QIBA US Biomarker Committee: Overview and Status Update - *Ultrasound Volume Blood Flow Biomarker*

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Quantitative Imaging Biomarkers Alliance® RSNA

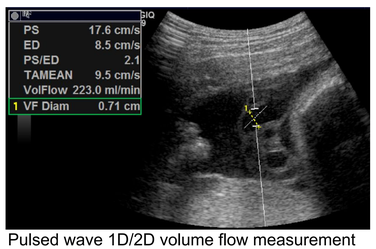
Significance

Clinical Need for Flow Quantification

- In many clinical practices, ultrasound scans commonly include a blood flow imaging component (*i.e.*, pulsed wave, color- or power mode Doppler) that is typically used to indicate the presence or absence of flow.
- Approximately 20% of ultrasound scans employ some degree of blood flow measurement and quantification.
- In the United States, there exist approximately 200,000 ultrasound machines (2014 Klein Report), that yield 136 million exams (2013 Klein Report), and thus annually 27 million ultrasound scans, where true flow measurements are potentially of interest.
- Most flow measures are heuristic and qualitative, semi-quantitative or just inaccurate, which indicates a need for a robust quantitative biomarker.

1D/2D Volume Flow Technique

- 1D flow velocity measurement based on range gate position in a 2D image
- Current volume flow is computed based on **several assumptions**:
  a. accurate user knowledge and selection of beam-to-flow angle
  b. accurate user knowledge and measurement of vessel diameter
  c. cylindrically symmetric flow velocity profile
  d. circular vessel cross section



Pulsed wave 1D/2D volume flow measurement in the umbilical vein

Anatomically configured flow phantom

Clinical Limitations

- Current 1D/2D volume flow technique is user dependent and is associated with poor accuracy and a time-consuming acquisition
- Time-dependent volume flow is not measured
- Turbulence or curved vessels prohibit meaningful volume flow estimation
- Dynamic changes in cross-sectional area influence volume flow estimation

Performance Sites

Mayo Clinic • MIT • University of Alabama at Birmingham • University of Michigan • University of Washington • University of Wisconsin • Hitachi Healthcare Americas • Toshiba America Medical Systems

Approach

3D Volume Flow Technique

- The volume flow biomarker measures blood volume flow rate (mL/min), in vessels with no need to make assumptions about the vessel cross sectional shape.
- The general principle of the technique is that the flow can be computed by multiplying blood velocity components along all US beams by local increments of the vessel cross-sectional area as "seen" from the transducer surface. These values are summed over a surface intersecting the vessel.

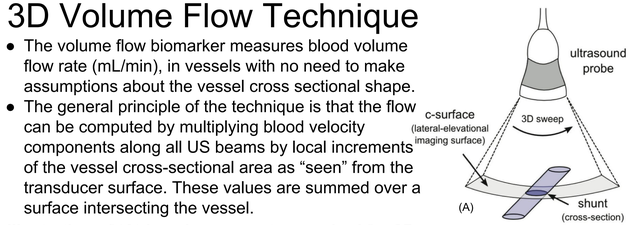
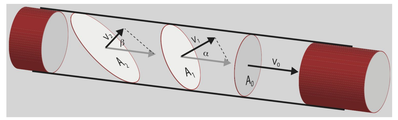
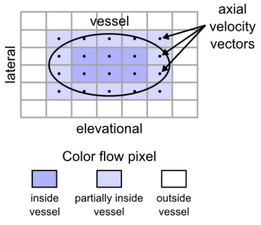


Illustration of (A) imaging geometry required for 3D volume flow measurement. Probe is oriented such that the lumen intersects the c-surface (lateral-elevational surface) in cross section. (B) Angle of c-surface intersection is an independent variable such that circular (θ_1) and ellipsoidal (θ_2 and θ_3) geometries all yield identical volume flow estimates without the need for any angle correction.



3D volume flow (Q) is computed by multiplying blood flow velocity (v_n), as measured by color flow, by the surface area of the intersected lumen (A_n). Given that $Q = A_0 \times v_0 = A_1 \times v_1 = A_2 \times v_2$, 3D volume flow is independent of angle. Specifically, $A_n = A_0 / \cos(\alpha_n)$ and $v_n = v_0 \times \cos(\alpha_n)$. Therefore, the cosine factor cancels when A is multiplied by v.

Partial volume effect in 3D volume flow measurement. Three types of color flow pixels exist. Color flow pixels inside the vessel correspond to 100% blood, those outside the vessel correspond to 0% blood, and those partially inside the vessel correspond to values between 0% and 100% blood. Color flow power is directly proportional to the amount of blood in each voxel and can therefore be used to correct the partial volume effect.



$$Q = \sum_{i \in S} v_i \cdot (A_i \times w_i)$$

Gauss' Theorem states that volume flow (Q) can be obtained by integrating the product $A_i \times v_i$ over the surface area (S), i.e., the c-surface. Power mode data is used to weight each area (A_i) in order to correct for partial volume effects.

