

## Intra- and inter-rater agreement of superior vena cava flow and right ventricular outflow measurements in late preterm and term neonates

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1 **The intra- and inter-rater agreement of superior vena cava flow and right**  
2 **ventricular outflow measurements in late preterm and term infants**

3

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13

14 Short Running Title: Superior vena cava flow and right ventricular outflow  
15 repeatability

16

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28 **Abstract**

29 **Objectives:** To explore the intra- and intra-rater agreement of superior vena cava  
30 flow (SVCF) and right ventricular outflow (RVO) in healthy and unwell late preterm  
31 infants (33-37 weeks gestational age) and term infants ( $\geq 37$  weeks gestational age),  
32 and infants receiving total body cooling.

33

34 **Methods:** The inter- and intra-rater agreement (n=25 and n=41 neonates  
35 respectively) of SVCF and RVO were determined by echocardiography in healthy  
36 and unwell late preterm and term infants using Bland-Altman plots, repeatability co-  
37 efficient (RC), repeatability index (RI) and inter-class co-efficients (ICC).

38

39 **RESULTS:** The intra-rater RI for SVCF was 41% and 31% for RVO with ICCs  
40 indicating good agreement for both measures. The inter-rater RI for SVCF and RVO  
41 were 63% and 51% respectively with ICCs indicating moderate agreement for both  
42 measures.

43

44 **CONCLUSION:** If SVCF or RVO were utilized in the hemodynamic management of  
45 neonates, sequential measurements should ideally be performed by the same  
46 clinician to reduce potential variability.

47

48 **Keywords:** Superior vena cava flow, right ventricular outflow, echocardiography,  
49 agreement

## 50 **Introduction**

51 The use of functional echocardiography has been highlighted as having potential for  
52 providing a better monitoring of the systemic blood flow in the developing circulatory  
53 system in preterm infants [1-3]. If echocardiography is utilized alongside clinical  
54 examination, improvements in the identification of cardiovascular compromise, its  
55 treatment and outcomes have been described [4]. Two common methods of  
56 determining systemic blood flow are right ventricular output (RVO) and superior vena  
57 cava flow (SVCF).

58

59 RVO represents the flow of blood returning to the right side of the heart and in the  
60 absence of intra-cardiac shunts, systemic blood flow [5,6]. A RVO measurement of  
61 less than 150ml/kg/min or decreases by up to 50% in septic infants is associated  
62 with increased morbidity and mortality [5-8]. The agreement of this technique is good  
63 with intra-rater differences in RVO diameter being reported to be as low as 4% [9].

64

65 SVCF has been proposed as a better measure of systemic blood flow because it is  
66 unaffected by intra-cardiac shunting such as the patent foramen ovale [10]. The  
67 interest in this method of measuring systemic blood flow has arisen from the  
68 association of low SVCF (<41ml/kg/min) and intraventricular hemorrhage in  
69 extremely preterm infants [4,10,11]. The agreement of this technique has been  
70 questioned in the literature as measurements of the SVC diameter are sometimes  
71 difficult to capture because of an infant's inflated lungs interfering with the ultrasound  
72 image acquisition. Moreover due to the lack of muscle within the venous vessel wall,  
73 and compression of the vessel by the aorta, the cross sectional area might is not  
74 truly circular [10,12]. Multiple volume time integral (VTi) measurements must be

75 taken into account for the variation seen with spontaneous respiration [13].  
76 Nevertheless, the intra- and inter-rater agreement is quoted to be as low as 8-17%  
77 and 14-29% respectively in extremely preterm and healthy term infants [14].  
78

79 Previous research has shown that HIE, its treatment with total body cooling or  
80 medications such as anti-seizure medication can lower an infant's heart rate, alter  
81 their behavior of the infant such as increased sedation [15,16]. These factors can  
82 significantly alter the eventual systemic blood flow measurement gained through its  
83 calculation or the ability to obtain accurate images respectively. As the side effects  
84 may potentially mitigate the variability that heart rate and infant behavior may have  
85 on the components of RVO and SVCF it appears to be an appropriate population to  
86 assess agreement.

87  
88 The physiology of the transitional circulation has not been well explored in late  
89 preterm infants [17]. Non-invasive measures such as SVCF and RVO therefore  
90 appear appropriate assessment that would be used in the exploration of this. Thus,  
91 their agreement should be formally assessed.

