

1 **Systemic Effects of Optos versus Indirect Ophthalmoscopy for Retinopathy**
2 **of Prematurity Screening**

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26 **Unstructured abstract**

27 A prospective randomised cross over study demonstrating for the first time that
28 bedside retinopathy of prematurity screening is more stressful with the Optos
29 California than with conventional binocular indirect ophthalmoscopy.

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50 Many regions of the world have a relative shortage of ophthalmologists trained
51 and willing to screen for retinopathy of prematurity (ROP).¹ As a result, many
52 regions have turned to retinal imaging and telemedicine.² Optos ultra-widefield
53 retinal imaging (Optos PLC, Dunfermline, UK) has recently been used as a
54 screening tool for ROP.^{3,4} However, there is no data available regarding the
55 systemic effects or stress induced by an ROP screening examination with the
56 Optos. In this prospective randomised cross over study we determined the
57 effects of Optos ultra-widefield screening examination on cardiorespiratory
58 indices, as a measure of stress, and compared the stress response to that of
59 conventional binocular indirect ophthalmoscopy (BIO) examination. The East
60 Midlands Leicester South Research Ethics Committee granted permission to
61 undertake the study. Written informed consents were obtained from the
62 mothers of all infants involved in the study. The study adhered to the tenets of
63 the Declaration of Helsinki.

64 Any infants born at ≤ 32 week's gestation or weighing ≤ 1500 grams at birth were
65 included. Each infant underwent bedside examination with the Optos California
66 (Optos) and BIO for all of its scheduled screening sessions. The order of the
67 examination methods performed was determined by randomisation via sealed
68 envelopes prepared remotely by a member of the team not involved in the
69 recruitment or screening of infants. Mydriasis was achieved with cyclopentolate
70 0.5% and phenylephrine 2.5% instilled in each eye at 30 minutes prior to
71 examination commencing. Optos examination began with the instillation of
72 proxymetacaine 0.5% into each eye followed by placement of a speculum in the
73 right eye. The infant was gently lifted out of the incubator or cot and held upright
74 to the Optos. Pseudocolour retinal images were acquired and the speculum was

75 then transferred to the fellow eye. Once images were captured from the fellow
76 eye, the speculum was removed and the examination was deemed complete. BIO
77 examination began with the instillation of proxymetacaine 0.5% into each eye
78 followed by insertion of a speculum in the right eye. A 28-diopter lens was used
79 together with an indirect ophthalmoscope to examine the retina of the infant in
80 the supine position. The speculum was then transferred to the fellow eye and the
81 retinal examination was repeated. Scleral indentation was not used. Once the
82 examination was completed in the fellow eye, the speculum was removed and
83 the examination was deemed complete. One neonatology nurse recorded
84 observations of SaO₂, HR in beats per minute, and respiratory rate (RR) in
85 breaths per minute on data collection forms for each examination method. SaO₂
86 and HR were measured using pulse oximetry, whereas the RR was recorded
87 manually. All of the above cardiorespiratory indices were recorded immediately
88 before instillation of topical anesthesia into both eyes (baseline values),
89 immediately after insertion of the speculum into the first eye to be examined,
90 immediately after the start and completion of the examination, and 10 minutes
91 after the completion of the examination. The examination time, measured from
92 the time of instillation of anesthetic drops to the removal of the speculum from
93 the second eye examined, was recorded for each examination method.

94 The results of 50 screening examinations with the Optos and BIO on 26 infants
95 (16 males and 10 females) were analysed. Of the 26 infants screened, two infants
96 had stage 3 ROP and one infant had stage 1 ROP. The rest of the infants had no
97 ROP. The mean gestational age was 27.9 weeks (standard deviation [SD], 2.2;
98 range, 24-34) and the mean birth weight was 1135 g (SD, 375.8; range, 684-
99 2110). The mean postnatal age at the time of examination was 34.5 weeks (SD,

100 2.2; range, 28-39). There was a median of two screening examinations per infant
101 (range, 1-4). Of the 50 screening examinations, 50% were randomised to have
102 the ROP screening examination starting with the Optos followed by BIO.

103 The cardiorespiratory indices over time for the two examination methods are
104 shown in Figure 1. Using the paired T-test, none of the three cardiorespiratory
105 indices varied significantly at baseline between the Optos and BIO. Some infants
106 in the study underwent more than one screening examination with the Optos
107 and BIO. Additionally, some infants underwent repeated measurements from
108 each screening examination, due to both multiple timepoints and measurements
109 by two examination methods. To account for this, a three level model linear
110 regression analysis was used with individual measurements nested within
111 individual screening examinations, which in turn was contained within infants.

112 By using multilevel linear regression analysis, we found no significant difference
113 in HR or RR between the two examination methods ($P = 0.49$ and $P = 0.56$,
114 respectively). However, a significant difference in SaO₂ ($P = 0.04$) between the
115 examination methods was found. The Optos examination method gave lower
116 SaO₂ values, with values being, on average, 0.8% lower for the Optos group than
117 for the BIO group. Handling of the infants required to position for image capture
118 with the Optos may explain this finding. Mean examination times were 3.0
119 minutes (SD, 0.7) in the Optos group and 1.8 minutes (SD, 0.5) in the BIO group
120 ($P < 0.001$). The longer duration of screening examination with the Optos might
121 be a contributing factor to the lower SaO₂ levels found when compared to BIO
122 examinations. No episodes of clinically significant bradycardia (HR < 100 beats
123 per minute) or respiratory distress (RR < 30 breaths per minute) occurred
124 during or after any screening examinations with the Optos or BIO. Of the 50

