POTENTIAL UTILITY OF FOVEAL MORPHOLOGY IN PRETERM INFANTS MEASURED USING HAND-HELD OPTICAL COHERENCE TOMOGRAPHY IN RETINOPATHY OF PREMATURITY SCREENING

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**Purpose:** To investigate dynamic foveal morphology with postmenstrual age, in preterm infants with and without retinopathy of prematurity using hand-held optical coherence tomography, adjusting for gestational age (GA) and birthweight (BW).

**Methods:** Prospective mixed cross-sectional/longitudinal observational study of 87 participants (23–36 weeks GA; n = 30 with, n = 57 without retinopathy of prematurity) using hand-held optical coherence tomography images (n = 278) acquired between 31 weeks and 44 weeks postmenstrual age excluding treated retinopathy of prematurity. Measurements included foveal width, area, depth, central foveal thickness, maximum slope, and parafoveal retinal thickness at 1,000 μm nasal and temporal to the central fovea.

**Results:** Retinopathy of prematurity was significantly correlated with only foveal width in either GA or BW adjusted statistical models. In contrast, severity of prematurity (GA, BW) correlated with foveal area (P < 0.005), depth (P ≤ 0.001), and slope (P < 0.01), although central foveal thickness (P = 0.007) and parafoveal retinal thickness (P < 0.001) correlated with GA, but not with BW.

**Conclusion:** Foveal width is independent of GA and BW with potential in retinopathy of prematurity screening assessment using hand-held optical coherence tomography. Foveal morphology could be graded in prematurity during development, with possible implications for future management of preterm infants.

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Preterm birth is defined by gestational birth age (GA) before 37 weeks and is associated with very low birthweight (BW) (less than 1,500 g) or extreme low BW (less than 1,000 g). Infants born at less than 32 weeks GA and those with extreme low BW are vulnerable to retinopathy of prematurity (ROP), a potentially blinding disease that requires primary screening and intervention during the period of retinal development before 42 weeks to 44 weeks postmenstrual age (PMA). Determining the infants that benefit most from ROP intervention is based on retinal appearance and is mainly subjective, varying between specialists. Therefore, a key goal of ROP study has been to investigate factors that identify preterm infants at risk of treatment requiring ROP.

Hand-held optical coherence tomography (HH-OCT) is a noninvasive imaging technology permitting high resolution detail of the central retina to be rapidly acquired from infants at the earliest stages of prematurity. Studies are now emerging that use HH-OCT to chart foveal changes in prematurity, for example, to compare the effect of treatments for ROP. Earlier HH-OCT studies in preterm infants report persistence of inner retinal layers across the foveal depression, increased thickness of the inner retina, shallow fovea, and reduced depth. However, because GA, BW, and ROP are all strongly correlated, the relationship between foveal changes observed on OCT with severity of prematurity and changes associated with ROP remains unclear.
Our aim was to investigate dynamic changes in foveal morphology parameters with PMA using HH-OCT to identify indicators that differentiate between diagnosis of ROP and non-ROP, which could not be accounted for by differences in GA or BW. To achieve this, we imaged preterm infants with and without ROP between 31- and 44-weeks PMA using HH-OCT. We excluded treated ROP infants and modelled the fovea using a difference of Gaussians (DoG) fit.

Methods

The study was conducted in accordance with the tenets of the Declaration of Helsinki and granted approval by a Local Ethics Committee (NRES committee, Nottingham, East Midlands, United Kingdom). Patients were recruited from the Leicester Royal Infirmary neonatal and maternity unit, United Kingdom. All preterm babies from 31 weeks to 44 weeks PMA who required ROP screening were eligible for inclusion in the study. Abnormal ocular examinations other than diagnosis of ROP, and treated ROP were exclusion criteria. Data from infants requiring treatment were included up until treatment was performed.

Retinopathy of prematurity screening, staging, and treatment criteria of preterm infants were performed according to the United Kingdom guidelines. For the purpose of the study, ROP was defined as Stages 1 to 3 using the United Kingdom guidelines (Stages 4 or 5: partial or total retinal detachment, respectively, were excluded from the study; see appendix C of the United Kingdom ROP Guidelines). Infant eyes were instilled with topical dilating drops (Cyclomydril = cyclopentolate hydrochloride 0.2% and phenylephrine hydrochloride 1%) and examined while awake, using a lid speculum. Binocular indirect ophthalmoscopy was used to establish the presence or absence of ROP. Documentation of demographic and clinical parameters for each preterm infant included: PMA, GA, and BW; presence or absence of ROP, the stage of ROP if present, single or multiple birth, sex, eye (right or left), and ethnicity (Caucasian or non-Caucasian). The number of infants who switched from no ROP to ROP and vice versa where ROP regressed spontaneously during the course of imaging, was also documented.

