

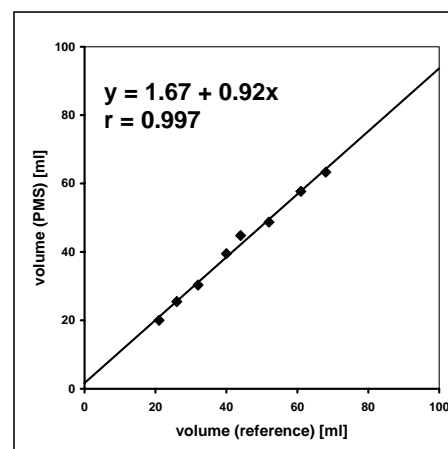
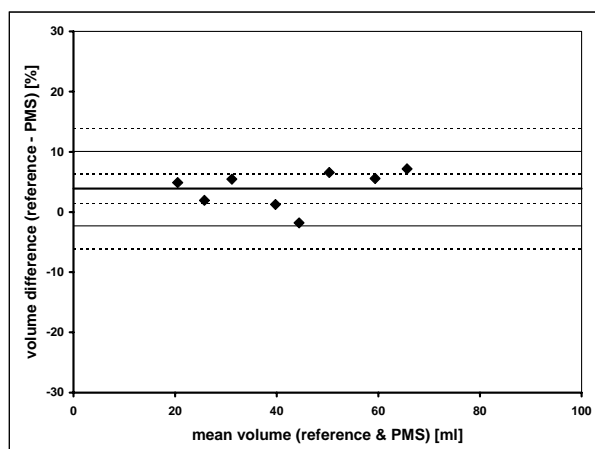
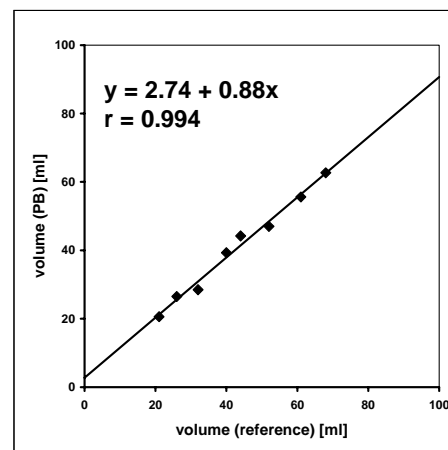
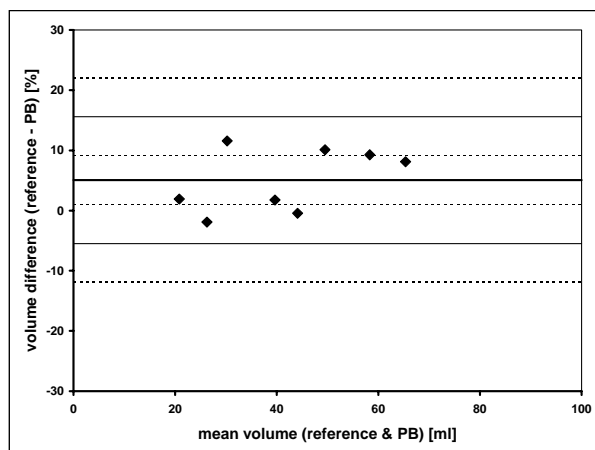
Appendix A

Validation of customized software (PB), developed by our group, versus View Forum software, R 5.1 Philips Medical Systems (PMS), Best, The Netherlands, for volumetry of the heart