92  
93 The agreement of SVCF and RVO has yet to be explored in healthy and unwell late  
94 preterm infants (33-37 weeks gestational age) or healthy and unwell term infants  
95 including those who are receiving total body cooling for hypoxic ischemic  
96 encephalopathy (HIE). The aim of this study was therefore to determine the intra-  
97 and inter-rater agreement of RVO and SVCF in these age groups.

## 98 **Materials and Methods**

99 This study included infants recruited to three prospective cohort studies investigating  
100 the use of echocardiographic measures of systemic blood flow over the first three  
101 days of life (The NeoAdapt 1, 2 and 3 studies). The NeoAdapt 1 study included  
102 infants born later than 33 weeks gestational age within 72 hours of birth receiving  
103 either routine care on the post-natal ward or special care on the Neonatal Unit of a  
104 tertiary centre [18]. The NeoAdapt 2 study included neonates born older than 33  
105 weeks gestational age within 72 hours of birth receiving intensive care on the  
106 Neonatal Unit of the same centre [18]. The NeoAdapt 3 study included infants born  
107 older than 36 weeks gestational age within 72 hours of birth receiving cooling  
108 therapy for HIE according to criteria set out by the “TOBY Trial” and local clinical  
109 guidelines [19]. A convenience sampling method was used for all three studies.  
110 Infants were excluded if they were considered to be non-viable, had congenital  
111 hydrops, cardiovascular malformations, believed to have chromosomal abnormalities  
112 or considered for surgical treatment within 72 hours of birth. Informed written consent  
113 was received from parents after the birth of an eligible infant.

114

115 Ethical approval for each study was gained from the City and East London National  
116 Research Ethics Committee. The protocols for each study were published on the  
117 website Clinicaltrials.gov (ClinicalTrials.gov Identifier: NCT02047916, NCT02051855  
118 and NCT02051894). Each study was adopted by the UK Clinical Research Network  
119 Study Portfolio (Study IDs: 16826, 16767 and 16768).

120

121 *2.1. Echocardiographic measures*

122 SVCF and RVO measurements were acquired using a HD11 XE (Phillips  
123 Healthcare, The Netherlands) ultrasound machine using a SD12-4 phased array  
124 probe. SVCF and RVO measurements were taken according to methods previously  
125 described in the literature [5,10,20]. SVCF VTi measurements were taken from a low  
126 subcostal view with pulsed Doppler measurements placed at the junction of the  
127 superior vena cava and the right atrium. Up to 10 VTi measurements were taken and  
128 the mean calculated in order to account for respiratory variation seen in SVCF. The  
129 diameter of the SVC was measured in M-mode in a true sagittal left mid parasternal  
130 window. Up to 10 measurements of the maximum and minimum diameter (5 each) of  
131 the SVC were used and the mean calculated (Figure 1).

132

-Insert Figure 1 Here-

134

135 RVO VTi measurements were gained from a modified parasternal long axis view of  
136 the heart. Up to 5 VTi measurements were measured and the mean calculated. The  
137 RVO diameter was measured in B-mode from a modified parasternal long axis view  
138 using the hinge points of the pulmonary artery during end systole determined  
139 through a frame by frame analysis of the echocardiographic images taken (Figure 2).

140

-Insert Figure 2 Here-

142

143 Each intra-rater SVCF and RVO measurement was performed on a single participant  
144 by one rater (LM) twice at different time points during a single echocardiographic  
145 assessment. Inter-rater measurements were taken from one participant by two



146 mutually blinded raters, one immediately after the other (LM and RF) during a single  
147 echocardiographic assessment.

148

149 Both raters (LM and RF) are experienced in neonatal echocardiography and have  
150 received specific training in SVCF and RVO echocardiographic measures as part of  
151 the Neo-CIRCulation studies .

152

153 All diameter and VTi measurements were either performed at the bedside using the  
154 inbuilt software on the ultrasound machine or after the examination using Intellispace  
155 PACs Enterprise program (Phillips Healthcare ®™, The Netherlands). In all cases  
156 where only one diameter or VTi measurement was taken by either rater, further  
157 diameter and VTi measurements were performed by one rater (LM) in order to  
158 produce mean values.