Scan Acquisition and Selection of Foveal B-Scan

Imaging was performed from 31 weeks to 44 weeks PMA at 1 to 2 weekly intervals. Optical coherence tomography scanning was conducted in both eyes using a portable noncontact high-resolution HH-OCT (Envisu C-Class; Leica Microsystems, Wetzlar, Germany). Scans were optimized for obtaining a single high-quality scan at the central retina consisting of 500 A scans and 100 B scans, covering a rectangular volume 5.0 mm × 10.0 × 2 mm. The total scan time was 2.9 seconds (5.8 milliseconds per B scan). The lateral distance settings (defined for adults on the machine) were corrected to account for the smaller axial lengths in the infant population using a conversion table according to PMA and GA from the data presented by Maldonado et al.

We aimed to acquire five HH-OCT images per infant per eye. From the HH-OCT scans acquired for each infant, those with the brightest and clearest components on retinal scanning were chosen for analysis. The successful identification of the foveal center was achieved by examining five uninterrupted B scans on either side of the B scan with the deepest point in the central retina. A foveal depression could always be identified on inspection. Repeated longitudinal images from each infant from 31 weeks to 44 weeks PMA were included in the study and analysis.

Image Segmentation and Foveal Contour Measurement

The fovea was modelled using a DoG customized fit based on previous literature and analysis of the images was performed using customized layer segmentation macros written in ImageJ software (United States National Institutes of Health, Bethesda, MD, https://imagej.nih.gov/ij/, downloaded on December
Foveal parameters included width, area and depth, central foveal thickness (CFT), steepest slope of the foveal wall, and parafoveal retinal thickness (pRT).

Foveal B-scans were flattened using the Bruch membrane as a reference line and translating individual A-scans vertically. Boundary detection of the internal limiting membrane (ILM) was performed automatically using the ABSnake plugin (http://imagejdocu.tudor.lu/doku.php?id=plugin:segmentation:active_contour:start downloaded on December 2013). Manual fine adjustment of the fitted line was used to generate the final segmentation.

Foveal shape dimensions were analyzed using an enhanced model based on the DoG principle described by Dubis et al. Because the fovea is asymmetric as reported by Liu et al, we modelled the nasal and temporal aspects of the fovea separately.

The DoG fits were calculated using Solver, an add-in tool in Excel (Microsoft Corporation, Seattle, WA). The aim of the Solver Tool was to reduce the root sum of squares of the differences between the actual and fitted values by adjusting the height and width terms of the Gaussians. An additional term was added to reduce the error between the bottom of the foveal pit values and the nasal and temporal fit. The starting points approximate to typical foveal profile consisting of a narrower inverted Gaussian which mainly fits the pit and a wider noninverted Gaussian which mainly fits the parafovea.

In the models by Dubis et al and Liu et al, the two rim points that determine the maximum diameter of the foveal depression were taken to be at the highest points on the two sides of the pit. This was determined from points of inflection, where the direction of the ILM changes direction and the slope is zero. However, in many preterm infant images, the foveal contour continues to increase beyond the foveal rim and the wider Gaussian fitting of the parafovea can also follow an inverted profile in contrast to adult retina. Hence, in our model, the foveal rim edge was defined as the maximum point of the third derivative of the ILM profile, which is the earliest indication of the falling away of the ILM to form the foveal pit. For consistency, this method was used on all images including those where the parafovea was fitted with a noninverted Gaussian.

Figure 1A illustrates the foveal metrics of width, depth, area, and CFT in relation to the ILM profile. Figure 1B shows the first derivative of the ILM and points that used to define the rim edges and maximum nasal and temporal foveal slope. Nasal and temporal parameters of slope, width, area, and pRT (1000 μm from the fovea) are illustrated in Figure 1A.