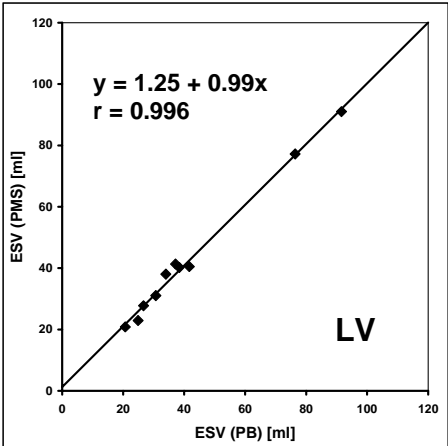
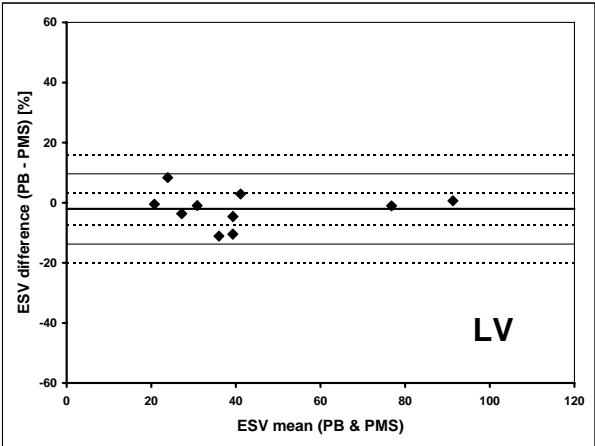
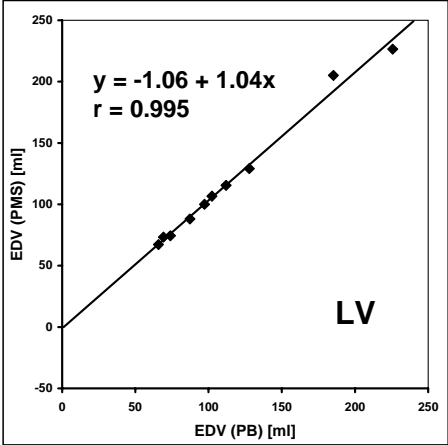
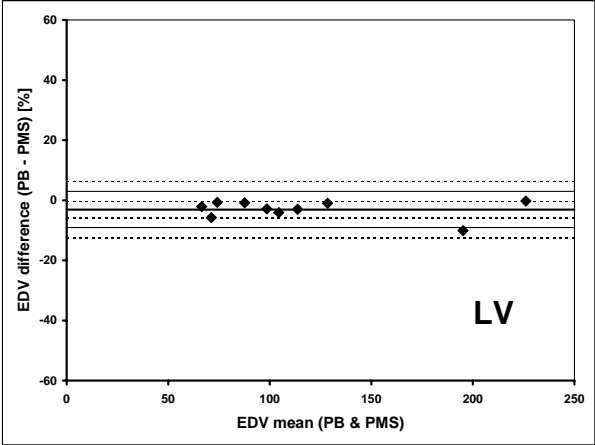
The calculation of sample size to detect a clinically significant difference in ventricular end-diastolic volume, end-systolic volume, stroke volume and ejection fraction (with a power of 90% and an alpha- error of 0.05) was performed according Grothues et al.¹

A 10 ml change in enddiastolic and endsystolic volume would therefore require sample sizes of 10 respectively 7 subjects. We therefore choose to examine 10 healthy subjects and 10 patients.

