INTRODUCTION

Craniosynostosis is the premature fusion of ≥1 cranial sutures. It affects as many as 1 in 1,500 live births and results in head shape abnormalities. The most common form of craniosynostosis is nonsyndromic sagittal synostosis, which accounts for approximately 41% of cases. Premature fusion of the sagittal suture results in an elongation of the head in an anterioposterior direction, which is known as scaphocephaly. Surgical correction is mandated to improve head shape and to decrease the risk of raised intracranial pressure. This study evaluated the utility of 3-dimensional (3D) imaging to quantify the volumetric changes of surgical correction. Currently there is no standardized method used to quantify the outcomes of surgery for craniosynostosis, with the cranial index (width : length ratio) being commonly used.

Methods: A method for quantification of head shape using 3D imaging is described in which the cranium is divided up into 6 compartments and the volumes of 6 compartments are quantified and analyzed. The method is size invariant, meaning that it can be used to assess the long-term postoperative outcomes of patients through growth. The method is applied to a cohort of sagittal synostosis patients and a normal cohort, and is used to follow up a smaller group of synostotic patients 1, 2, and 3 years postoperatively.

Results: Statistical analysis of the results shows that the 6-compartment volume quantification method is more accurate in separating normal from synostotic patient head shapes than the cranial index.

Conclusions: Spring-mediated cranioplasty does not return head shape back to normal, but results in significant improvements in the first year following surgery compared with the preoperative sagittal synostosis head shape. 3D imaging can be a valuable tool in assessing the volumetric changes due to surgery and growth in craniosynostosis patients.

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most commonly used is the cephalic index (CI). The CI is defined as the ratio of calvarial width to length and has traditionally been used to assess scaphocephaly severity, treatment outcomes and to define the normal range of CI. However, the sensitivity of the ratio is low and does not account for specific anomalies of head shape. Three-dimensional (3D) imaging methods can be used to acquire head shapes. Currently there is no standardized method for 3D head shape quantification that has been applied across different surgical approaches for craniosynostosis.

The present study aimed to: (1) describe a 6-compartment volume measurement for quantification of the outcomes of spring-mediated cranioplasty for sagittal synostosis cases, (2) show how this method can be used with computed tomography (CT) and 3D photogrammetry data, and (3) demonstrate use of the method to quantify volume distribution differences between normal and sagittal craniosynostosis head shapes.

METHODS

Ethics approval was obtained to collect retrospective CT and photogrammetry data for pre- and postoperative craniosynostosis patients and normal head shape CTs. Ethics approval for the study was sought from the South Eastern Sydney Local Health District—Human Research Ethics Committee (HREC). Study title “Quantifying head shape in craniosynostosis using 3D analysis,” HREC No. 15/105. Ethics approval for the study was granted on August 5, 2015.

Data Collection and Sample Composition

The craniofacial database of a tertiary referral craniofacial unit was used to identify patients undergoing spring-mediated cranioplasty for sagittal synostosis. Patients underwent 3D digital photogrammetry imaging (3dMD, Atlanta, GA) at preoperative and at postoperative review (1 year, 2 years, and 3 years postoperatively).

Age at surgery ranged from 13 days to 6.5 years. There were 58 males and 40 females included in the total normal group (n = 98), with 22 males and 19 females in the normal preoperative comparison group ranging from 13 days to 1.55 years (564 days) old (n = 41). There were 15 males with 12 females (and 3 sex unrecorded) included in the preoperative craniosynostosis group ranging from 32 days old to 1.27 years (464 days) old (n = 30).

The surgical technique was a lazy S incision followed by sagittal osteotomy and mobilization of medial parietal bones, insertion of 2 or 3 springs (depending on patient). The wound was closed with a drain. The springs were removed 3 months post (initial) operation.

CT scans for the control (normal head shape) database were from patients aged between 0 and 6 years. Scans were excluded where pathology affecting head shape was noted.

