.9	111.5±5.6	74.3±4	457.2±27	800.8±88.6
	NA	<6 M	NA	NA	NA	NA	NA	NA
	8	6M-2Y	324.8±13.2	163.8±7.7	128.3±6.5	78.5±5.3	492.5±21.2	1098.7±137
	8	2Y-5Y	1149.1±41.9	178.8±8	132.7±6.4	74.3±3.8	523.2±37	1239.0±133.8
	NA	>5Y	NA	NA	NA	NA	NA	NA

Appendix

Table A1. Regression analysis of the data presented in Fig 2. The intercept corresponds to the mean value of the reference class i.e. control females at “age zero”. For example, the mean skull length for the males with sagittal synostosis at 2 months of age was: 116.9 + 3.227 + 12.94 + 2 x 2.603 + 2 x (0.429 x 1) = 139.1 mm. Note, the penultimate term of the aforementioned equation refers to the fact that it is necessary to multiply 2.603 by 2 because it is the coefficient, to be multiplied by the age in months i.e. 2. Then the last term of the aforementioned equation is an interaction term i.e. it would be necessary to add “(2 months) x 1 (SS = yes) = 2 x (0.429 x 1)” in the previous calculation. The calculation of SD is not as easy, but it could be done in the same way with the limits of the 95% confidence interval (mean +/- 2 x SD). The male parameter was significant (p<0.001), as well as the sagittal synostosis (p<0.001) and age at the CT scan (p<0.001) parameters. However, the growth over age was not significantly different from the sagittal synostosis group (p=0.067).

	Value	SD	p
Skull length			
Intercept	116.9	1.316	
Male	3.227	0.917	**< 0.001**
Sagittal synostosis	12.94	1.774	**< 0.001**
Age at CT scan	2.603	0.139	**< 0.001**
Age at CT scan x Sagittal synostosis	0.429	0.234	0.067
Skull width			
Intercept	101.8	1.218	
Male	3.690	0.848	**< 0.001**
Sagittal synostosis	-6.158	1.640	**< 0.001**
Age at CT scan	1.793	0.128	**< 0.001**
Age at CT scan x Sagittal synostosis	0.224	0.216	0.301
Cephalic index			
Intercept	86.71	0.862	
Male	0.686	0.600	0.254
Sagittal synostosis	-12.78	1.161	**< 0.001**
Age at CT scan	-0.275	0.091	**0.003**
Age at CT scan x Sagittal synostosis	0.097	0.153	0.526
Skull circumference			
Intercept	317.8	5.678	
Male	14.37	3.953	**< 0.001**
Sagittal synostosis	27.58	7.649	**< 0.001**
Age at CT scan	9.622	0.598	**< 0.001**
Age at CT scan x Sagittal synostosis	1.099	1.008	0.276
Intracranial volume			
Intercept	557.9	20.74	
Male	88.07	14.44	**< 0.001**

Sagittal synostosis	-1.834	27.93	0.948
Age at CT scan	39.49	2.185	**< 0.001**
Age at CT scan x Sagittal synostosis	7.954	3.681	**0.031**

Table A2. Regression analysis of the data presented in Fig 3, 4 and A1. The reference classes were female controls. For example, the H group had a lower CI than controls (-8.441 ± 1.425, p<0.001) and there were no differences over age between the two groups (p=0.262).