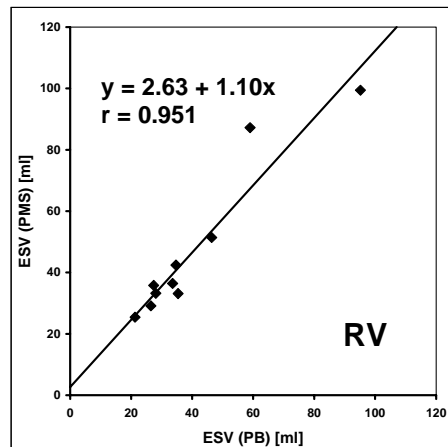
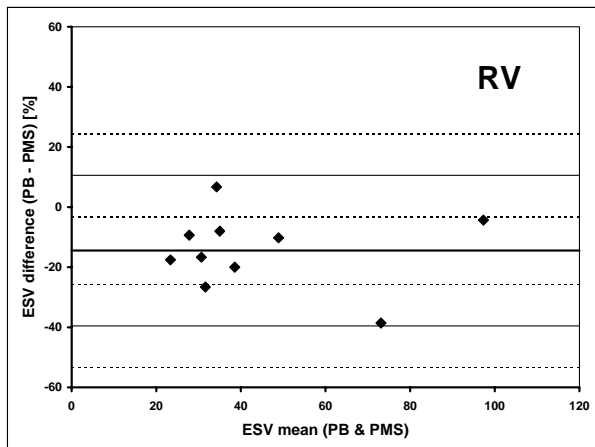
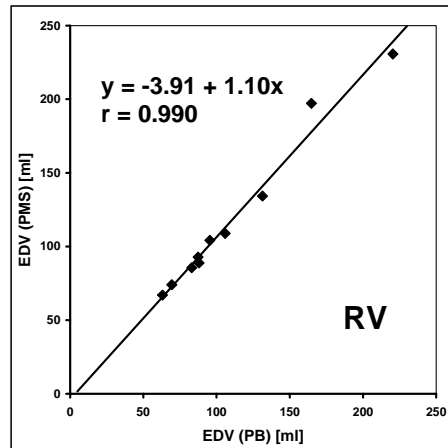
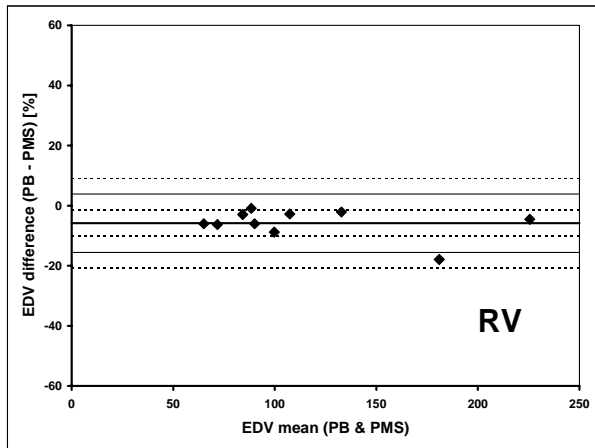
Prior to the validation in humans we performed phantom studies, where we examined **water filled balloons (reference)** with a definitive volume with our software (PB) versus View Forum software (PMS). Linear regression and the Bland-Altman plots are given below and show a very good correlation to the volumes of the reference balloons by both softwares.



