Achievements, Challenges, and Present Status of QIBA's Ultrasound Volume Blood Flow Committee

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Disclosures

Histosonics – One of the Founders and Scientific Advisors with financial interest.

Philips Healthcare – Research collaborations

GE Healthcare – Research collaborations

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QIBA Committee Leadership

- Co-chairs
  - J. Brian Fowlkes, PhD
  - Oliver D. Kripfgans, PhD
  - James Jago, PhD

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AIUM/QIBA Volume Flow Biomarker Subcommittee

Member	*Institution*
Oliver Kripfgans, PhD, Co-chair	University of Michigan
J Brian Fowlkes, PhD, Co-chair	University of Michigan
James Jago, PhD, Co-chair	Philips Healthcare
Kazuya Akaki	Toshiba
Ajaj Anand	Carestream
Cristel X. Baiu	Cristel X. Baiu
Matt Bruce, PhD	University of Washington
Paul Carson, PhD	University of Michigan
Shigao Chen, PhD	Shigao Chen, PhD
Yi Hong Chou, MD	Taipei Veterans General
Hyo-Min Cho, PhD	Korea Research Institute of Standards and Science
David Dubberstein, PhD	GE Healthcare
Todd Erpelding, PhD	Toshiba
Jing Gao, MD,	Weill Cornell Medical College
Timothy Hall, PhD	Wisconsin Institutes for Medical Research
Mauro Hanaoka, MD	University of São Paulo
Mark Holland	Indiana University
Ron Leichner, PhD,	Philips Healthcare
Adrian Lim	Imperial College London
Mark E. Lockhart, MD, MPH,	Univ. of Alabama at Birmingham
Ted Lynch, PhD	CIRS, Inc.
Ravi Managuli, PhD	Hitachi Aloka Medical America, Inc
Andy Milkowski	Siemens
Shigeto Ono	CIRS, Inc

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Stephen Pinter	University of Michigan
Michelle Robbin, MD	University of Alabama
Jonathan M. Rubin, MD, PhD,	University of Michigan
Anthony Samir, MD, MPH	Harvard - Massachusetts General Hospital
Timothy Stiles	Kettering University
Randall S. Sung, MD,	University of Michigan
Rimon Tadross, PhD	GE Healthcare
Kai Thomenius, PhD	Visiting Scientist Institute of Medical Engineering and Science, MIT
Marijean Trew, PhD	Gammex Inc.
Theresa Tuthill, PhD	Morton General Hospital
Nikolay Tzaribachev, MD (RSNA)	Research Institute, Germany
Wang Xueding	University of Michigan
Guan (Gary) Xu	University of Michigan
James Zagzebski, PhD	University of Wisconsin
Andy Milkowski, PhD	Siemens
Anne Hall	
Adrian Lim	Imperial College London
Shigeto One	CIRS
Chi-Yin Lee	Siemens

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Participating Institutions (Alphabetical)

- Food and Drug Administration
- Korea Research Institute of Standards and Science
- Hammersmith Hospital
- Harvard Medical School
- Mayo Clinic
- Rocky Vista University
- Taipei Veterans General
- University of Alabama at Birmingham
- University of Michigan
- University of Mississippi
- University of São Paulo
- University of Washington
- University of Wisconsin

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Participating Companies (Alphabetical)

- Aloka Medical America
- CIRS
- Gammex - Sun Nuclear
- GE Healthcare
- Hitachi
- Pfizer Inc.
- Philips Healthcare
- Siemens Healthcare
- Canon Medical Systems

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Doppler Equation

$$f_D = 2f \cos\theta \; v_o/c$$

f = center frequency of transmitted ultrasound
θ = Angle of motion with respect to sound propagation
v_o = velocity of blood
c = sound speed

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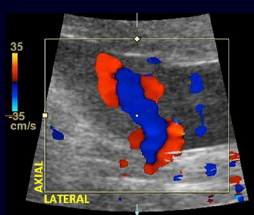
Tortuous Umbilical Cord Flow



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Flow Indices and Metrics

$$f_D = 2f \cos\theta \; v_o/c$$

- Variety of flow indices used for assessing flow.
  - Less operator dependence than absolute flow measures
- S/D ratio = (systolic / diastolic ratio)
- Resistance index (RI) = [(systolic velocity - diastolic velocity) / systolic velocity]
- Pulsatility index (PI) = [(systolic velocity - diastolic velocity) / mean velocity]

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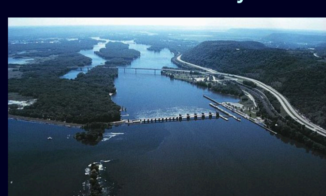
Volume Flow vs. Flow Velocity

https://www.bathselect.com/



https://www.worldatlas.com/

Same flow velocity but VERY DIFFERENT VOLUME FLOW!!!!!

