

QIBA Ultrasound Biomarkers: Shearwave Speed Imaging, Contrast Enhanced Ultrasound, Blood Flow Quantification (Part 1)

Coordinating Committee Cochairs: Brian Garra, MD, PhD, Brian Fowlkes, PhD Recent Former Cochair: Timothy Hall.



Relevance of QIBA Ultrasound Biomarker Efforts

Volumetric Blood Flow Quantification

Committee Cochairs: Brian Fowlkes, PhD; James Jago, PhD; Oliver Kripfgans, PhD

Active ultrasound biomarker committees

Committee participants and current and past documents can be found with the following QR codes. The Rosters are near the top left of the text of those pages.



- Ultrasound Shear Wave Speed Quantification



- Contrast Enhanced Ultrasound Quantification



- Volumetric Blood Flow Quantification (joint effort with AIUM)

Importance of Quantitative US Measurements

Ultrasound has been a clinical standard of practice in quantitative measurements of the fetus and of the heart. The three ultrasound biomarker committees are pursuing biomarkers that have not been established clinically or have suffered claims by some as being less reliable with ultrasound than with another imaging modality. Thus QIBA efforts at documenting good performance and reducing bias and variance, are particularly relevant in these cases.

Biomarker Evaluation

To aid evaluation of the relevance of a biomarker effort, a diagram of the relevant variables is proposed as illustrated in Figure B2. This is a graphical “figure” of merit. If normalization of the axes can be standardized, it could be a rapid method of initiating comparison of the impact of different biomarker efforts.

3D Technique based on Color Flow

Background: Quantitative blood flow measurements using pulsed-wave ultrasound rely on difficult-to-meet conditions. Surrogate markers were introduced, such as resistive index, but they fail to quantify actual volumetric flow.

Purpose: To evaluate a QIBA supported, user independent ultrasound method for quantitatively measuring volumetric blood flow.

Hypothesis: Volumetric flow can be quantified without assumptions using the c-plane of a color flow 3D volume scan (Figure A1). This is possible on mechanically swept arrays as well as 2D matrix probes. Color flow velocities are multiplied with pixel geometry as defined by the scanner (Figure A2). Color flow power is used to correct for pixels being only partially filled with blood (partial volume correction). No angle correction or segmentation is needed. Absolute flow in milliliters per minute is computed.