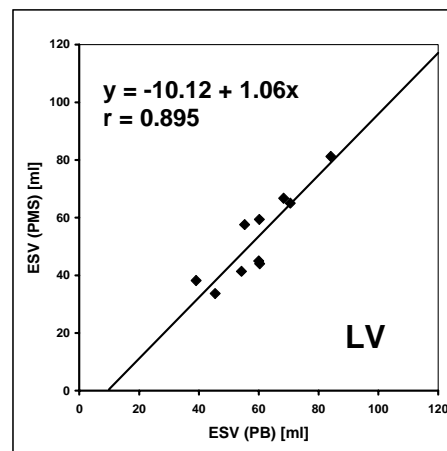
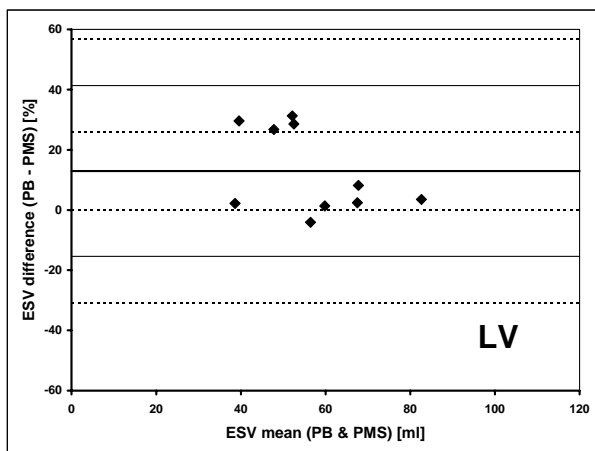
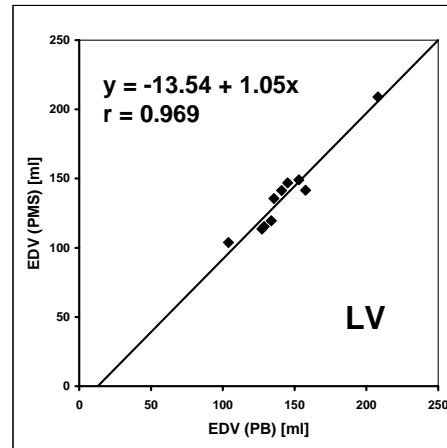
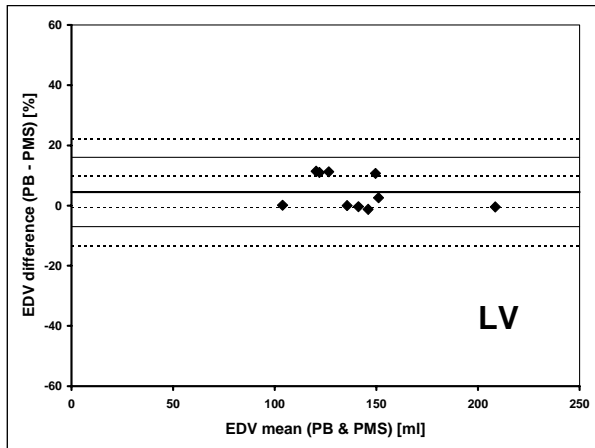
We then performed volumetry in 10 **healthy subjects** with our software (PB) versus View Forum software (PMS). Linear regression and the Bland-Altman plots of the **left ventricle**.



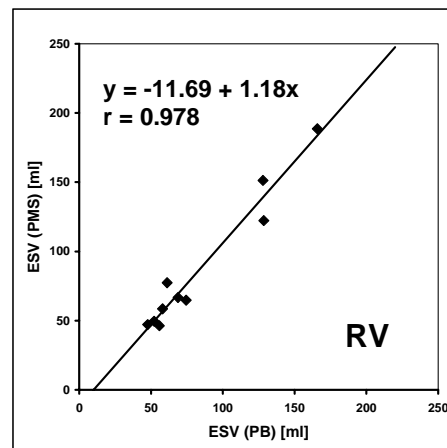
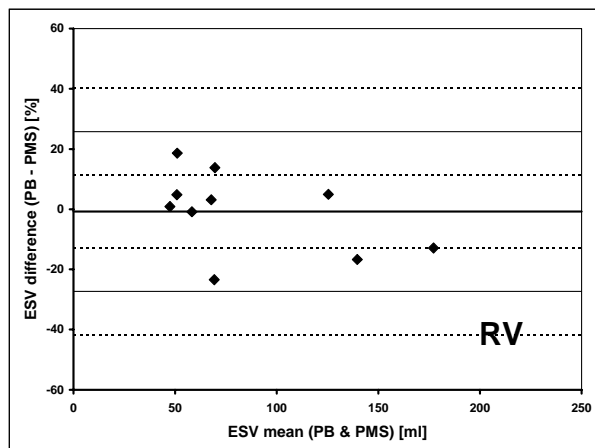
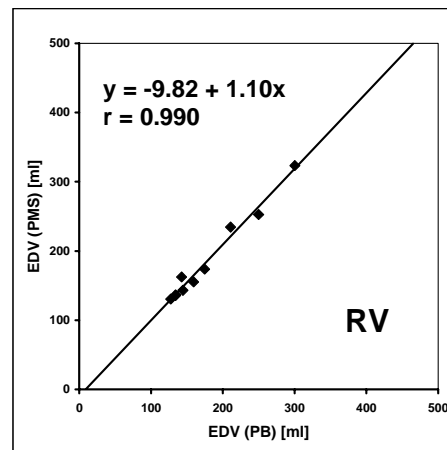
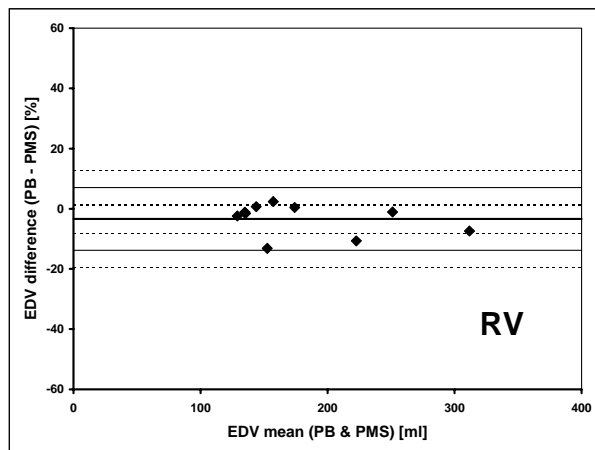
Linear regression and the Bland-Altman plots of the **right ventricle** in healthy subjects.