	Value	SD	p
Cephalic index			
H < 6	-8.441	1.425	**< 0.001**
H < 6 x Age at CT	0.059	0.045	0.262
H > 6	-9.758	2.512	**< 0.001**
H > 6 x Age at CT	0.061	0.096	0.521
Modified H	-10.08	1.588	**< 0.001**
Modified H x Age at CT	0.169	0.040	**0.025**
TVR1	-11.49	1.728	**< 0.001**
TVR1 x Age at CT	0.067	0.043	0.193
TVR2	-3.300	5.591	0.556
TVR2 x Age at CT	-0.087	0.160	0.588
endoscopic	-18.75	26.85	0.486
endoscopic x Age at CT	0.685	1.493	0.647
2 springs	-4.317	1.924	**0.026**
2 springs x Age at CT	-0.031	0.040	0.466
3 springs	-6.617	2.105	**0.002**
3 springs x Age at CT	-0.007	0.037	0.861
Skull circumference			
H < 6	28.06	8.764	**0.002**
H < 6 x Age at CT	-0.487	0.258	0.132
H > 6	12.35	62.18	0.843
H > 6 x Age at CT	4.271	2.369	0.073
Modified H	10.33	13.31	0.438
Modified H x Age at CT	0.652	0.476	0.264
TVR1	12.51	15.70	0.426
TVR1 x Age at CT	1.212	0.553	0.093
TVR2	-105.8	28.71	**< 0.001**
TVR2 x Age at CT	4.659	0.821	**< 0.001**
endoscopic	-68.48	134.1	0.610
endoscopic x Age at CT	4.055	7.457	0.578
2 springs	73.46	12.49	**< 0.001**
2 springs x Age at CT	-0.791	0.429	0.108
3 springs	177.9	57.99	**0.002**
3 springs x Age at CT	-5.860	1.559	**0.020**
Intracranial volume			
H < 6	104.5	37.97	**0.006**
H < 6 x Age at CT	-2.361	1.240	0.130
H > 6	12.35	62.18	0.843
H > 6 x Age at CT	4.271	2.369	0.073

Modified H	128.9	52.98	**0.016**
Modified H x Age at CT	-2.735	1.876	0.241
TVR1	40.43	64.19	0.529
TVR1 x Age at CT	3.157	2.259	0.235
TVR2	-167.8	127.7	0.190
TVR2 x Age at CT	9.409	3.653	**0.011**
endoscopic	82.26	606.9	0.892
endoscopic x Age at CT	0.636	33.75	0.985
2 springs	158.9	46.78	**0.001**
2 springs x Age at CT	-6.086	1.179	**0.001**
3 springs	177.9	57.99	**0.002**
3 springs x Age at CT	-5.860	1.559	**0.020**

Table A3. Regression analysis of the data presented in Fig 5 A-F, 6 A-F. The reference classes were female in the H group. For example, the 2 springs group had a higher CI than the H group (+3.667 ±1.730, p=0.043). The change over age in CI between both groups was however not significantly different (p=0.058).

	Value	SD	p
Cephalic index			
H > 6	0.274	3.363	0.936
H > 6 x Age at CT	-0.008	0.032	0.813
Modified H	-0.080	1.886	0.966
Modified H x Age at CT	0.002	0.024	0.944
TVR1	-1.052	1.954	0.594
TVR1 x Age at CT	-0.022	0.026	0.403
TVR2	1.647	3.801	0.668
TVR2 x Age at CT	0.023	0.102	0.825
endoscopic	-17.01	27.36	0.540
endoscopic x Age at CT	0.875	1.490	0.563
2 springs	3.667	1.730	**0.043**
2 springs x Age at CT	-0.082	0.040	0.058
3 springs	0.911	2.135	0.673
3 springs x Age at CT	-0.079	0.040	0.071
Skull circumference			
H > 6	18.78	22.27	0.406
H > 6 x Age at CT	0.097	0.195	0.635
Modified H	13.99	11.89	0.248
Modified H x Age at CT	-0.156	0.164	0.364
TVR1	2.619	16.15	0.872
TVR1 x Age at CT	-0.088	0.309	0.781
TVR2	36.59	32.85	0.275
TVR2 x Age at CT	0.209	0.880	0.814
endoscopic	38.15	156.7	0.810
endoscopic x Age at CT	-0.706	8.537	0.935
2 springs	71.24	14.40	**< 0.001**
2 springs x Age at CT	-0.878	0.430	0.061
3 springs	75.25	19.03	**0.001**
3 springs x Age at CT	-0.571	0.625	0.381
Intracranial volume			
H > 6	-35.99	96.06	0.710
H > 6 x Age at CT	-0.449	0.917	0.640
Modified H	39.24	54.47	0.476
Modified H x Age at CT	-1.156	0.738	0.148
TVR1	-17.60	74.02	0.814
TVR1 x Age at CT	-1.468	0.971	0.159
TVR2	273.0	140.5	0.063
TVR2 x Age at CT	-4.108	3.774	0.286

endoscopic	894.1	818.9	0.285
endoscopic x Age at CT	-37.24	44.61	0.412
2 springs	101.6	66.22	0.137
2 springs x Age at CT	-5.127	1.287	**0.001**
3 springs	122.7	75.76	0.118
3 springs x Age at CT	-5.882	1.153	**< 0.001**

Table A4. Regression analysis of the data presented in Fig 5 G, 6 G.