Segmentation and 3D Reconstruction of Data

All CT scans were segmented in Materialise Mimics (version 16.0; Leuven, Belgium). 3D surface model reconstructions were made for both the skin and bone for each CT. The skin reconstructions were edited in Materialise 3-Matic (version 8.0) to remove any extraneous material captured by the scan and then reimported into Mimics to check the final 3D surface models were accurate representations of the head shape (see Fig. 1). Note, hair is not visible on segmented CT, so does not influence head shape.

Photogrammetry data were reconstructed into 3D models using 3dMD software and edited in Materialise’s 3Matic (version 8.0). Shape abnormalities caused by the head cap worn by subjects and the bunching of hair were edited to minimize the potential influence on head shape (see figure, Supplemental Digital Content 1, which displays before (off-white) and after (light blue-green) cleaning and editing photogrammetry data, http://links.lww.com/PRSGO/B20).

Alignment

Three orthogonal planes (axial, coronal, sagittal) were established with their origin point at the pituitary fossa (see figure, Supplemental Digital Content 2, which displays alignment with planes using bone reconstruction. Skin surface reconstruction is shown in gray, and bone reconstruction is shown in pale yellow. Alignment in the anterioposterior direction for each model was achieved with reference to the “atlas” model, http://links.lww.com/PRSGO/B21).

An initial normal CT 3D reconstruction was aligned to these planes manually using a combination of bone reconstruction and skin reconstruction and used as an “atlas” scan to align other CT scan reconstructions. Using an inferior view of the base of the skull, the midpoint of the nose, opisthion, and basion were used as landmarks to align the sagittal plane in an anterioposterior direction (see figure, Supplemental Digital Content 3, which displays homologous landmark point registration of another patient (gray) to atlas (yellow), http://links.lww.com/PRSGO/B22).

The external occipital protuberance, posterior fontanelle, and sagittal sutures were then used to correct the alignment to the sagittal plane. The supraorbital foramina were used to align the crania in the coronal plane. The crania were rotated so that the axial plane passed through nasion and external occipital protuberance.

CT scan reconstructions were aligned to the atlas model in a similar fashion (Fig. 4). The coronal and lambdoid sutures of the atlas were used to align the other reconstructions during anterioposterior rotation.

Preoperative photogrammetry reconstructions were aligned to preoperative CT scan (for patients where both were available) using iterative closest point registration. Postoperative photogrammetry reconstructions were scaled to the preoperative CT anterioposterior length, iterative closest point aligned, then manually aligned to the preoperative CT before rescaling to the original size. All areas below the axial plane, as well as the ears, were then removed from each reconstruction.

Data Analysis

The total sample size (N) was 128 individuals, which included 98 normals and 30 synostosis patients. The total number of scans used was 156 (98 normal, 30 preoperative
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synostosis, 14 P1, 9 P2, 5 P3 where P1, P2, and P3 scans were from a subset of the 30 preoperative synostosis patients). Patient scans were separated into 5 groups for pre- and postoperative analysis:

1. Controls (control, n = 98). Subset of 41 patients aged 0–15 months,
2. Preoperative sagittal synostosis cases (preoperative, n = 30), age range 0–15 months,
3. Postoperative patients 0–1 year after surgery (P1, n = 14),
4. Postoperative patients 1–2 years after surgery (P2, n = 9),
5. Postoperative patients 2–4 years after surgery (P3, n = 5).

Definition of 6 Compartments

Planes were constructed that passed through the pituitary fossa to the middle of the anterior and posterior fontanelles of each CT model, and the average angles calculated from normal cranial anatomy (84 degrees clockwise from the anterior axial and 31 degrees anticlockwise from the posterior axial planes Figs. 2, 3). These compartments were then separated by the sagittal plane to give anterior, middle, and posterior compartments for the left- and right-hand sides. The volumes of these compartments were then calculated as a percentage of total volume. As the cephalic index (CI) is still widely used to quantify head shape, we also calculate the CIs for the study groups. A superior axial view was used to measure the maximum width and length of each aligned reconstruction to calculate the CI.