Courtesy of Jonathan Rubin

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Courtesy of Jonathan Rubin

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Courtesy of Jonathan Rubin

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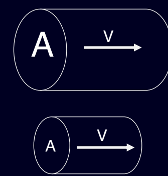
Volume Flow (Q) vs. Flow Velocity (V)



$$Q = \oint_S \vec{v} \cdot d\vec{A}$$

Same flow velocity but VERY DIFFERENT VOLUME FLOW!!!!!

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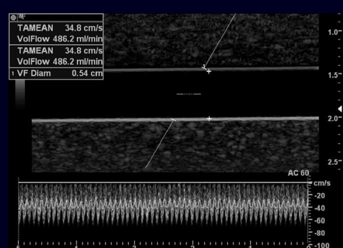
Traditional Doppler Volume Flow

- Required for Measurement
  - Doppler Angle
  - Diameter
  - Circular Cross Section
  - Axial Symmetry



Hoyt K, *et al*, J Ultrasound Med, 28(11):1511-8, 2009.

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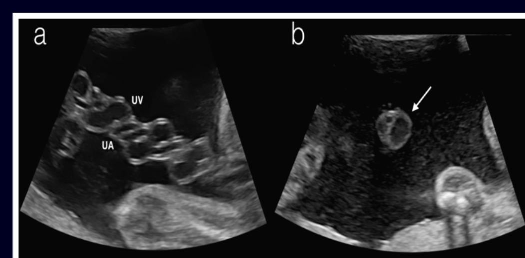
Umbilical Cord Flow



Doppler Angle? Circular Cross Section?

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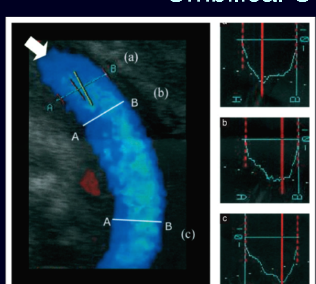
Umbilical Cord Flow



Axial Symmetry?

Pennati G, *et al. Ultrasound Obstet Gynecol.* 2004;23:131-7.

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So what do we do about this?

Alternative method for estimating blood flow (mL/min) using 3D/4D Doppler ultrasound

Eliminate the limitations of pulsed-wave Doppler

- Doppler Angle
- Vessel Diameter/Circularity
- Flow Symmetry

Proposed 3D/4D method overcomes limitations

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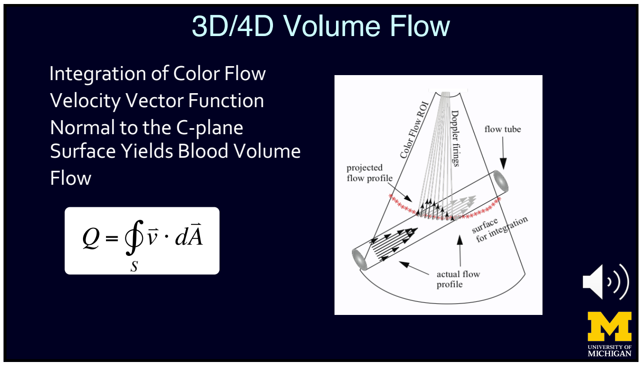

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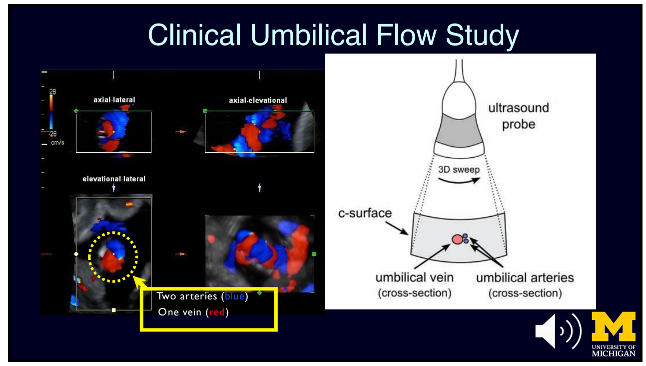

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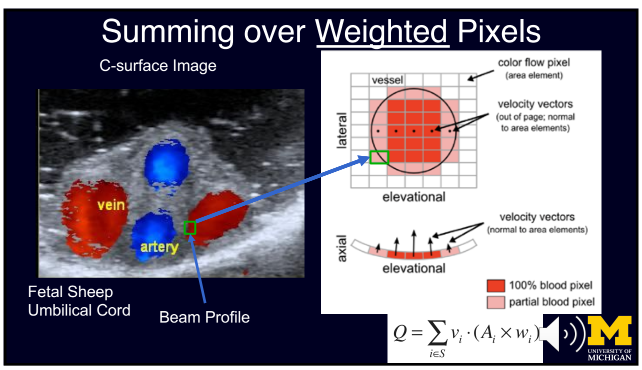