	Value	SD	p
Cephalic index			
3 springs	-2.286	1.998	0.272
3 springs x Age at CT	0.006	0.035	0.862
Skull circumference			
3 springs	2.635	19.99	0.897
3 springs x Age at CT	0.219	0.791	0.786
Intracranial volume			
3 springs	32.12	81.02	0.698
3 springs x Age at CT	-0.718	1.228	0.568

Table A5. Regression analysis of the data presented in Fig 5 H, 6 H.

	Value	SD	p
Cephalic index			
endoscopic	-8.017	31.49	0.804
endoscopic x Age at CT	0.627	2.197	0.781
Skull circumference			
endoscopic	17.65	318.5	0.957
endoscopic x Age at CT	-3.489	22.22	0.878
Intracranial volume			
endoscopic	-574.8	1112	0.617
endoscopic x Age at CT	33.40	77.60	0.676

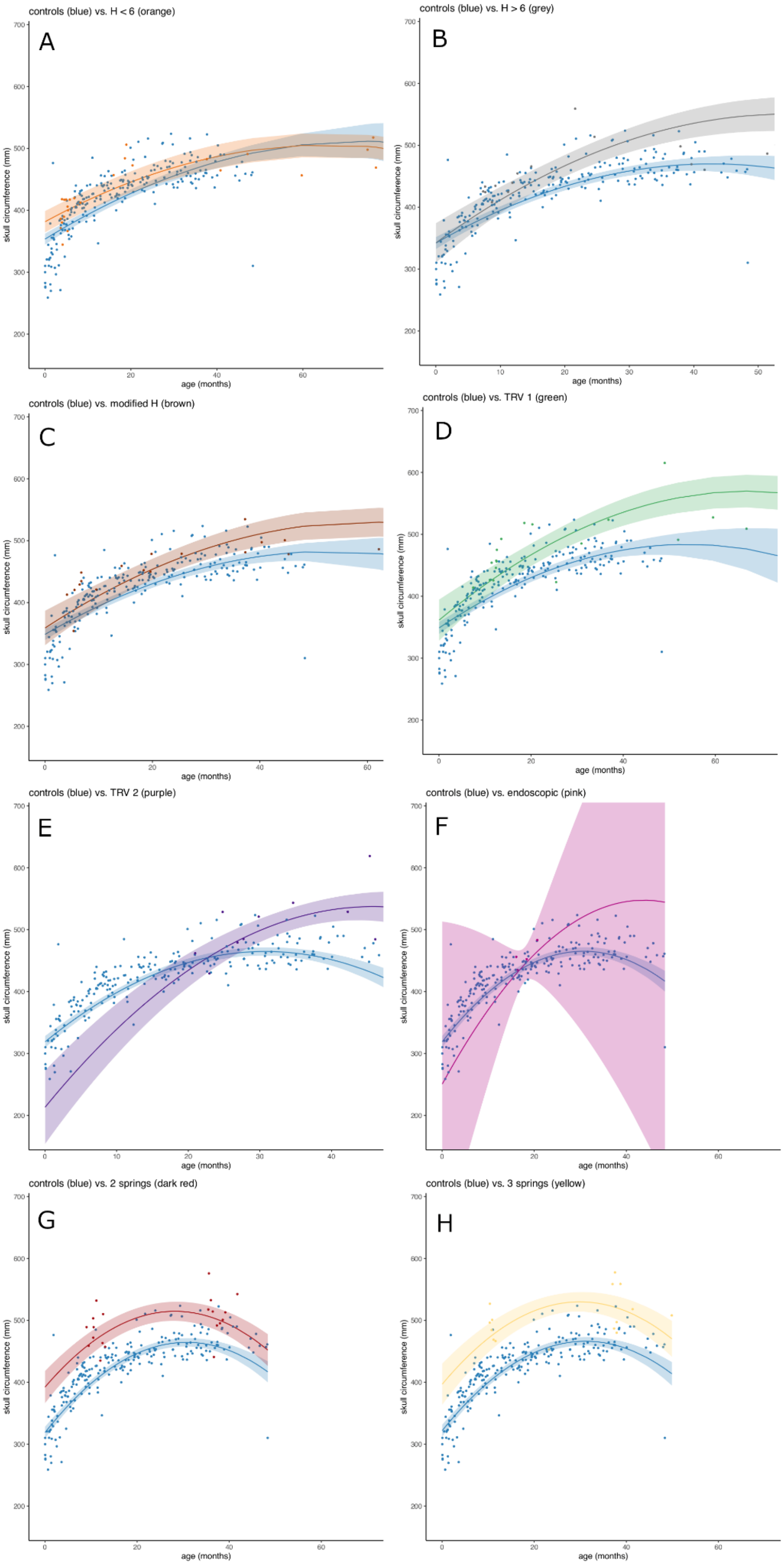


Fig A1: Comparing post-operative skull circumference measurements versus normal skulls.

