

REPRODUCIBILITY OF FETAL BIOMETRY AND DOPPLER FOR DIAGNOSIS OF LATE FETAL GROWTH RESTRICTION

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Background	Key Results	Table 1 – Intra- and Interobserver Reproducibility	Table 2 – Validation Sensitivity Analysis																																																																																																																	
Fetuses with late growth restriction (FGR) have higher risk of poor outcomes than appropriately grown fetuses, including increased risk of stillbirth, neonatal death and neonatal unit admission. Ultrasound detection and monitoring is the mainstay of clinical management. Reproducibility of ultrasound parameters significantly contributes to variation in centile calculations and diagnostic accuracy. ISUOG guidelines aim to improve reproducibility by defining cross-sectional planes and referring standards of variability. Previous reproducibility studies have not investigated variability in FGR fetuses exclusively. Given that guidelines on timing of delivery depend on these measurements, it is crucial to know how reliable they are. Aim: To report intra- and interobserver reproducibility of ultrasound biometry and Doppler parameters for diagnosis of late FGR, and to produce standards for quality control.	Mean systematic differences: <4 g (EFW) • <1 mm (AC) • <0.03 (Dopplers) 95% LOA: <250 g (EFW) • <16 mm (AC / AC drop) • <14% all biometry EFW interobserver: - Hadlock-4: 221 g (11.5%), z ±0.68 - INTERGROWTH-21st: 249 g (13.8%), z ±0.89 - Hadlock significantly narrower than IG-21st (p<0.05) AC interobserver: 95% LOA 15.6 mm (5.7%), z ±0.87–0.98 (Chitty / IG-21st) No significant difference between chart methods Doppler ratios: - UCR equally reproducible to CPR (see Table 1) - CPR interobserver LOA significantly wider than intraobserver (p=0.041)	<table><tr><th>Parameter</th><th>Observer</th><th>Mean diff (g / mm / abs)</th><th>95% LOA (g / mm / abs)</th><th>95% LOA (%)</th><th>95% LOA (z-score)</th></tr><tr><td rowspan="2">EFW Hadlock</td><td>Intra</td><td>−2.5 g</td><td>177 g</td><td>9.1%</td><td>±0.54</td></tr><tr><td>Inter</td><td>−1.6 g</td><td>221 g</td><td>11.5%</td><td>±0.68</td></tr><tr><td rowspan="2">EFW IG-21st</td><td>Intra</td><td>−3.0 g</td><td>191 g</td><td>10.5%</td><td>±0.68</td></tr><tr><td>Inter</td><td>4.2 g</td><td>249 g</td><td>13.8%</td><td>±0.89</td></tr><tr><td rowspan="2">AC Chitty</td><td>Intra</td><td>−0.1 mm</td><td>11.8 mm</td><td>4.3%</td><td>±0.66</td></tr><tr><td>Inter</td><td>0.2 mm</td><td>15.6 mm</td><td>5.7%</td><td>±0.87</td></tr><tr><td rowspan="2">AC IG-21st</td><td>Intra</td><td>−0.1 mm</td><td>11.8 mm</td><td>4.3%</td><td>±0.76</td></tr><tr><td>Inter</td><td>0.2 mm</td><td>15.6 mm</td><td>5.7%</td><td>±0.98</td></tr><tr><td rowspan="2">AC drop Chitty</td><td>Intra</td><td>0.2 c</td><td>12.5 c</td><td>N/A</td><td>±0.66</td></tr><tr><td>Inter</td><td>−0.8 c</td><td>16 c</td><td>N/A</td><td>±0.80</td></tr><tr><td rowspan="2">UCR</td><td>Intra</td><td>0.00</td><td>0.21</td><td>N/A</td><td>±0.79</td></tr><tr><td>Inter</td><td>0.00</td><td>0.24</td><td>N/A</td><td>±0.92</td></tr><tr><td rowspan="2">CPR</td><td>Intra</td><td>0.02</td><td>0.61</td><td>N/A</td><td>±1.48</td></tr><tr><td>Inter</td><td>−0.03</td><td>0.72</td><td>N/A</td><td>±1.75</td></tr></table> <i>EFW: estimated fetal weight; IG-21st: INTERGROWTH-21st; AC: abdominal circumference; c: centile drop; UCR: umbilical cerebral ratio; CPR: cerebroplacental ratio.