Supplemental Online Content

Mangalesh S, Sarin N, McGeehan B, et al; BabySTEPS Group. Preterm infant stress during handheld optical coherence tomography vs binocular indirect ophthalmoscopy examination for retinopathy of prematurity. *JAMA Ophthalmol*. Published online April 1, 2021. doi:10.1001/jamaophthalmol.2021.0377

eMethods.

eTable 1. List and description of events collected for optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination during the study

eTable 2. Intra-observer reproducibility results for both the observers for the collection of stress factors in 5 infants with 11 examinations during optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO)

eTable 3. Baseline characteristics of the study cohort and categories of respiratory support used during the optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination for retinopathy of prematurity screening

eTable 4. Occurrence of stress events for optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination

eTable 5. Comparison of studies reporting the impact of retinopathy of prematurity (ROP) examinations with imaging modalities versus with the standard binocular indirect ophthalmoscopy examination on infant stress

eFigure. Behavioral and physiologic measures of stress at baseline (within 10 minutes before optical coherence tomography (OCT) imaging/binocular indirect ophthalmoscopy (BIO) examination), and during first and second eye OCT imaging/BIO examination

This supplemental material has been provided by the authors to give readers additional information about their work.

eMethods: Enrollment of infants to the stress sub-study

Enrollment for BabySTEPS was from August 2016 through November 2019. The stress sub-study included 26 consecutive infants enrolled June 25-November 30, 2019; eight transferred, were discharged or withdrew from the study and two died, all before OCT imaging. The remaining 16 infants had 73 eligible examination sessions. Per ICN general practice, any unstable infant had BIO first, followed by OCT imaging, if the infant was thought to be stable enough. Thus clinical BIO examinations were performed for all 73 eligible sessions, but for two visits of one infant, OCT imaging--a research activity--was deferred by the care team due to infant instability, resulting in 71 visits with both OCT imaging and BIO for this sub-study.

eTable 1: List and description of events collected for optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination during the study**.** We included and modified the CRIES neonatal pain measurement score (C-Crying; R-Requires increased oxygen administration; I-Increased vital signs; E-Expression; S-Sleeplessness)[14] based on the ease of access and relevance for the collection of stress factors during OCT imaging and BIO examination in the intensive care nursery.

Variable collected during OCT imaging and BIO modified components based on the CRIES score	Collected at 3-time points	Conventional CRIES
Crying	0=No crying, 1=Moans or cries minimally, 2=Appropriate crying (not irritable), 3=High pitched, 4=Inconsolable,	0=No cry or cry which is not high pitched 1=Cry high pitched but easily consoled 2=Cry high pitched and inconsolable
Facial expression	0=Relaxed with no grimace, 1=Grimace only,	0=No grimace 1=Grimace alone 2=Grimace and grunt
Heart rate	beats per minute	Increased vital signs (Heart rate(HR) and blood pressure(BP)): 0=HR & BP unchanged or less than baseline 1=HR or BP increased <20% 2=HR or BP increased >20%
Respiratory rate	breaths per minute	Not included
O_2 saturation	percentage	Requires O_2 for saturation >95%: 0=No oxygen required 1=<30% oxygen required 2=>30% oxygen required
Stress Events based on preset alarms for each infant	Bradycardia Tachycardia Oxygen desaturation	Sleepless: 0=Continuously asleep 1=Awakened at frequent intervals 2=Awake constantly
Additional variables collected for each visit		
Pharmacological dilation	Yes/No	
Lid speculum	Yes/No	

Lubricant	Yes/No If yes, a. preservative-free artificial tears b. preservative-free artificial gel
Oral Sucrose	Yes/No
Pacifier	Yes/No
Number of examiners	Number
Time between two exams	in minutes
Examination performed first	1=BIO 2=OCT
Enteral nutrition status	1= *nil per os* 2=Partial enteral feeds 3=Full enteral feeds
Respiratory Support	1=Ventilator 2=Continuous positive airway pressure 3=Nasal cannula 4=No support

eTable 2: Intra-observer reproducibility results for both the observers (SM, NS: same observers as the primary stress study) for the collection of stress factors in 5 infants with 11 examinations during optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO). There was 100% agreement for all categorical variables collected including pharmacological dilation, use of comfort aids, respiratory support, infant cry score, facial expression score and occurrence of bradycardia, tachycardia and oxygen desaturation.