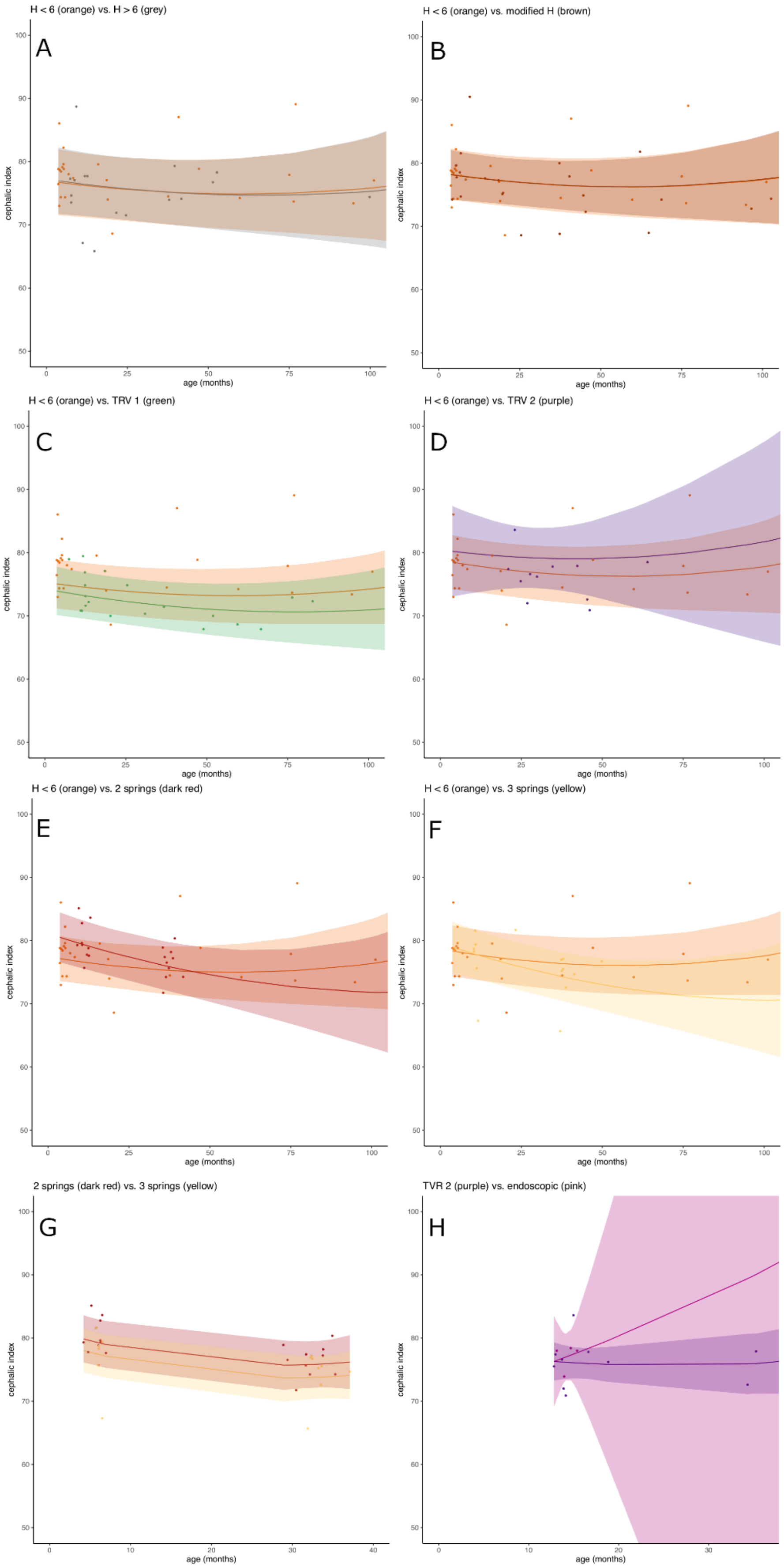


Fig A2: Comparing cephalix indexes between different techniques plotted over age.