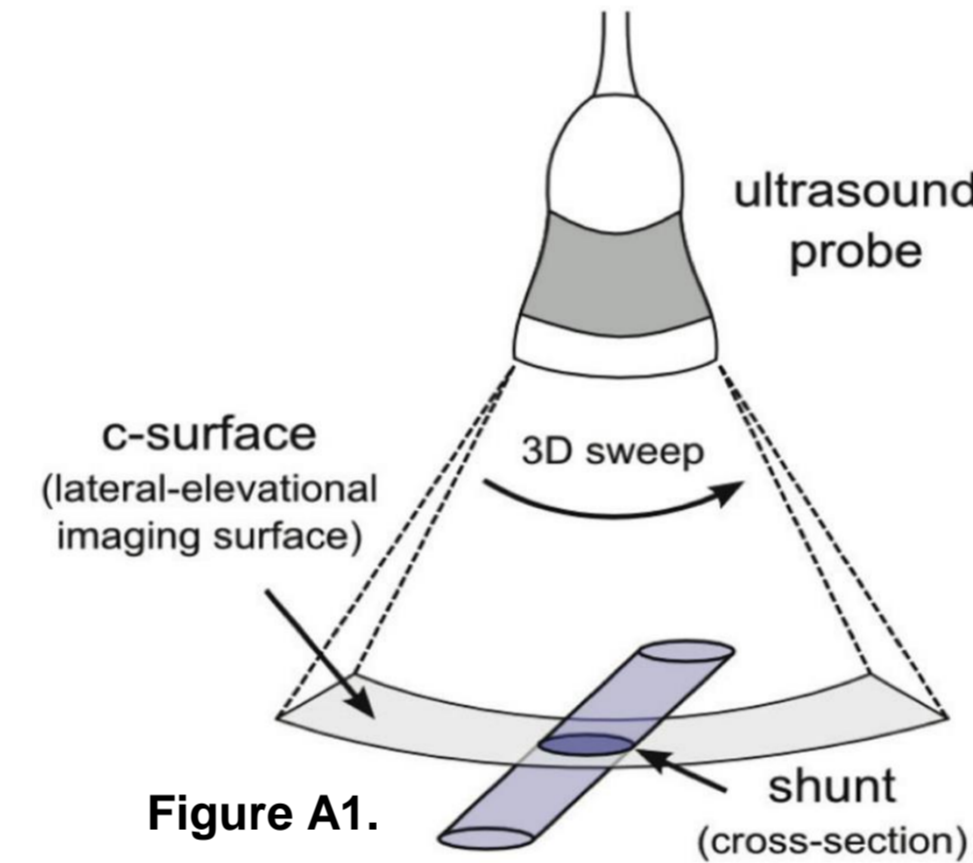


Figure A1.

Multi-Site Flow Phantom Evaluation

Materials and Methods: A prototype phantom was used for 3D volume flow assessment in realistic *in situ* conditions, with curved, stenotic and non-circular tubing sections. Nominal lumen diameter was 5 mm. Flow rates ranged from 30 to 750 mL/min (12 steps). Depths ranged 2.5 to 7.5 cm (11 steps). Color flow receive gain was stepped from no visible flow to full blooming (11 steps). Constant and pulsatile (60 bpm) flows were tested. Evaluation took place at three laboratories for each of the three enrolled systems.

Results: Detailed results for flow and depth testing are given below. Color flow gain is user selectable. Average absolute biases (across labs) for constant/pulsatile flow after filling the lumen with color pixels were 6.3%/18.5%, 8.5%/9.0% and 16.6%/6.2%, for constant/pulsatile flow for three systems, respectively. Coefficients of variation (COV) were 11.9%/5.9%, 9.3%/9.2%, and 5.4%/4.8%. Compensating for sensitivity reduced COV for one system from max 26% to 7% (Figure A3).

Conclusion: Ultrasound measurement of volumetric blood flow has potential to become a clinical biomarker. It shows promising performance with respect to bias and variation in this multi-site, multi-system study. We now have 13 university or standards lab sites, 5 system suppliers, 2 phantom companies and one drug company participating.