159

160 Both SVCF and RVO were calculated using the equation below [10]:

161 
$$Q = \frac{VTi \times HR \times (\pi \times d^2 / 4)}{BW}$$

162  $Q$  = blood flow,  $VTi$  = volume time integral,  $HR$  = heart rate,  $d$  = vessel diameter  
163 and  $BW$  = body weight

164

## 165 2.2. Data Analysis

166 Demographic data of subjects for intra- and inter-rater assessments were compared  
167 using the Mann Whitney U and Chi-Squared tests. Comparisons of heart rates  
168 between intra- and inter-rater echocardiographic measurements was performed  
169 using the Wilcoxon rank test. The agreement of echocardiographic measures was

170 assessed using Bland-Altman plots [21]; these plot the difference between two  
171 measurements on the y-axis against the mean of the two measurements on the x-  
172 axis. The repeatability coefficient (RC) was also calculated from the standard  
173 deviations between measurements multiplied by 1.96. The RC is the maximum  
174 allowed difference between repeated measures for there to be a 95% probability that  
175 the measurements did not occur by chance alone [21,22]. The repeatability index  
176 (RI) can be calculated from this by dividing the repeatability coefficient by the mean  
177 of all values. This is expressed as a percentage with increasing repeatability index  
178 representing poorer repeatability [21,22]. The inter-class coefficients (ICC) were also  
179 calculated for all measurements. ICC is a mean squares analysis of variance that  
180 estimates variability in a set of measures [23]. Intra-rater measurements ICC were  
181 calculated using a two-way mixed model with absolute agreement, with inter-rater  
182 measurements ICC using a two-way random model with absolute agreement. These  
183 were reported according to standard guidance with r-values <0.5 representing “poor”  
184 reliability, values between 0.5 - 0.75 representing “moderate” reliability, values  
185 between 0.75 - 0.9 representing “good” reliability with values >0.9 representing  
186 “excellent” reliability [23]. A p-value of less than 0.05 was considered significant. All  
187 statistical results and graphs were calculated using Prism version 6.05 for Windows  
188 (GraphPad Software, La Jolla California USA) apart from ICC which were calculated  
189 using IBM® SPSS Statistics® Subscription for Mac (Build 1.0.0.580, Armonk, NY:  
190 IBM Corp).

191 **Results**

192 A total of 41 and 25 infants were included for intra- and inter-rater analyses  
193 respectively. The demographic details of the subjects included in the intra- and inter-  
194 rater agreement are outlined in Table 1. The only significant difference noted was the  
195 gestational age of infants included in the intra- and inter-rater analyses. Eight  
196 recordings were excluded from the intra-rater echocardiographic agreement analysis  
197 due to poor image acquisition or problems in accessing images.

198

199 -Insert Table 1 Here-

200

201 Table 2 displays the hearts rates measured between at the time of intra- and inter-  
202 rater echocardiographic measurements. No significant differences were found  
203 between the heart rates of either intra- and inter-rater echocardiographic  
204 measurements.

205

206 -Insert Table 2 Here-

207

208 Table 3 outlines the results of the intra- and inter-rater echocardiographic agreement  
209 analysis. Figures 1, 2, 3 and 4 outlines Bland-Altman plot for intra- and inter-rater  
210 agreement of RVO and SVCF. These plot the difference between two measurements  
211 on the y-axis against the mean of the two measurements on the x-axis.

212

213 -Insert Table 3 Here-

214

215 -Insert Figure 3, 4, 5 & 6 Here-

216

217 Table 3 shows that the ICC for intra-rater measurement for SVC diameter, VTi and  
218 flow were 0.7, 0.85 and 0.88 respectively representing moderate to good reliability.  
219 ICC of intra-rater measurements for RVO ranged between 0.82 to 0.94 indicating  
220 good to excellent reliability. When considering the 95% confidence intervals for intra-  
221 rater ICC for both SVCF and RVO the reliability ranges from moderate to excellent.

222

223 The ICC for inter-rater measurements for SVC diameter, VTi and flow were 0.54,  
224 0.80 and 0.69 respectively representing moderate to good reliability. The ICC intra-  
225 rater measurements for RVO were 0.7, 0.87 and 0.75 indicating moderate to good  
226 reliability. However, the 95% confidence interval for both RVO and SVCF measures  
227 were wide ranging (0.17-0.94) indicating poor to excellent reliability.