Examination	Measure	Mean Difference	Standard deviation	Lower LOA	Upper LOA	ICC
OCT	Heart rate (beats per minute)	1.12	3.59	-5.92	8.16	0.98
	Oxygen saturation (%)	-0.27	1.74	-3.68	3.13	0.89
	Respiratory rate (breaths per minute)	0.00	8.29	-16.25	16.25	0.93
BIO	Heart rate (beats per minute)	2.27	8.39	-14.17	18.71	0.94
	Oxygen saturation (%)	-0.18	1.47	-3.07	2.71	0.95
	Respiratory rate (breaths per minute)	0.21	8.46	-16.37	16.80	0.74
LOA: limits of agreement; ICC: Intraclass correlation coefficient						

eTable 3: Baseline characteristics of the study cohort and categories of respiratory support used during the optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination for retinopathy of prematurity screening.

Characteristic	N= 16 infants
Gestational age in weeks, mean (SD)	27 (3)
Birth weight in grams, mean (SD)	869 (277)
Male, n (%)	8 (50)

Race, n (%)
    African American
    White
    Mixed
	
	7 (44)
	7 (44)
	2 (12)

Ethnicity, n (%)
    Hispanic
    Non-Hispanic
	
	3 (18)
	13 (82)

Postmenstrual age at examination (weeks),
    Mean (SD)
    Median (Range)
	
	39 (4)
	38 (31-51)

The time between exams, minutes,
    Mean (SD)
    Median (Range)
	
	32 (32)
	17 (1-130)

	Episodes of OCT imaging and BIO examination (N=71)

Exam performed first, n (%)
    OCT Imaging
    BIO
	
	44 (62)
	27 (38)

Respiratory support status at time of exam, n (%) Ventilator	 1 (1)
Continuous positive airway pressure	7 (10)
Nasal cannula	25 (35)
No respiratory support	38 (54)

Enteral nutrition status, n (%)
    nil per os
    Partial enteral feeds
    Full enteral feeds
	
	5 (7)
	31 (44)
	35 (49)

eTable 4: Occurrence of stress events for optical coherence tomography (OCT) imaging and binocular indirect ophthalmoscopy (BIO) examination

	OCT imaging (N=71)	BIO exam (N=71)	P-value
Bradycardia			.33
Yes	3 (4%)	1 (1%)	
No	68 (96%)	70 (99%)	
Tachycardia			.06
Yes	1 (1%)	8 (11%)	
No	70 (99%)	63 (89%)	
O$_2$ desaturation			.77
Yes	8 (11%)	9 (13%)	
No	63 (89%)	62 (87%)	

eTable 5: Comparison of studies reporting the impact of retinopathy of prematurity (ROP) examinations with imaging modalities versus with the standard binocular indirect ophthalmoscopy examination on infant stress

Study by first author and (year published)	Objective	Study arms and modalities	No. of infants	GA, weeks Mean (SD)	BW, grams Mean (SD)	PMA at examination, weeks Mean (SD)	Measurement time points	Outcome measures	Results
Studies monitoring stress during exam									
Current Study (2020)	Evaluate preterm infant stress during ROP examination with OCT imaging versus BIO examination	All infants had both modalities: OCT imaging and BIO examination	16 (71 visits)	27 (3)	869 (277)	39 (4)	1. Before exam/imaging: baseline (10 min) 2. During first eye OCT imaging/BIO examination 3. During second eye OCT imaging/BIO examination	1. Cry 2. Facial expression 3. Heart rate 4. Respiratory rate 5. Oxygen saturation Stress events: bradycardia, tachycardia, desaturation (based on preset alarms for each infant)	Lower change in cry, facial expression & heart rate from baseline to during first and second eye OCT imaging/BIO examination Stress events: 12 with OCT and 18 with BIO OCT less stressful than BIO examination
Fung et al[26] (2018)	Effect of Optos ultrawide-field upright ("flying-baby pose") screening on cardiorespiratory indices with that of conventional BIO	All infants had both modalities: Optos imaging and BIO exam	26 (50 visits)	28 (2)	1135 (376)	34.5 (2)	1. Baseline: before topical anesthesia 2. Immediately after insertion of speculum into the 1st eye 3. after start & completion of imaging/exam	1. Heart rate 2. Respiratory rate 3. Oxygen saturation	Clinically significant desaturation (<85%) in 10% of the Optos group and 2% of the BIO examination group Optos is more stressful than BIO examination

	examination for ROP						4. 10 min after		
Wade et al[24] (2015)[#]	Adverse events associated with ROP evaluation procedures (BIO+ RetCam imaging)	All infants had both modalities : BIO exam and RetCam imaging	1257	27	864	36.3 (2.6)	1. 12 hours before exam 2. During exam/imaging 3. 12 hours after exam	1. Apnea, Bradycardia, Hypoxia 2. Tachycardia 3. Emesis 4. Epistaxis 5. Retinal hemorrhage	Adverse events during exam: 8% during ophthalmoscopy, 15% during RetCam imaging BIO and RetCam imaging performed together is safe