RESULTS

Normal Versus Preoperative Sagittal Synostosis

A least squares linear regression analysis on the natural log (Ln) transformed total cranial vault volumes (cubic millimeter) against Ln transformed age (days) showed no significant difference \((P = 0.05)\) between 30 sagittal synostosis cases and 41 controls (normals) within the same age range (0–1 year and 3 months) (Fig. 4). A separate analysis showed no significant difference between males and females for these 2 groups \((P = 0.05)\).

Cephalic Index

The mean CI in the normal group was significantly higher at 83 compared with the preoperative synostosis group at 71 \((P < 0.05)\) (Fig. 5). There was a significant difference between the normals and postoperative year 1 synostosis group (83 versus 77, respectively, \(P < 0.05\)). No significant differences at the \(P = 0.05\) level were identified between any of the postoperative synostosis groups and the preoperative synostosis group. Mean CIs: normal (83.1) > P1 (76.6) > P3 (75.8) > P2 (75.0) > preoperative (71.2).

Symmetry of Volume Distribution across the Midsagittal Plane

There was no correlation between asymmetric volume distribution (more volume in the left- or right-side compartments) and age.
Six-compartment Volume Analysis

*Left Anterior Compartment*

The left anterior volume in the normal cases was less than those in the preoperative synostosis group (14.58% vs 17.05%, *P* < 0.05). Following surgery, P1 was significantly different from both preoperative and normal groups lying between 2 at 15.85% (*P* < 0.05). There was a trend in anterior compartment volume P3 back toward the preoperative group volume distribution with P3 not significantly different at the *P* = 0.05 level from the preoperative sagittal synostosis group. Trend: normal (14.58%) < P1 (15.85%) < P2 (16.23%) < P3 (16.80%) < preoperative (17.05%).

*Right Anterior Compartment*

Normal cases had less right anterior volume than preoperative cases (15.12% versus 17.47%, *P* < 0.05). Following
Fig. 4. Least squares linear regression plot of ln transformed total volume vs ln transformed age for normal and sagittal cases. Red points and line represent the sagittal synostosis cases, and blue points and line represent the normal cases. Translucent bands show the 95% confidence intervals (to dashed lines), with the dotted lines showing the 99% confidence intervals. Note that these confidence intervals overlap considerably, showing that there is no significant difference between the regression lines. The best fit lines were (sagittal) $y = 12.34 + 0.31x$ ($R^2 = 0.88$) and (normal) $y = 12.31 + 0.30x$ ($R^2 = 0.85$).

Fig. 5. CI frequency distribution of normals (dark blue) vs preoperative (red) vs postoperative 1 (orange) vs postoperative 2 (cyan) vs postoperative 3 (green).

surgery, all postoperative groups were still significantly different from the normal group. P1 and P2 were also different (significant reduction in percentage volume) from the preoperative sagittal synostosis group at the $P<0.05$ level (16.59% and 16.35%, respectively). Postoperative 3 was not significantly different from the preoperative group at the $P=0.05$ level. Trend: normal (15.12%) < P2 (16.35%) < P1 (16.59%) < P3 (17.12%) < preoperative (17.47%).

**Left Middle Compartment**

The normal left middle volumes were more than the preoperative group (24.75% versus 22.11%, $P<0.05$) and significantly different from all postoperative groups ($P<0.05$). Postoperative 1 was significantly different from both the normal group and preoperative group lying between the 2 (23.07%, $P<0.05$), as was P2 (22.94%, $P<0.05$). As with the anterior left compartment, P3 was not significantly different from preoperative at the $P=0.05$ level. Trend: normal (24.75%) > P1 (23.08%) > P2 (23.88%) > P3 (23.00%) > P2 (22.94%) > preoperative (22.11%).