228

229 The repeatability index for both intra- and inter-rater SVC diameter measurements  
230 was higher than corresponding SVC VTi measurements. With regard to RVO  
231 measurements the RI for both intra- and inter-rater RVO diameter measurements  
232 were lower than the corresponding RVO VTi measurements. The repeatability  
233 indices of both of the final flow measurements (SVCF and RVO) were higher than  
234 those of each of their contributing diameter and velocity measurements.

235 Furthermore, the RI of RVO diameter and VTi were less than that of SVCF. These  
236 results are therefore responsible for the overall higher intra- and inter-rater RI of  
237 SVCF compared to RVO (40% and 64% vs 26 and 49% respectively).

238

239 The Bland-Altman plots show that the spread of intra-rater measurements is less  
240 than that of inter-rater measurements. Furthermore, the spread for SVCF  
241 measurements are relatively more dispersed than that of the RVO measurements.

## 242 **Discussion**

243 Our results add to the published literature by investigating the agreement of SVCF and  
244 RVO in healthy and unwell late preterm infants or healthy and unwell term infants  
245 including those who are receiving total body cooling for hypoxic ischemic  
246 encephalopathy. The intra- and inter-rater agreement index of SVC was 41% and 62%  
247 respectively and is similar to previously quoted values in extremely preterm and  
248 healthy term neonates (31%, 53% and 104%). This combined with the ICC values of  
249 0.88 and 0.61 indicate good to moderate reliability of this technique [10,12,20,24]. In  
250 keeping with previous research the greatest degree of variability in SVCF appeared to  
251 be contributed by intra- and inter-rater diameter measurements [12]. This is likely to  
252 be due to the difficulty in acquiring good images of the SVC vessel in a sagittal plane  
253 due to interference by the expanding lungs. This is of particular importance as the  
254 diameter measurement is squared during the calculation of systemic blood flow. It is  
255 important to highlight that our methodology involved the taking of repeated images of  
256 SVC diameter and VTi thus increasing the potential for differences to be seen in SVCF  
257 values gained. This differs from previous studies such as the study by Lee *et al.* where  
258 intra- and inter-rater calculations of SVCF agreement were assessed using the one  
259 image which was analysed by different raters [12]. This study therefore reflects more  
260 closely the variability which might be expected in the clinical or research situation using  
261 sequential measurements over time within the same patient.

262

263 Whilst the ICC indicated excellent reliability, the 19% intra-rater repeatability index for  
264 RVO diameter gained in our study is much greater than in previous research (3.9%)  
265 [9]. Similarly, the study by Goodman *et al.* assessed the agreement of the components  
266 of RVO calculation were assessed within or between raters using the same image

267 whereas our study involved raters taking repeated images and measurements thus  
268 further influencing the repeatability values [9]. Interestingly both the intra- and inter-  
269 rater (23% and 25% respectively) repeatability index measurements of RVO VTi were  
270 similar to that of RVO diameter. Previous research in preterm and term neonates found  
271 that measuring RVO VTi through a long axis position led to significant differences in  
272 the values gained [9]. Thus, in our analysis both components of RVO calculation  
273 appear equally responsible for the intra- and inter-rater RI values observed (31% and  
274 51%). The improved agreement for RVO compared to SVCF is likely to be due to RVO  
275 being less affected by respiratory movements interfering with either the  
276 echocardiographic window for diameter measurements or the VTi waveforms gained.  
277 The variability may have been improved in this study by measuring RVO VTi in a short  
278 axis plane as previous research has found this to be the most repeatable way to  
279 measure VTi [9].

280

281 A potential flaw in analysing the agreement in the method chosen is the potential to  
282 disturb an infant through repeated echocardiographic examinations and therefore  
283 interfere with acquisition of images but also disturb their physiology which may  
284 influence the SVCF and RVO results gained. However, the difference seen in values  
285 gained could not be explained by difference in heart rate as we did not find any  
286 significant differences in the heart rate between intra- or inter-rater  
287 echocardiographic measurements. Future studies should consider including  
288 information such as respiratory rate and the behaviour of the baby (e.g. crying) as  
289 this will influence the VTi values gained for SVCF [5,10].