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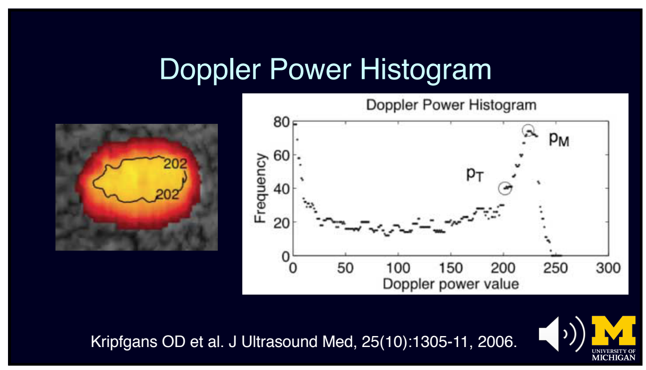

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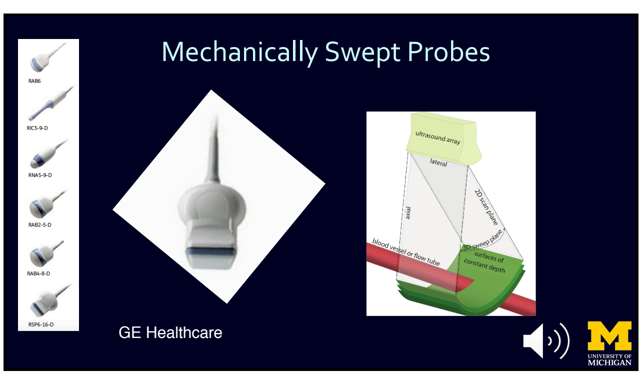

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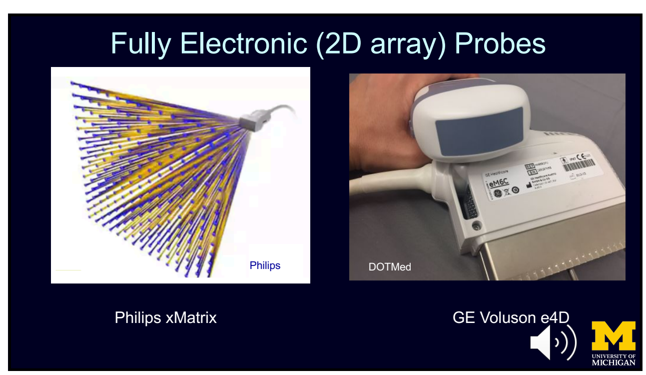

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Clinical Umbilical Flow Study

- 35 patients each with a singleton pregnancy
  - Recruited from a population at an increased risk of preeclampsia.
- Classified into 3 groups:
  - 21 at-risk patients
  - 5 with preeclampsia (29.7-34.3 weeks GA)
  - 9 with normal pregnancies (25.9-34.7 weeks GA)

Pinter SZ, *et al*, J Ultrasound Med, 2017.

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Clinical Umbilical Flow Study

- Images acquired on a LOGIQ E9 with a 2.0–8.0-MHz bandwidth array transducer (RAB6-D)
- Three different free loop positions along the length of the cord.
- Intra-subject and intra-measurement relative standard error (RSE) were 12.1 ± 5.9 and 5.6 ± 1.9 % (mean ± SD), respectively.

Pinter SZ, *et al*, J Ultrasound Med, 2017.

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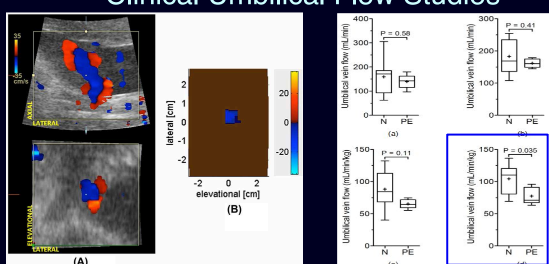
Clinical Umbilical Flow Studies



d. Depth-corrected, weight-normalized flow

Pinter SZ, *et al*, J Ultrasound Med, 2017.