**Statistical Analysis**

Multivariate mixed models were generated (see Supplemental Digital Content 1, http://links.lww.com/IAE/B43) to investigate the effect of diagnosis of ROP on foveal parameters described above with PMA, adjusting for the degree of prematurity (GA and BW) and other potential factors that may influence foveal morphology: ethnicity, birth (single/multiple) sex, and eye (right, left). Foveal asymmetry was also explored by comparing nasal and temporal measures of steepest slope of the foveal wall and pRT.

**Results**

One hundred and seventy-four preterm infants were recruited to the study over 42 months (91 boys and
83 girls). Poor quality images for both eyes were discarded with the result that data could not be analyzed for 62 participants (36%) (31 boys and 31 girls). A further 25 infants (14%) developed cystic appearances (identical to cystoid macular edema) of the central retina\(^5\)\(^{-}\)\(^\text{23}\) distorting foveal structure, and these infants were also excluded from the foveal morphology analysis. The remaining 87 participants (47 boys and 40 girls) and 278 images were analyzed in the study. Fifty-seven infants (65%) never had ROP at any imaging session, whereas 19 infants (22%) had ROP recorded at every imaging session and 11 infants (13%) had ROP on at least one imaging session. In this last group (mixed ROP/no ROP), seven infants developed ROP in one eye, whereas one infant developed ROP in both eyes. In two infants, the ROP regressed spontaneously and another infant initially had no ROP recorded, which then developed into ROP and then subsequently spontaneously regressed. Details of the infant cohort are shown in Table 1. Further summary details of 1) number of successfully analyzed repeated images; 2) details of ethnicity, multiplicity, and sex; and 3) characteristics according to BW and GA are shown (see Supplemental Digital Contents 2–4, http://links.lww.com/IAE/B44, http://links.lww.com/IAE/B45, and http://links.lww.com/IAE/B46, respectively).

Figure 2 shows predicted mean fits (with 95% confidence intervals) of statistical models adjusted for GA for: 1) foveal width (Figure 2B), 2) area (Figure 2C), 3) depth (Figure 2D), and 4) CFT (Figure 2E), and Figure 3 for: 5) steepest slope of the foveal wall (Figure 3B) and 6) pRT (Figure 3C). Separate plots are provided where statistical models demonstrate a factor that significantly affects the foveal parameter (e.g., presence or absence of ROP for foveal width, Figure 2B).

Differences Between Retinopathy of Prematurity and Non-Retinopathy of Prematurity Infants

Figure 4 (see also Figure 2B) shows the results of multivariate modelling for GA and BW on foveal width, with predicted mean fits (with 95% confidence intervals) shown in Figure 4, B and D, respectively, and results of statistical modelling shown in Figure 4, C and E, respectively. Similar formats are used for foveal area (see Supplemental Digital Content 5, http://links.lww.com/IAE/B47), foveal depth (see Supplemental Digital Content 6, http://links.lww.com/IAE/B48), CFT (see Supplemental Digital Content 7, http://links.lww.com/IAE/B49), steepest slope of foveal wall (slope) (see Supplemental Digital Content 8, http://links.lww.com/IAE/B50) and pRT (see Supplemental Digital Content 9, http://links.lww.com/IAE/B51), respectively.

Foveal width was the only parameter where diagnosis of ROP had a significant effect, with a highly significant interaction between absence/presence of ROP and PMA (\(P < 0.001\)). Foveal width decreased when ROP was absent, at a mean (±SEM) rate of \(-11.18 ± 4.46\) \(\mu m\) per week, but increased when ROP was present at a rate of \(+24.96 ± 6.92\) \(\mu m\) per week (Figure 4, B and C). This