**Right Middle Compartment**

The normal right middle volumes were larger than the preoperative group (25.03% vs 22.12%, $P<0.05$). P1, P2, and P3 were significantly different from both the preoperative group and normal group lying between the 2 (23.88%, 23.71%, and 23.08%, respectively; $P<0.05$). P3 was not significantly different from preoperative at the $P=0.05$ level. Trend: normal (25.03%) > P1 (23.88%) > P2 (23.71%) > P3 (23.08%) > preoperative (22.12%).
Left Posterior Compartment
The P3 volumes for the left posterior compartment were less than the preoperative group (9.34% versus 10.16%, respectively), which was the only significant difference found between any groups for the right middle volume \((P < 0.05)\). Trend: P3 (9.34%) < P2 (9.71%) < P1 (9.72%) < normal (9.78%) < preoperative (10.16%).

Right Posterior Compartment
The normal volumes for the right posterior compartment were less than the preoperative group (9.62% versus 10.08%), which was the only significant difference found between any groups for the right middle volume \((P < 0.05)\). Trend: P3 (9.53%) < normal (9.62%) < P1 (9.86%) < P2 (9.96%) < preoperative (10.08%).

Principal Component Analysis (PCA) of 6-compartment Volumes
PCA is a multivariate statistical analysis method allowing for the volumes of the 6 compartments to be analyzed together.\(^{20,21,24}\) PCA identifies the main (principal) modes (components) of difference within the sample. The main variation is distributed along the first principal component (PC) axis. The analysis also identifies the relative weighting of each of the 6 volumes in each of the components.

PC1 captured 71.42% of the variance in volume distribution among the 6 compartments with PC2 explaining 16.18%, PC3 explaining 6.94%, and PC4 explaining 4.73%. Together, PC1–4 captured 99.28% of the variance in volume distribution in the sample. An analysis of variance (ANOVA) of PC1 scores was able to differentiate between the normals and preoperative (Figs. 6, 7), normals and P1, normals and P2, normals and P3, preoperative and P1, preoperative and P2 \((P < 0.01)\) and preoperative and P3 \((P < 0.04)\) (Fig. 6).

DISCUSSION
The use of virtual and physical 3D modeling for assessing head shape has become more common place in the last decade.\(^{25–29}\) A significant drawback in methods presented by previous studies has been the reliance on CT scans for data acquisition, subjecting the patients to ionizing radiation and a general anesthetic. Wong et al.\(^{30}\) demonstrated that a photogrammetric method using the 3dMD system could be effective in capturing cranial measurements. Photogrammetric methods to analyze craniosynostosis have also been validated in other studies\(^{31,32}\) and in nonsynostotic craniofacial deformities.\(^{33}\)

Total Volume Analysis
There is a concern with that craniosynostosis could limit brain growth and neurological development by limiting in the cranial vault size.\(^{34–36}\) Hence, measurements of intracranial volume (ICV) have been used to quantify the outcomes of surgery.\(^{9,35,37–40}\) Comparisons of the ICVs of normal and sagittal synostosis patients have found limited evidence of decreased ICV with sagittal synostosis.\(^{3,9,38}\) Our results showed no significant difference in cranial volume between normal and sagittal synostosis patients (0–15 months; Fig. 4). This supports conclusions of Fischer et al.,\(^{39}\) Heller et al.,\(^{9}\) and Posnick et al.\(^{40}\) that sagittal synostosis volumes are equal to, or larger than, normal volumes.