290

291 One of the weaknesses of this study is that where mean values were needed, extra  
292 tracing of diameter and VTi measurements were performed by one rater (LM)  
293 sometimes using different software. This may have influenced agreement results  
294 seen as it does exclude the bias that one may see from different observers  
295 performing such measurements and also assumes that measurements made  
296 between different software programmes are comparable. The latter is indeed a  
297 potential source of variation as previous research has shown that with a variety of  
298 echocardiographic techniques (e.g. speckle tracking) differences in measures are  
299 found between vendors or even updates to existing software [25,26]. An additional  
300 analysis that would have strengthened the study would be to investigate the  
301 agreement of raters repeating SVCF and RVO calculations on established first  
302 images. The gestational ages of infants included in the inter-rater analysis are of a  
303 statistically significantly lower gestation age than those in the intra-rater analysis.  
304 This combined with the trend for those infants included the former analysis being of a  
305 lower birthweight may have influenced the ability to acquire accurate ultrasound  
306 images and thus the agreement values gained. For example, in smaller babies, even  
307 if variation in measurement of SVC diameter is the same, proportionally the variation  
308 would be larger compared with the actual diameter measurement obtained.

309

310 In newborn infants, values of  $<150$  ml/kg/min for RVO and  $<41$  ml/kg/min for SVCF  
311 have been considered pathological [8,27]. Our inter-rater reliability coefficient results  
312 of 123 and 79 ml/kg/min respectively might be considered too large for them to be  
313 considered a reliable measure of systemic blood flow in the clinical domain. This  
314 assertion is further reinforced by the wide ranging 95% confidence interval for ICC  
315 for inter-rater RVO and SVCF. All measurements of intra-rater agreement are better



316 than for inter-rater agreement, supporting the notion that the same  
317 clinician/investigator should, ideally, perform sequential measurements.

318

319 To improve the robustness of echocardiographic measures of systemic blood flow  
320 further studies should investigate the use of repeated measurements of stroke volume  
321 combined with pre-defined median-weight corrected measurements of vessel  
322 diameter in order to improve their agreement in SVCF [28]. The fact that VTi is more  
323 repeatable and that it is not squared during the calculation of systemic blood flow  
324 means that the agreement of these echocardiographic biomarkers would improve.  
325 However, this approach does ignore the finding that the diameter of the SVC changes  
326 over the first three days of life [12]. There is also a suggestion that novel ways of  
327 exploring SVC VTi and diameter, such as through a suprasternal or parasternal view,  
328 may reduce variability [29]. A recent study by Ficial *et al* found that measuring SVC  
329 VTi from a suprasternal view and SVC area via a modified short axis view improved  
330 both accuracy and agreement of this echocardiographic measure of systemic blood  
331 flow [30]. However, these new techniques of measuring SVCF have not been used in  
332 intervention studies and therefore require further exploration.

333

334 In summary, this study presents measurements of agreement of SVCF and RVO in  
335 healthy and unwell late preterm infants or healthy and unwell term infants including  
336 those who are receiving total body cooling. These measurements demonstrate that  
337 reasonable assessments of SVCF and RVO can be made in these groups of patients.  
338 In future studies which might assess changes in these parameters in response to  
339 interventions, careful attention should be made to study design to minimize areas of  
340 variability. In particular, when sequential measurements are required they should

341 ideally be performed by the same observer. Further work could be undertaken to  
342 investigate whether the use of 'standardized' vessel diameters would improve  
343 reliability further. Furthermore this study highlights, with the increasing use of  
344 ultrasound in the neonatal setting, that if measures such as SVCF and RVO are to be  
345 routinely used in the haemodynamic management of sick infants, that's it is of  
346 paramount importance that these measures of systemic blood flow are included in the  
347 development of a structured training for neonatal echocardiography to improve their  
348 robustness [31,32].