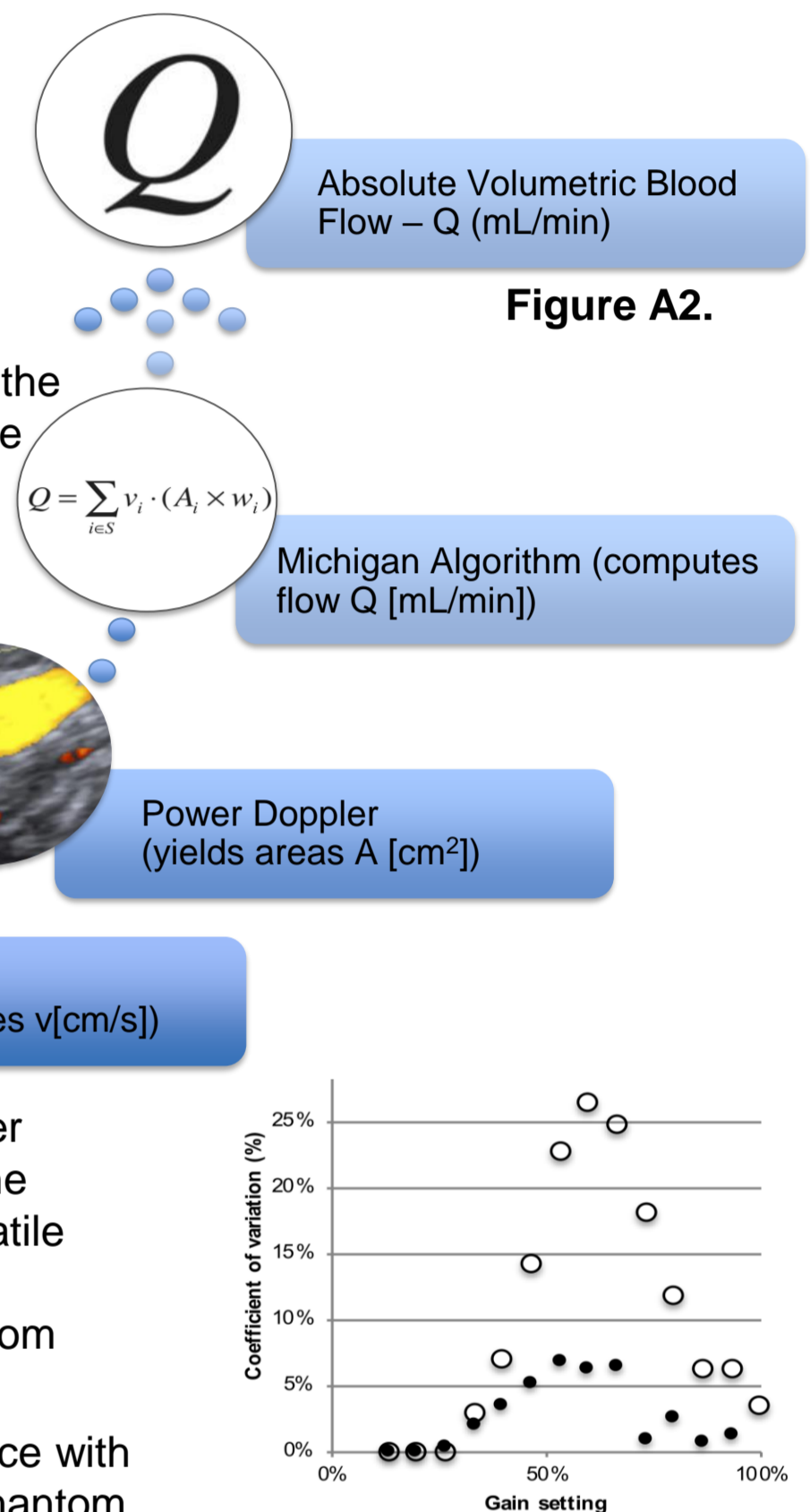


Figure A2.