Cephalic Index
CI has been widely used to assess the outcome of surgery for craniofacial deformities\(^{25–9,12–16}\) as the CI is generally able to distinguish between normal and scaphocephalic head shapes.\(^{2,5,6}\) Although the present study found significant differences between the preoperative sagittal synostosis group and the normal group, this difference is not “clear cut” with considerable overlap between the 2 groups (see Fig. 5). The CI improved from an av-

Fig. 6. A scatter plot of PC1 (x-axis) vs PC2 (y-axis) scores for the PCA of the 6-compartment volumes with convex hulls showing the distribution of each of the groups. Normals = blue (mean represented by N). Preoperative = red (mean represented by S). Postoperative 1 = orange (mean represented by S-Po1). Postoperative 2 = cyan (mean represented by S-Po2). Postoperative 3 = green (mean represented by S-Po3). The polygon shapes denote the convex hulls for each of the groups.
average of 71–77 from the preoperative group compared with the P1 but was not significant at the \( P = 0.05 \) level. P2 and P3 both reported slightly decreased CI relative to P1, but these differences were not significant. This trend is supported by studies by Windh et al.\(^5\) and van Veelan et al.\(^6\) who also report a trend toward a scaphocephalic head shape following surgery using the CI at 1- and 3-year postoperative time points.

### Compartment Volume Analysis

Although the CI fails to characterize the location of change following surgery, the 6-compartment volume analysis introduced here has shown promise in defining postoperative changes. David et al.\(^4\) using a frontal volume to characterize improvements following Spring Mediated Cranioplasty (SMC) and Wikberg et al.\(^41\) using a ratio of the frontal volume to total volume to assess postoperative changes for metopic synostosis. A comprehensive study of volume analysis by Wilbrand et al.\(^32\) divided the head into 4 compartments and used the ratio of the compartment volumes to quantify the outcome of surgery for a variety of single-suture cases. Although the use of 4 compartments allows for improved quantification and localization of the areas affected by surgery, it is limited in its use for isolating the affected area of change. For example, it cannot differentiate between an increase in the frontal volume and a decrease in the posterior volume based on ratios alone.

The present study also applied the 6-compartment volume distribution method to sagittal synostosis patients following spring-mediated cranioplasty to quantify the effects of the surgery on the volume distribution in the head. Since a volume distribution is used, the method is size invariant, which was shown by the lack of a relationship between volume distribution and age. The method aimed to use the minimum number of compartments that could (1) account for asymmetry and (2) be sensitive (precise) enough to identify differences in the main anatomical regions of the crania that are affected by synostosis.

The 3 sagittal split lines are based on anatomical regions of (normal) crania (see Figs. 2, 3).

The PCA of the 6-compartment volume distributions showed that the anterior and middle compartments were more useful in differentiating between normal, preoperative, and postoperative patients. The PCA and ANOVAs showed an increase in the volume distribution in the anterior compartment, a similar (unchanged) volume distribution in the posterior compartments and a decrease in the volume distribution in the middle compartments of sagittal synostosis patients compared with normal (see Fig. 8). Although the anterior and middle compartment results were expected, we also expected an increase in the posterior compartments as this would fit the classic scaphocephalic description of an elongation and narrowing of the head; however, this was not what the present study found. The ANOVA of the PC1 results demonstrated significant differences between normals, the preoperative group, and postoperative groups, showing that 6-compartment volume distribution method is effective for differentiating between these head shapes in these groups.
When examining the trends for the anterior and middle compartments, it is notable that all the postoperative groups were between the normal and preoperative groups and significantly different from the preoperative group. This means that while the spring-mediated cranioplasty did not fully restore the head shape of patients to the normal group shape, it significantly improved their head shape compared with their preoperative state. Unlike the CI, the 6-compartment volume analysis was able to identify significant differences between the preoperative group and P1, which potentially indicates greater sensitivity in the 6-compartment volume distribution analysis method than the CI measurement.

P1 was situated closest to the normal group in 3 of 4 compartments with the most significant differences (anterior and middle compartments). This suggests that the biggest impact on head shape is in the first year following spring-mediated cranioplasty, after which there may be a shift back toward the preoperative shape. The small sample sizes in P2 and P3 are a clear limitation of this study and future studies with an increased number of postoperative follow-ups would allow for statistically significant long-term postoperative trends to be determined.

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