349

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Table 1. Echocardiographic intra- and inter observer variability subject characteristics

		<b>Intra-rater subject characteristics N=41</b>	<b>Inter-rater subject characteristics N=25</b>	<b>p-value</b>
<b>Gestational age (weeks)</b>		37 ( $\pm$ 3.0)	36 ( $\pm$ 2.9)	0.04
<b>Type of care received by infants n (%)</b>	Special Care	20 (49)	15 (60)	0.54
	Intensive Care	12 (29)	7 (28)	
	Total Body Cooling	9 (22)	3 (12)	
<b>Respiratory support at recording n (%)</b>	No	38 (67)	19 (76)	0.39
	Yes	19 (33)	6 (24)	
<b>Birth weight (gram); mean (SD)</b>		3010 ( $\pm$ 810)	2628 ( $\pm$ 741)	0.07
<b>Age of infant (hours); mean (SD)</b>		38 ( $\pm$ 20.1)	32 ( $\pm$ 17)	0.24

471

Data displayed as mean (standard deviation) or N (%)

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Table 2: Neonatal heart rate analysis during intra- and inter echocardiographic studies

		<b>n</b>	<b>Rater 1</b>	<b>Rater 2</b>	<b>p-value</b>
<b>Intra-rater echocardiographic studies heart rate; median (IQR)</b>	SVCF	57	114 (106-130)	116 (105-130)	0.30
	RVO	54	120 (106-129)	121 (103-129)	0.83
<b>Inter-rater echocardiographic studies heart rate; median (IQR)</b>	SVCF	25	126 (113-132)	128 (108-141)	0.22
	RVO	25	125 (111-136)	127 (111-141)	0.35

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Data displayed as median (interquartile range)

Table 3. Echocardiographic agreement analysis

<b>Intra-rater echocardiographic agreement analysis</b>								
<b>Measure</b>	<b>n</b>	<b>Mean value</b>	<b>Inter-Class Coefficient (95% Confidence intervals)</b>	<b>Mean Bias</b>	<b>Standard Deviation of Bias</b>	<b>95% Limits of Agreement</b>	<b>Repeatability Coefficient</b>	<b>Repeatability Index</b>
SVC diameter (mm)	56	4.9	0.70 (0.54-0.81)	-0.01	0.08	-0.17, 0.15	0.16	33%
SVC VTi (cm)	57	15.9	0.85 (0.76-0.91)	0.27	2.41	-4.45, 4.99	4.70	30%
SVCF (ml/kg/min)	56	122.1	0.88 (0.80-0.93)	-0.52	25.3	-50.1, 49.1	49.6	41%
RVO diameter (mm)	54	8.3	0.94 (0.90-0.97)	0.005	0.08	-0.07, 0.08	0.16	19%
RVO VTi (cm)	54	10.1	0.82 (0.72-0.89)	-0.13	1.20	-2.49, 2.22	2.35	23%
RVO (ml/kg/min)	54	224.9	0.86 (0.76-0.91)	2.70	36.2	-68.3, 73.7	70.9	31%
<b>Inter-rater echocardiographic agreement analysis</b>								
SVC diameter (mm)	24	4.5	0.54 (0.17-0.77)	0.04	0.07	-0.1, 0.2	0.15	33%
SVC VTi (cm)	25	15.6	0.80 (0.56-0.91)	15.6	2.37	-5.8, 3.5	4.63	30%
SVCF (ml/kg/min)	24	122.8	0.61 (0.29-0.81)	13.0	40.3	-66.1, 92.0	79.1	63%
RVO diameter (mm)	25	7.7	0.70 (0.43-0.86)	0.03	0.08	-0.1, 0.2	0.16	21%
RVO VTi (cm)	25	10.3	0.87 (0.71-0.94)	0.58	1.36	-2.1, 3.2	2.66	26%
RVO (ml/kg/min)	25	236.2	0.75 (0.50-0.88)	24.7	62.8	-98.4, 47.8	123.1	51%

476 Figure. 1. Echocardiographic images measuring SVC diameter in M-mode and VTi  
477 via pulsed wave Doppler

478

479 Figure. 2. Echocardiographic images measuring RVO diameter in B-mode and VTi  
480 via pulsed wave Doppler

481

482 Figure. 3. Bland-Altman plots of intra-rater agreement of (A) SVC diameter, (B) SVC  
483 VTi and (C) SVCF echocardiographic measurements

484

485 Figure. 4. Bland-Altman plots of intra-rater agreement of (A) RVO diameter, (B) RVO  
486 VTi and (C) RVO echocardiographic measurements

487

488 Figure. 5. Bland-Altman plots of inter-rater agreement of (A) SVC diameter, (B) SVC  
489 VTi and (C) SVCF echocardiographic measurements

490

491 Figure. 6. Bland-Altman plots of inter-rater agreement of (A) RVO diameter, (B) RVO  
492 VTi and (C) RVO echocardiographic measurements