We then performed volumetry in 10 **patients** with our software (PB) versus View Forum software (PMS). Linear regression and the Bland-Altman plots of the **left ventricle**.



Linear regression and the Bland-Altman plots of the **right ventricle** in patients.



There was a very good overall correlation of our software (PB) to View Forum software (PMS) proofing our semi-automatic, threshold-based contour finding algorithm to be accurate for the use in clinical and scientific settings. We did not perform additional comparison of muscle mass determination as there would not be any principle difference between both softwares with the outer ventricle wall contour being manually traced in both.

Table A:

Volume evaluation tools (PB vs. PMS). Except the correlation coefficient r, all values are given in percent.

	LV-EDV	LV-ESV	RV-EDV	RV-ESV
SW-Evaluation Variability				
- healthy subjects -				
Mean difference	-3.1	-2.0	-5.8	-14.5
LOA	-9.1 to 3.0	-13.7 to 9.6	-15.5 to 3.9	-39.5 to 10.6
COV	2.2	3.1	4.1	11.2
r	0.995	0.996	0.990	0.951
SW-Evaluation Variability				
- patients -				
Mean difference	4.5	13.0	-3.4	-0.8
LOA	-7.0 to 16.0	-15.4 to 41.3	-13.8 to 7.0	-27.3 to 25.8
COV	3.5	9.7	2.9	7.1
r	0.969	0.895	0.990	0.978

LOA = limits of agreement; COV = coefficient of variation; r = correlation coefficient

The validation of our customized software (PB) for **phase-contrast flow** measurements has been described in detail by our group in two previously published Circulation-papers^{2,3}.

The volumetric analysis tool has been used for compilation of pediatric reference values and was part of the review process for this paper.⁴

References:

1. Grothues F, Smith GC, Moon JC, Bellenger NG, Collins P, Klein HU, Pennell DJ. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. *Am J Cardiol.* 2002 Jul 1;90(1):29-34.
2. Beerbaum P, Koerperich H, Barth P, Esdorn H, Gieseke J, Meyer H. Noninvasive quantification of left-to-right shunt in pediatric patients: phase-contrast cine magnetic resonance imaging compared with invasive oximetry. *Circulation* 2001;103:2476-82.
3. Beerbaum P, Koerperich H, Gieseke J, Barth P, Peuster M, Meyer H. Rapid left-to-right shunt quantification in children by phase-contrast magnetic resonance imaging combined with sensitivity encoding (SENSE). *Circulation.* 2003;108(11):1355-1361.
4. Sarikouch S, Kuehne T, Peters B, Gutberlet M, Leismann B, Kelter-Klopping A, Koerperich H, Beerbaum P. Gender Specific Pediatric Percentiles for Ventricular Size and Mass As Reference Values for Cardiac Magnetic Resonance Imaging. *Circ Cardiovasc Imaging* 2010 Jan;3(1):65-76.