Dhaliwal et al[25] (2010)	Compare the pain effects of BIO exam and wide- field digital retinal imaging (RetCam) screening for ROP	All infants had both modalities : RetCam imaging and BIO exam	76	29 (24-35)*	1208 (610-1970)*	34 (30-40)*	1. Baseline
							2. During exam /imaging
								PIPP score
								  a. Gestational age
								  b. Behavioral state
								  c. Heart rate & oxygen
								     saturation
								  d. Facial actions
									Greater increase in heart rate during RetCam than during BIO exam.
									
									RetCam imaging and BIO exam with eyelid speculum are similarly painful.

Mukherjee et al[28] (2006)	Effect of RetCam screening versus BIO	Group 1: RetCam	52	28 (2)	1112 (370)	36 (2)	1. Immediately before speculum	1. Mean arterial blood Pressure 2. Heart rate	Significant impact on cardiorespiratory indices with both techniques. However,

	exam on cardiovascular indices as a measure of stress (2 ICN units)	Group 2: BIO exam	34	28.5 (2)	1088 (263)	36 (2)	insertion 2. During exam/imaging 3. 1 hour after	3. Oxygen saturation 4. Respiratory rate	RetCam was associated with less stress compared to BIO exam
**Studies monitoring stress before and after exam**									
Prakalapakorn et al[20] (2018)	Evaluate the safety profile of imaging with a non-contact retinal camera compared to the BIO examination	All infants had both modalities: BIO and Pictor (non-contact retinal camera)	99	-	-	26-51*	1. Before exam: midnight to when dilating eye drops instilled 2. From completion of exam/imaging for 10 minutes following exam And 10 minutes following imaging	1. Bradycardia <80bpm, 2. Tachycardia >230bpm 3. Desaturation <80% 4. Apnea >20 seconds.	Safety events occurred after 0.8% (n=1) of imaging sessions and 5.8% (n=18) of clinical examinations Less safety events after the Pictor imaging when compared to after the BIO examination
Moral-Pumarega et al[27] (2012)	Compare pain and stress responses measured with specific assessment scales when performing wide-field digital retinal imaging (RetCam) and	All infants had both modalities: RetCam imaging first and BIO exam after an interval of 3 to 5 days	24 (70 visits)	27 (2)	895 (171)	6^ (1)	1.Baseline (prior to application of cycloplegic) 2. 30 seconds after Exam/imaging 3. 1 hour after exam/imaging 4. 24 hours after exam/imaging	1. PIPP score 2. CRIES score	Lower mean (SD) PIPP, 6.2 (1.9) vs 7.4 (2.3)) and CRIES score, 1.6 (1.1) vs 2.5 (1.4)) at 30 seconds after RetCam versus after BIO examination Less pain and stress after RetCam when compared to BIO

	BIO examination								examination at 30 sec after

GA: Gestational age; BW: Birth weight; SD: Standard deviation; BIO: Binocular indirect ophthalmoscopy; OCT: Optical coherence tomography; PIPP: Premature Infant Pain Profile; CRIES: Crying, Requires oxygen, Increased vital signs, Expression and Sleeplessness

[#]e-ROP study;

*Range;

^Mean postnatal age

eFigure: Behavioral (a,b) and physiologic (c,d,e) measures of stress at baseline (within 10 minutes before optical coherence tomography (OCT) imaging/binocular indirect ophthalmoscopy (BIO) examination), and during first and second eye OCT imaging/BIO examination. (a,b) represent the percentage of cry and facial expression score at baseline and each eye exam. (c,d,e) represent box and whisker plots showing the median, first quartile, third quartile, maximum and minimum values of heart rate, respiratory rate and oxygen saturation at the three timepoints. All values are comparable at baseline except respiratory rate **(Table 2)**.