### Table 1. Participant and Image Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Always Had ROP</th>
<th>Never Had ROP</th>
<th>Mixed (ROP or No ROP)</th>
</tr>
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<tbody>
<tr>
<td>No. of children</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total 87 (100%)</td>
<td>19 (22)</td>
<td>57 (65)</td>
<td>11 (13)</td>
</tr>
<tr>
<td>Male</td>
<td>7</td>
<td>33</td>
<td>7</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>Caucasian</td>
<td>9</td>
<td>29</td>
<td>4</td>
</tr>
<tr>
<td>Non-Caucasian</td>
<td>10</td>
<td>28</td>
<td>7</td>
</tr>
<tr>
<td>Single birth</td>
<td>14</td>
<td>52</td>
<td>9</td>
</tr>
<tr>
<td>Multiple birth</td>
<td>5</td>
<td>5</td>
<td>2</td>
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<tr>
<td>Mean (± SD) GA, BW, PMA</td>
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</tr>
<tr>
<td>GA (weeks)</td>
<td>26.1 ± 1.98</td>
<td>28.6 ± 2.43</td>
<td>26.6 ± 1.79</td>
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<tr>
<td>BW (grams)</td>
<td>807 ± 170</td>
<td>1,154 ± 423</td>
<td>864 ± 179</td>
</tr>
<tr>
<td>PMA (weeks)</td>
<td>36.5 ± 2.63</td>
<td>36.1 ± 2.45</td>
<td>36.0 ± 3.18</td>
</tr>
<tr>
<td>No. of images</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total 278 (100%)</td>
<td>73 (26)</td>
<td>156 (55)</td>
<td>49 (18)</td>
</tr>
<tr>
<td>Stage 1</td>
<td>12</td>
<td>—</td>
<td>11</td>
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<tr>
<td>Stage 2</td>
<td>57</td>
<td>—</td>
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</tr>
<tr>
<td>Stage 3</td>
<td>4</td>
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<td>2</td>
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<tr>
<td>Right eye</td>
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<td>73</td>
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</tr>
<tr>
<td>Left eye</td>
<td>33</td>
<td>83</td>
<td>18 ROP</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>9 no ROP</td>
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</table>
interaction was independent of GA and BW, neither of which were correlated with foveal width ($P = 0.11$, $P = 0.30$). Exceptions to this trend were observed in 14.3% of infants without ROP (where foveal width increased $5\%$ per week) and 18.2% of infants with ROP (where foveal width decreased $5\%$ per week). For the three infants where ROP regressed, one infant showed an increase in foveal width (i.e., $5\%$ per week between 32 and 37 weeks PMA), whereas two infants remained the same ($<5\%$ change per week).

The difference in trajectories with ROP absent and present resulted in a significant difference for the earliest PMA. On average, when ROP was present, foveal width was 76% of the value when ROP was absent at 32 weeks PMA (mean $\pm$ SE: $1,203.6 \pm 84.40 \mu m$ compared with $1,584.9 \pm 77.25 \mu m$, respectively).

The results for the other foveal parameters as described above are shown (see Supplemental Digital Contents 5–9, http://links.lww.com/IAE/B47, http://links.lww.com/IAE/B48, http://links.lww.com/IAE/B49, http://links.lww.com/IAE/B50, and http://links.lww.com/IAE/B51, respectively) (see also Figures 2 and 3 to directly compare changes in parameters with PMA). In contrast to foveal width, absence or presence

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**Fig. 2.** Foveal parameters (A), predicted mean fits (with 95% confidence intervals) of statistical models adjusted for GA for change with PMA: (B) foveal width, (C) area, (D) depth, and (E) CFT. Predicted mean fits are displayed for GA 24, 26, 28, and 30 weeks illustrated using colored lines, with matching shaded regions representing 95% confidence intervals of the mean. Absence/presence of ROP was only significant for foveal width, and hence plots for these two conditions are displayed in (B).
of ROP had no statistically significant effect on other parameters.

Parameters significantly correlated with gestational age and birthweight. Both GA and BW were significantly correlated with increasing foveal area \((P < 0.001, P = 0.004)\) (see Supplemental Digital Content 5, http://links.lww.com/IAE/B47), depth \((P < 0.001, P = 0.001)\) (see Supplemental Digital Content 6, http://links.lww.com/IAE/B48), slope \((P < 0.001, P = 0.009)\) (see Supplemental Digital Content 8, http://links.lww.com/IAE/B50), and pRT \((P < 0.001, P = 0.013)\) (see Supplemental Digital Content 9, http://links.lww.com/IAE/B51). However, only GA was a significant predictor for CFT \((P < 0.001)\) (see Supplemental Digital Content 7, http://links.lww.com/IAE/B49), which decreased with increasing GA.

Other variables. Sex, ethnicity, and birth (single/multiple) were not significant predictors for any parameter in either model using GA or BW. The steepest foveal slope was greater in the right eye compared with the left eye \((P < 0.01)\) (see Supplemental Digital Content 8, http://links.lww.com/IAE/B50). The nasal aspect of the fovea was significantly steeper \((P = 0.001)\) and pRT significantly thicker \((P < 0.001)\) compared with the temporal aspect (see Supplemental Digital Contents 8 and 9, http://links.lww.com/IAE/B50 and http://links.lww.com/IAE/B51) respectively.