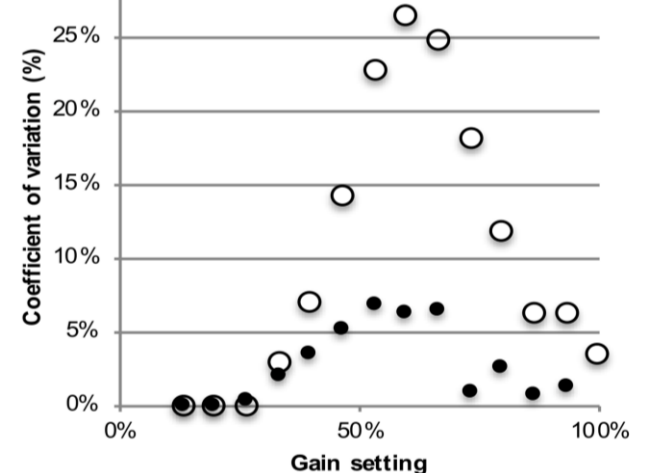
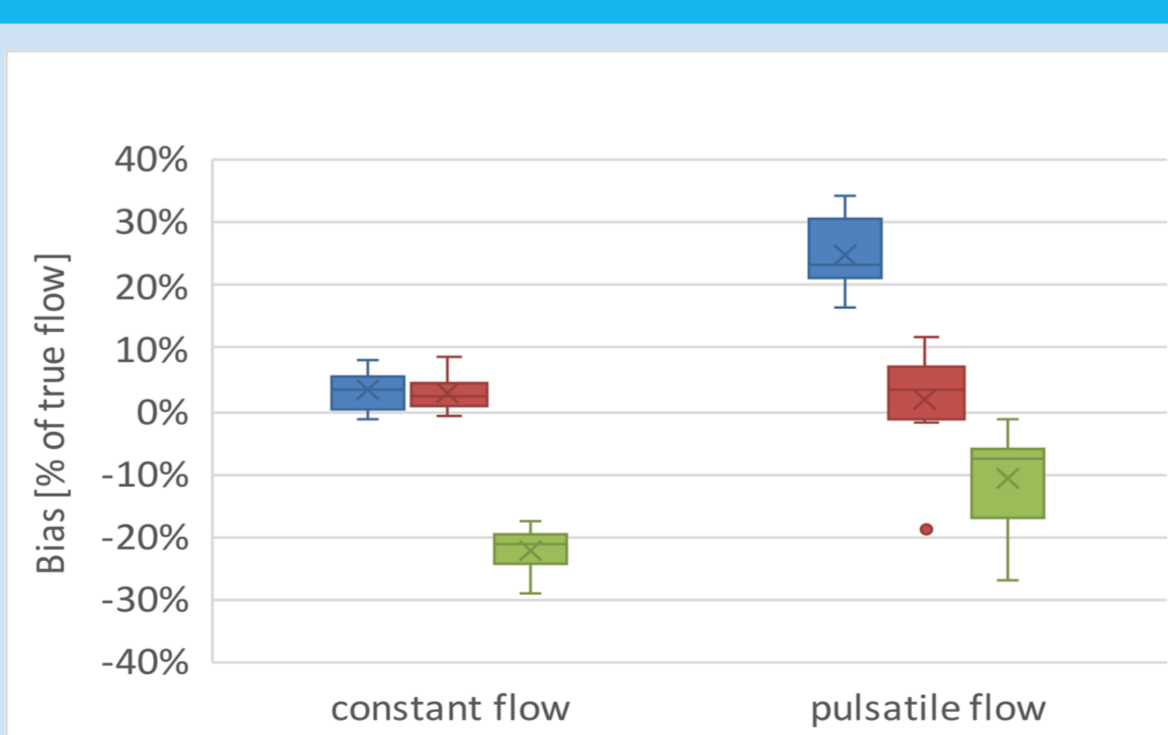


