Characterising Optic Nerve Head Morphological Variation in Craniosynostosis using Handheld Optical Coherence Tomography: A Cohort Study

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Introduction: Craniosynostosis is associated with intracranial hypertension (IH), which can damage the brain and optic nerve head (ONH) if unaddressed. In this world-first prospective cohort study, we used handheld OCT (Figure 1) in children with non-IH associated craniosynostosis, to assess ONH morphological variation.

Methods:

Single-centre, prospective cohort study: Feb 2020 – Feb 2022

Inclusion criteria:

- Children <18 years with craniosynostosis.
- Handheld OCT successful.
- Normal ICP on direct intracranial measurement, OR
- Stable VEPs, stable VA and no swelling on fundoscopy ≥4 months.

Main outcome measures:

- ONH parameters (Figure 2) for craniosynostosis (including FGFR1/2 mutations: Crouzon, Apert and Pfeiffer syndromes) vs. control data derived from normative dataset.[1]
- Handheld OCT feasibility in craniosynostosis.

Analysis:

- ImageJ (https://imagej.nih.gov/ij/) used for OCT segmentation.
- 3-way linear mixed model: control data vs. non-FGFR1/2 craniosynostosis vs. FGFR1/2 craniosynostosis, accounting for age, eye (right/left) and spherical equivalent, using SPSS Statistics 22.0.

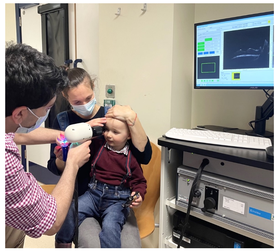


Figure 1: Handheld OCT

Image taken with parental consent.

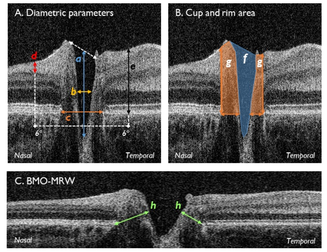


Figure 2: Optic nerve head parameters

A: cup depth; b: cup width; c: disc width; d: RNFL thickness, e: retinal thickness; f: cup area; g: rim height, width and area; h: Bruch's membrane opening minimum rim width.

Results:

Handheld OCT was successful in 50 of 55 (91%) eligible children; 21 (42%) were female, 41 (82%) had non-FGFR1/2-associated craniosynostosis and 9 (18%) FGFR1/2-associated (Crouzon=4; Apert=3; Pfeiffer=2). Median age at OCT was 51 months (range: 2-157; IQR: 37-73); median follow-up was 10 months (range: 4-20; IQR: 7-12). Control data were available for 107 children. Figure 3 displays ONH parameters demonstrating significant morphological variation (cup and rim parameters). Figure 4 displays examples of variation in ONH morphology. Interestingly, there were no significant differences for RNFL thickness and retinal thickness – these are likely to be useful OCT measures for IH in our ongoing diagnostic accuracy study.[2]

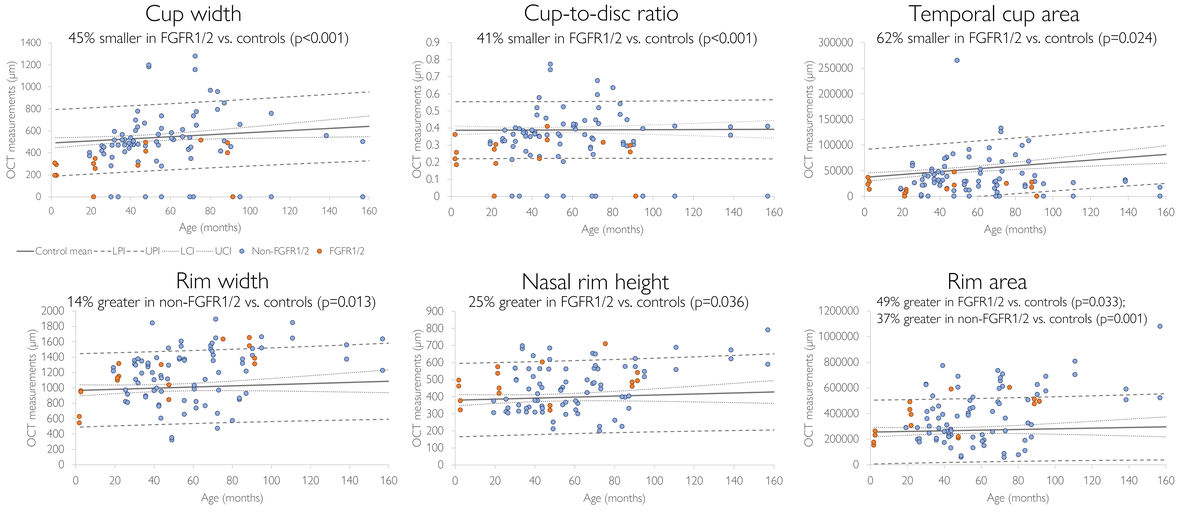


Figure 3: Optic nerve head parameters demonstrating significant variation

Our 3-way linear mixed model demonstrated significant differences in the displayed ONH parameters. Solid grey line = control mean; dashed grey lines = control lower/upper 95% prediction interval (LPI/UPI); dotted grey lines = control lower/upper 95% confidence interval (LCI/UCI); blue spots = non-FGFR1/2-associated craniosynostosis eyes; orange spots = FGFR1/2-associated craniosynostosis eyes (Crouzon, Apert and Pfeiffer syndromes).

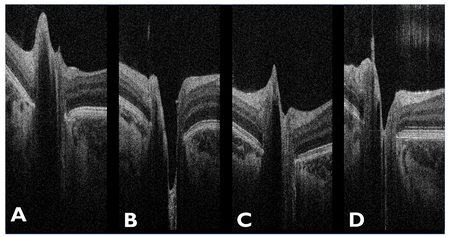


Figure 4: Examples of variation in optic nerve head morphology

A. 21-month-old male with Apert syndrome; B. 26-month-old male with sagittal synostosis (non-syndromic, for comparison); C. 91-month-old female with Crouzon syndrome; D. 85-month-old male with sagittal synostosis (non-syndromic, for comparison). Note how the two examples with FGFR1/2-association craniosynostosis, A and C, have much smaller cups compared to B and D. This is not always the case in FGFR1/-associated craniosynostosis, but highlights that the cup can appear small despite normal ICP in these patients.

Conclusions: We found excellent feasibility of handheld OCT and significant variation in ONH morphology in this cohort: greater rim measurements in craniosynostosis, with smaller cups in FGFR1/2 mutations. Our findings could help guide the clinical management of craniosynostosis.

References: 1. Patel A, et al. Ophthalmology. 2016 Oct;123(10):2147-57.
2. Rufai SR, et al. BMJ Open. 2022 Jan 11;12(1):e048745.

The RIO Study

Recognition of Intracranial Hypertension in Children using Handheld Optical Coherence Tomography

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