Significant changes with postmenstrual age. All foveal parameters had significant dynamic mean rates of change with increasing PMA using both predictive models \((P \leq 0.01)\). Foveal depth (see Supplemental Digital Content 6, http://links.lww.com/IAE/B48), CFT (see Supplemental Digital Content 7, http://links.lww.com/IAE/B49), and steepest slope (see Supplemental Digital Content 8, http://links.lww.com/IAE/B50) all demonstrated significant nonlinear changes with PMA that were modelled with a quadratic term. The change in parameters with PMA are shown dynamically in the video animation (see Supplemental Digital Content 10, http://links.lww.com/IAE/B52) illustrating the change in the DoG model fits of ILM with increasing PMA for ROP and non-ROP groups. Particularly noteworthy is reducing foveal width in the group without ROP, which is not apparent in the group with ROP.

Parafoveal retina. An inverted Gaussian fitted the parafovea more often in the ROP group (75.7%) compared with the non-ROP group (55.5%) (chi-square test: \(P = 0.001)\). This can be observed in the video animation (see Supplemental Digital Content 10, http://links.lww.com/IAE/B69), where the parafovea slopes in more toward the fovea in the ROP group, especially at early PMAs.
**Discussion**

We show that foveal width demonstrates a different trajectory of development depending on the presence or absence of ROP/non-ROP that is independent of GA and BW, factors that are clearly associated with the degree of prematurity. This is evident from a highly significant interaction between presence of ROP and PMA ($P < 0.001$), because of foveal width increasing in the ROP group and decreasing in the non-ROP.
study27 developed a model based on GA, weight gain, torial nature of the risk in prematurity. The e-ROP
ROP could be related to the size of the foveal
width of older children and adults with a history of
Retinopathy of Prematurity
Foveal Width, Foveal Avascular Zone and
gels using GA, BW, weight gain, and color image
is a promising method that could be used with risk mod-
of GA and BW. This suggests that HH-OCT of the fovea
foveal width as an early predictor variable independent
of ROP. Future studies of the inner retinal layers at
the FAZ using OCT during early active development
of ROP may provide more information to explain the
differences we found in foveal width between pre-
term infants with and without ROP.

Foveal Width as a Potential Early Indicator of
Retinopathy of Prematurity
Risk algorithms to identify treatment requiring ROP
(Type 1 ROP) are based on BW, GA, and weight gain as
predictive variables in multivariate logistic regression
models.25 The prospective PINT ROP study26 investi-
gated such a model in extreme low BW infants; how-
ever, one infant with severe ROP, but not requiring
treatment was missed. The authors highlight that factors
associated with ROP in univariate analysis were not sig-
nificant in multivariate analysis underlining the multifac-
torial nature of the risk in prematurity. The e-ROP
study27 developed a model based on GA, weight gain,
respiratory support data, and analysis of color image
findings to predict ROP requiring treatment, producing
risk scores. The results showed that image criteria pre-
dicted treatment requiring ROP better than GA and that
this was best at 34 weeks PMA or earlier. In our study,
we analyzed image characteristics using HH-OCT on
foveal morphology and GA, BW, PMA, and identified
foveal width as an early predictor variable independent
of GA and BW. This suggests that HH-OCT of the fovea
is a promising method that could be used with risk mod-
els using GA, BW, weight gain, and color image
findings.

Foveal Width, Foveal Avascular Zone and
Retinopathy of Prematurity
It has been suggested that differences in the foveal
width of older children and adults with a history of
ROP could be related to the size of the foveal
avascular zone (FAZ).28 The FAZ is determined by
an absence of vessels in the macula, and has been
correlated with foveal shape, continuation of the
inner nuclear layer at the fovea, and increased foveal
thickness.24,29–31 Chui et al31 studied 11 healthy
adults and found that a smaller FAZ was associated
with a thicker, narrower fovea. A small FAZ has also
been noted in children aged between the ages of 1
year and 17 years with a history of prematurity.32
Falavarjani et al33 compared the FAZ in 15 preterm
children (including those with ROP) with 11 age-
matched controls between the ages of 4 years and
12 years using OCT angiography. They showed an
abnormal FAZ in preterm children born less than 29
weeks GA. We found a significant correlation
between earlier GA and increased CFT which is
not influenced by diagnosis of ROP, suggesting that
prematurity could result in the development of a
smaller FAZ independently of the diagnosis of
ROP. Future studies of the inner retinal layers at
the FAZ using OCT during early active development
of ROP may provide more information to explain the
differences we found in foveal width between pre-
term infants with and without ROP.