Figure A3. Reduction in Variation

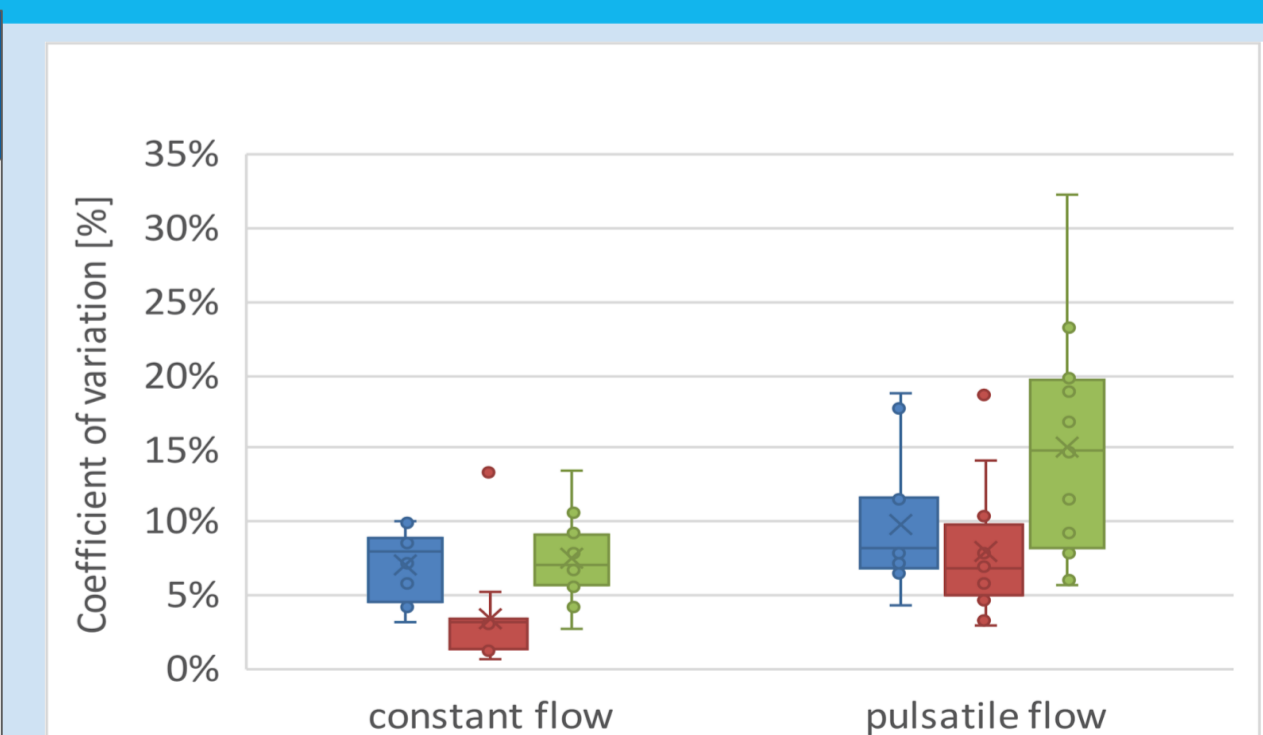
Bias across three sites



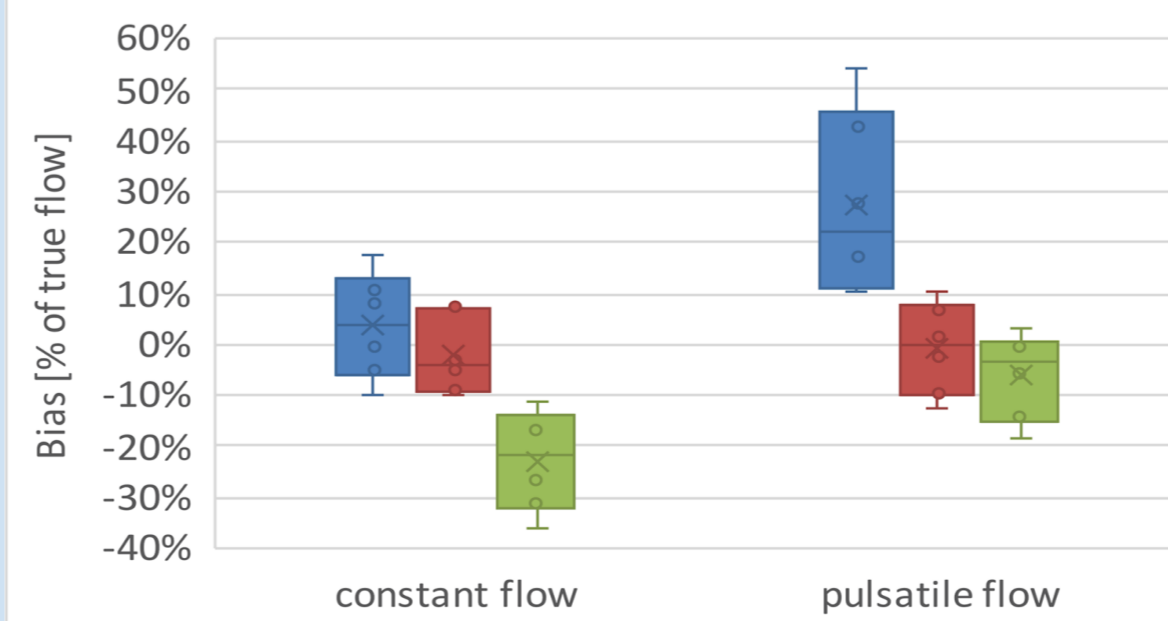
Flow Dependence

Left: Measurement bias between sites. Systems anonymously represented by color. Box plots show median (bar), error bars, mean ('x') and 25-75% range (boxes). Median biases are 3.5%/23.4%, 2.6%/3.5%, and -21.2%/-7.4% for constant/pulsatile flow for three systems, respectively. Pulsatile flow may experience algorithmic instabilities during diastole, which we seek to address in the future. **Right:** Variation between sites averaged across 12 flow rates. Coefficients of variation were 7.9%/8.2%, 3.2%/6.7%, and 7.1%/14.9%, for constant/pulsatile flow for three systems, respectively.

Variation across three sites



Bias of estimating flow over depth range



Depth Dependence

Left: Bias in the measurement of volume flow as a function of depth (limited to the range of 2.5 to 5 cm). Each color represents one system. Constant and pulsatile flow cover similar ranges in bias. Although the green system has a comparatively tighter spread over depth, it shows a larger overall bias. **Right:** Variation is mostly between 10 and 20% except for outliers which may be subsequently removed as outside the operating range for a given imaging probe, i.e. large depth for a high frequency array. For changes in imaging depth, biases for constant/pulsatile flow were 3.9%/22.5%, -4.1%/-0.4%, and -21.7%/-3.2%. COVs for constant/pulsatile flow were: 10.6%/11.2%, 2.3%/7.6%, and 5.6%/9.6%.

Variation of estimating flow over depth range