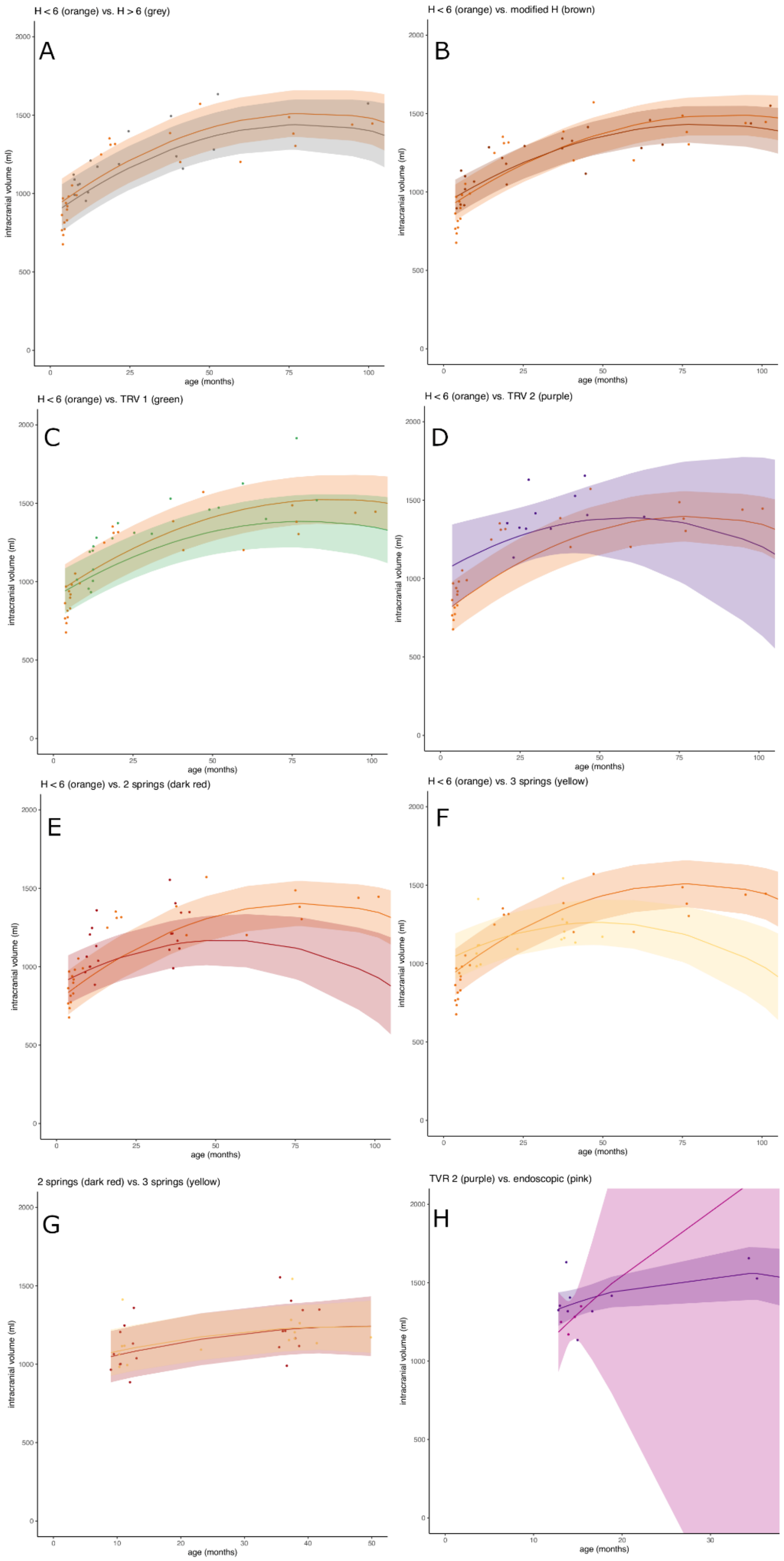


Fig A3: Comparing intracranial volume between different techniques plotted over age.