125 screening examinations, 5 (10%) in the Optos group and only 1 (2%) in the BIO
126 group developed clinically significant oxygen desaturation ($\text{SaO}_2 < 85\%$) during
127 examination, precluding statistical analysis. No additional supplemental oxygen
128 administration to the infants during these screening examinations was required
129 as SaO_2 levels increased spontaneously or with stimulation. All episodes of
130 clinically significant oxygen desaturation occurred for screening examinations
131 performed in infants in the intensive care unit of the neonatology department.
132 Limitations of our study include firstly the small number of infants in a single
133 center. Further studies with larger number of infants are required to verify our
134 findings. Secondly, our institution provides only level 2 neonatal care and our
135 study population may not be generalisable to sicker infants with more co-
136 morbidities. Thirdly, the majority of the infants screened in this study had no
137 ROP. Examination with BIO in this study may therefore have been less extensive
138 or caused less distress to the infants than would normally be experienced in
139 neonatology units that have infants with more severe forms of ROP. Finally,
140 further studies that measure both the physiological and behavioural responses of
141 stress are required to determine the complete stress response of infants to
142 screening with the Optos.

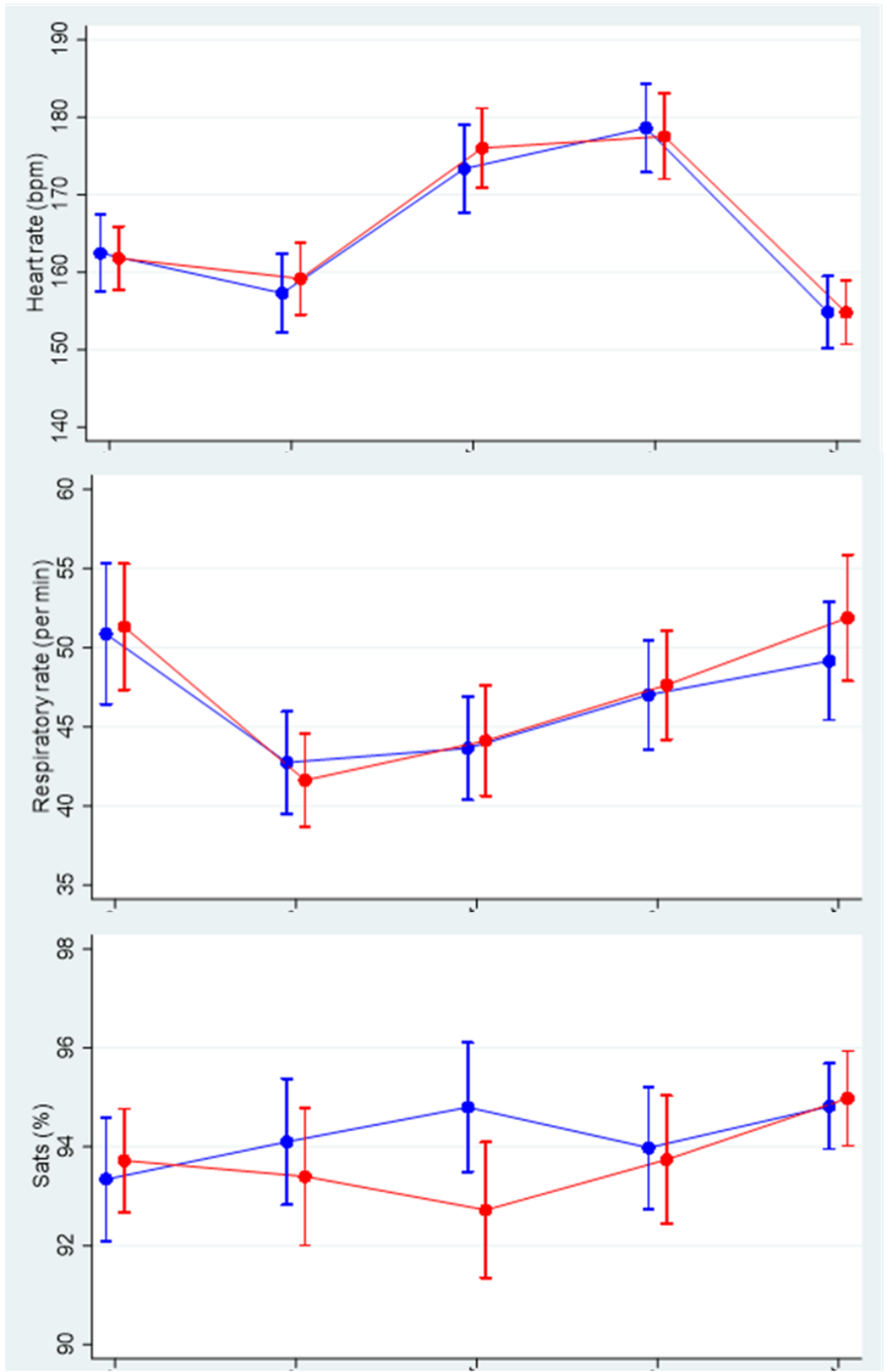
143 In summary, the statistical difference in SaO_2 and the difference in the number of
144 clinically significant oxygen desaturations found may indicate that ROP
145 screening is more stressful with the Optos than with BIO. Careful handling and
146 close monitoring of SaO_2 should be performed when the Optos is used for
147 bedside screening. Greater attention should be paid to the sicker infants in the
148 intensive care unit who seem to be the most vulnerable to clinically significant
149 oxygen desaturations with the Optos examination.

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Baseline During screening During imaging After screening 10 min. later

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167 **Figure 1. Cardiorespiratory indices during OPTOS and BIO examinations**

168 Recordings during BIO are represented in blue and during OPTOS in red.

169 bpm, beats per minute; Sats, oxygen saturation level