Foveal Parameters Dependant on Gestational Age
and Birthweight
Previous studies in infants and ex-preterm children
including ROP, report increased CFT with ROP,
which is in contrast to our study, where CFT was
independent of ROP. However, these conclusions are
based on studies comparing preterm with full-term
children,19 small numbers of non-ROP children,8 trea-
ted preterm children with ROP,21 or retrospective
data.23,34,35

Our results on GA and CFT in preterm infants are
in keeping with previous reports of older ex-preterm
children that describe an association between CFT
with GA, but not with diagnosis of ROP.36–40 Tariq
et al39 showed that both GA and BW were signifi-
cant predictors for increased foveal retinal thickness.
Similarly, Bowl et al40 reported a cross-sectional
analysis of RT at the foveal center and found inverse
correlation between GA and BW with total retinal
thickness in preterm children with and without ROP
compared with full-term born children aged between
6 years and 13 years. However, by using separate
predictor models, we found only a relationship for
GA and not for BW, which is in contrast with these
large studies of older preterm children. This may
reflect either a change in foveal thickness between
preterm birth and foveal maturity in childhood or
differences in sample size.
Our finding of a greater early GA effect on CFT supports that of Wang et al\textsuperscript{38} who suggested that before 28 weeks GA, there is an increased likelihood of delayed migration of the inner retina away from the foveal center with persistence of the inner retina and increased CFT. A recent investigation by Mollan et al\textsuperscript{41} reported a strong association between central macular thickness and GA before 27 weeks in preterm children, after adjusting for ROP and sex. We also found that GA interacts with foveal depth similar to Rosen et al,\textsuperscript{42} who investigated foveal depth in preterm children aged 6.5 years including ROP. The correlation of increased CFT and reduced foveal depth with early GA in both preterm infants and older former preterm individuals suggests that extreme preterm birth interferes with the normal mechanisms of inner centrifugal retina migration at the fovea.

**Differences due to Sex and Ethnicity**

Adults with normal foveae show differences between race and sex,\textsuperscript{43} male gender being associated with increased central macular thickness in preterm children.\textsuperscript{41} Our results present no differences in foveal dimensions between Caucasians and non-Caucasians, multiple/single birth infants, or sex, possibly because changes are not present in very early foveal development or because of insufficient numbers to reach significance.

**Limitations**

Limitations of this study include conducting our study using one horizontal scan through the central fovea without analysis of the entire volume of the fovea. Also, we did not incorporate specific systemic confounders in our analysis such as oxygen therapy or illness with each individual, and it is known that these may relate to the severity and development of ROP. To adjust for the variability between the ROP and non-ROP groups for systemic factors, a larger number of participants would be needed to adjust for each disease category and oxygen delivery method.

A number of infants included in this study (n = 19) were only successfully scanned on one visit, although 78% (n = 68) were imaged ≥2 times and 49% (n = 43) infants were imaged ≥3 times. To investigate changes with time more systematically, it would be useful to develop a more consistent repeated scanning protocol for future studies.

We also did not incorporate FAZ measurements from fluorescein angiography in our investigation, because we were primarily concerned with modelling foveal morphology using OCT. The advent of portable OCT angiography in vivo would further our understanding of the relationship between ROP, the FAZ, and the foveal development.

**Conclusions**

Foveal width in early PMA appears to have a significant relationship with ROP when adjusting for GA and BW. Further study may determine whether this has the potential to predict Type 1 ROP during screening using HH-OCT. The finding that only GA significantly influences CFT, supports the view that early birth interferes with inner retinal migration at the fovea, despite continuing development of the fovea. The EPICure@19 Study\textsuperscript{44} has reported a correlation between increased retinal thickness with a reduction in best-corrected visual acuity in adults born extremely preterm. The best-corrected visual acuity reduction was found to be similar in untreated ROP and non-ROP, suggesting that prematurity and not presence of ROP per se, has an impact on retinal thickness and vision.

A longitudinal HH-OCT study grading foveal morphology, GA, and visual acuity could be useful in understanding the changes that occur during visual development and in the management of children who are born preterm.

Key words: foveal morphology, hand-held optical coherence tomography, prematurity, preterm infant.

**Acknowledgments**

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**References**