</i>	Parameter	Observer	Mean diff (g / mm / abs)	95% LOA (g / mm / abs)	95% LOA (%)	95% LOA (z-score)	EFW Hadlock	Intra	−2.5 g	177 g	9.1%	±0.54	Inter	−1.6 g	221 g	11.5%	±0.68	EFW IG-21st	Intra	−3.0 g	191 g	10.5%	±0.68	Inter	4.2 g	249 g	13.8%	±0.89	AC Chitty	Intra	−0.1 mm	11.8 mm	4.3%	±0.66	Inter	0.2 mm	15.6 mm	5.7%	±0.87	AC IG-21st	Intra	−0.1 mm	11.8 mm	4.3%	±0.76	Inter	0.2 mm	15.6 mm	5.7%	±0.98	AC drop Chitty	Intra	0.2 c	12.5 c	N/A	±0.66	Inter	−0.8 c	16 c	N/A	±0.80	UCR	Intra	0.00	0.21	N/A	±0.79	Inter	0.00	0.24	N/A	±0.92	CPR	Intra	0.02	0.61	N/A	±1.48	Inter	−0.03	0.72	N/A	±1.75	<table><tr><th>Parameter</th><th>N at standard threshold</th><th>95% LOA (z-score)</th><th>Adjusted threshold (z)</th><th>N still meeting criteria (%)</th></tr><tr><td>EFW Hadlock (<10th centile)</td><td>681/843 (80.8%)</td><td>±0.68</td><td>−1.96</td><td>303 (35.9%)</td></tr><tr><td>EFW IG-21st (<10th centile)</td><td>681/843 (80.8%)</td><td>±0.89</td><td>−2.17</td><td>197 (23.4%)</td></tr><tr><td>AC Chitty (<10th centile)</td><td>746/845 (88.3%)</td><td>±0.87</td><td>−2.15</td><td>454 (53.7%)</td></tr><tr><td>AC IG-21st (<10th centile)</td><td>746/845 (88.3%)</td><td>±0.98</td><td>−2.26</td><td>392 (46.4%)</td></tr><tr><td>UCR Arduini (>95th centile)</td><td>35/856 (4.1%)</td><td>±0.92</td><td>2.57</td><td>13 (1.5%)</td></tr></table>	Parameter	N at standard threshold	95% LOA (z-score)	Adjusted threshold (z)	N still meeting criteria (%)	EFW Hadlock (<10th centile)	681/843 (80.8%)	±0.68	−1.96	303 (35.9%)	EFW IG-21st (<10th centile)	681/843 (80.8%)	±0.89	−2.17	197 (23.4%)	AC Chitty (<10th centile)	746/845 (88.3%)	±0.87	−2.15	454 (53.7%)	AC IG-21st (<10th centile)	746/845 (88.3%)	±0.98	−2.26	392 (46.4%)	UCR Arduini (>95th centile)	35/856 (4.1%)	±0.92	2.57	13 (1.5%)
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Study design: Multi-centre prospective cohort study, January–July 2022. Nine tertiary fetal medicine centres across Europe (TRUFFLE-2 trial sites). 164 women recruited. Inclusion criteria: - Age ≥18 years, singleton non-anomalous pregnancy - Gestational age 32+0 to 36+6 weeks - Suspected FGR: EFW and/or AC <10th centile, or >50 centile drop in AC growth velocity Measurements: Two blinded sonographers performed biometry (BPD, HC, AC, FL) and Doppler (UA PI, MCA PI) per ISUOG guidelines. CPR (MCA PI / UA PI) and UCR (UA PI / MCA PI) were calculated. Each measurement obtained twice per operator. Statistics: Bland-Altman plots; mean difference and 95% limits of agreement (LOA) calculated as absolute values, %, z-scores and conditional SD scores (cSDS). Paired t-tests (p<0.05 significant).	Under extreme reproducibility conditions (LOA z-scores applied as adjusted thresholds), fetuses still meeting FGR criteria: EFW Hadlock: 36% (adjusted z = −1.96) EFW IG-21st: 23% (adjusted z = −2.17) AC Chitty: 54% (adjusted z = −2.15) AC IG-21st: 46% (adjusted z = −2.26) UCR (Arduini): 1.5% (down from 4.1%) ~50% reduction in FGR diagnoses under extreme variability — underscoring the need for standardised quality control.																																																																																																																			
UCR versus CPR: Equivalent Reproducibility UCR Intraobserver 95% LOA: ±0.21 (z ±0.79) Interobserver 95% LOA: ±0.24 (z ±0.92) CPR Intraobserver 95% LOA: ±0.61 (z ±1.48) Interobserver 95% LOA: ±0.72 (z ±1.75)* <i>* No significant difference in reproducibility between UCR and CPR. CPR interobserver LOA significantly wider than intraobserver (p=0.041).</i>																																																																																																																				
Conclusions - Ultrasound biometry and Dopplers in suspected late FGR are reproducible and can be relied upon for clinical management decisions. - Reproducibility is comparable to normally grown fetuses, independently of the parameter, formula or centile chart used. - UCR performs equally to CPR, supporting its use as an acceptable alternative in clinical practice and in the TRUFFLE-2 trial. - Standards of reproducibility presented here should be adopted for quality control and standardisation in clinical practice and research. - This is the first study reporting inter- and intra-observer variability for biometry and Doppler exclusively in suspected late FGR.																																																																																																																				