Protocol and Data

- Provide sites with minimal and uniform guidelines for system setup and allow for adequate user vessel positioning and parameter selection (gain, PRF, WF).
- Collect data for the identification and assessment of bias and inter- and intra-observer variability (reproducibility and repeatability) across operators, systems, and centers.

Participating Laboratories and Vendors

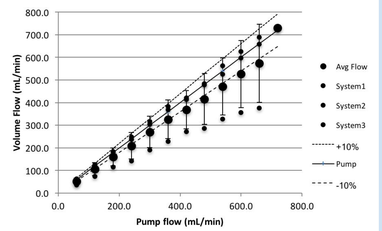
[3]University of Washington, [4]University of Michigan, [5]Korea Research Institute of Standards and Science, [6]Hammersmith Hospital, [7]University of Mississippi, [9]Weill Cornell University, [10]University of Wisconsin, [11]University of São Paulo, [13]University of Alabama at Birmingham, [17]Harvard Medical School, [18]Mayo Clinic, [20]Food and Drug Administration, [21]Taipei Veterans General, and [1]Toshiba America Medical Systems, [2]Gammex, [8]GE Healthcare, [12]Philips Healthcare, [14]CIRS, [15]Hitachi Aloka Medical America, [16]Siemens Healthcare, [19]Pfizer Inc.

Preliminary Round-Robin Results and Discussion

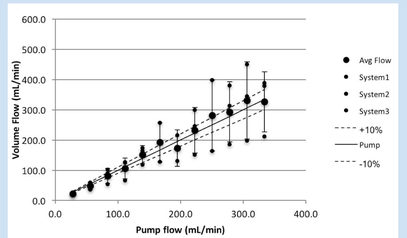
Round-Robin Flow Phantom Evaluation

Prototype phantom for 3D volume flow assessment in realistic *in situ* conditions, with curved, stenotic and non-circular tubing sections (see photo of phantom in Significance section). Nominal lumen diameter is 5 mm, flow rates range from 30 to 750 mL/min, and the stenotic section consists of a 40% reduction (5 to 3 mm). Note: For all results, systems 1 and 2 represent means of evaluation at 3 sites, system 3 only at one site so far. Large symbols represent the mean of the 3 systems tested.

Constant Flow

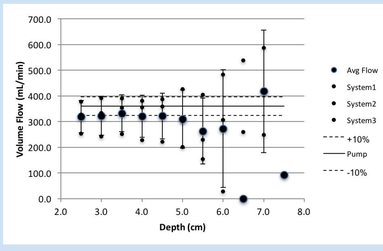


Pulsatile Flow



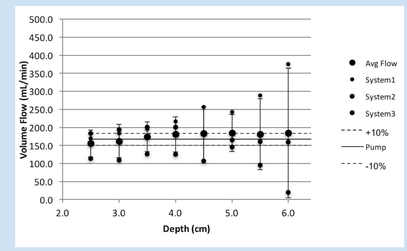
Flow Dependence

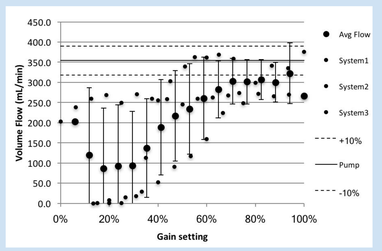
Volume flow estimation tracks with actual flow rate. One system underestimates systematically (for both constant and pulsatile flow). Another system overestimates under pulsatile flow conditions. Two systems track within ±10% of constant flow and one for pulsatile flow. These systematic dependences are currently under investigation. Note: We intentionally plot all systems with the same symbol to hide their identities.



Depth Dependence

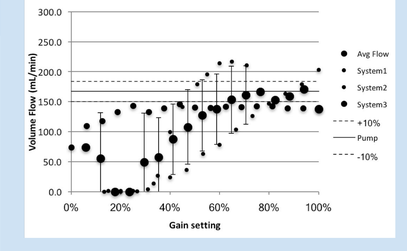
Volume flow remains within ±10% of true flow in the range from 2.5 to 5 cm depth. Deviations at deeper sites might arise from depth of penetration limitations of high frequency color flow probes or other reasons, such as diverging beams past their elevational focal zone.

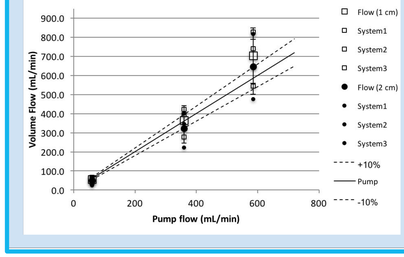




Gain Dependence

As expected for low gain, there is generally an underestimation for volumetric flow. As the gain is increased, volume flow increases to a stable yet slightly underestimated average. The partial volume approach handles the high gain settings even as the color begins to bloom and sensitivity to low flow is maximized. Limitation: Even though the individual gain settings were normalized, it is difficult to compare them across platforms.





Stenosis Influence

Post stenotic flow can be turbulent, although there was no obvious visual evidence in the color images. Estimates were taken 1 and 2 cm away from the center of the stenosis and are depicted with hollow and solid symbols, respectively. Volume flow continues to scale with true flow, though there is a tendency to overestimate the flow at higher true flow.