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Quantitative Imaging Biomarker Alliance (QIBA)

- **QIBA Mission: Improve the value and practicality of quantitative imaging biomarkers by reducing variability across devices, sites, patients, and time.**

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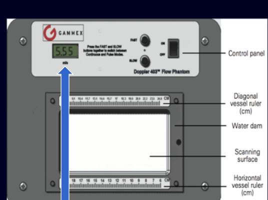
Complex Flow Phantom



Calibrated Volumetric Flow

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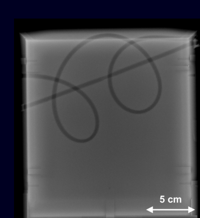
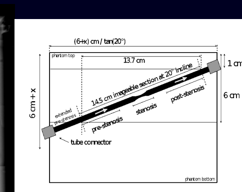
QIBA Phantom





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Ultrasound Systems in this Study*

- Canon (formerly Toshiba) Aplio 500 with a mechanically swept 9CV2 probe
- GE Logiq LE9 with a mechanically swept RSP6-16 probe
- Philips Epiq 7 with an X6-1 2Dmatrix array

* Other participating companies have systems in development.

Kripfgans et al. Radiology, Accepted

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Scope of Study

Table 1: Structure of the multi-system and multi-site study, with 3 systems at 3 sites each. The study at each site included four tests (flow, depth, gain, and stenosis) taken under constant and pulsatile flow each. This results in a total of 738 datasets consisting of 18,450 image volumes.

Dataset size		No. volumes scanned	
No. systems	3	No. systems	3
No. sites	3	No. sites	3
No. flow modes	2	No. volumes (per flow mode)	20 (constant) 30 (pulsatile)
No. parameter steps (per test)	12 (flow) 11 (depth) 12 (gain) 6 (stenosis)	No. parameter steps (per test)	12 (flow) 11 (depth) 12 (gain) 6 (stenosis)
Total no. datasets	738	Total no. volumes	18,450

Kripfgans et al. Radiology, Accepted

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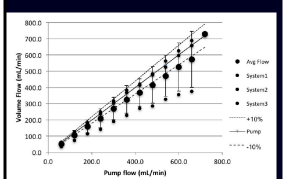
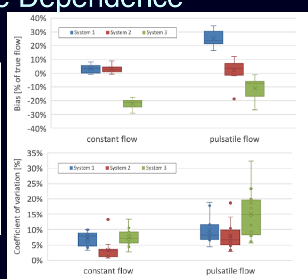
Flow Range Dependence





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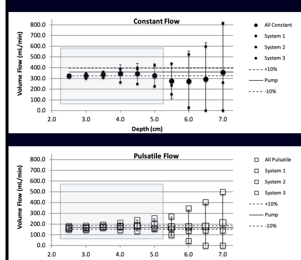
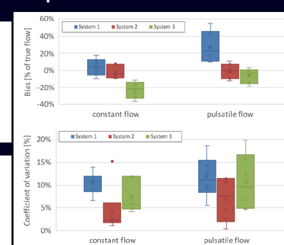
Depth Range Dependence





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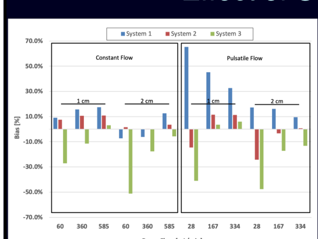
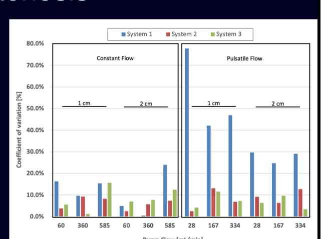
Effect of Stenosis





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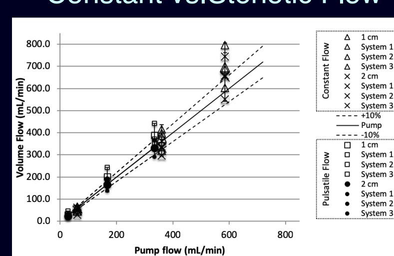
Constant vs.Stenotic Flow



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Summary of Phantom Results

- Volume flow estimated by 3D color flow ultrasound was
  - Accurate (11.5% mean bias)
  - Reproducible (10.4% mean within-subject CV)
- There were differences among systems that are still being examined.
- There are changes being made to systems expecting to improve performance.
- Phantom accuracy?
  - Data collected over several months (03/2017 to 03/2019).
  - Phantom was not recalibrated during this period.
  - Two phantoms were circulated.
  - Flow meter accuracy 0.5% of reading (+/- 0.25% based on measurements made with a blood mimicking fluid (matched viscosity) and 2000 mL flask)

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Pinter et al. Umbilical Venous Study Results

Table 1. Volume Flow Estimate Variability (All Patients, Absolute Flow)

Statistic	Value
Intrapatient relative SD (CV), %	20.3 ± 10.1
Intrameasurement relative SD (CV), %	29.6 ± 9.6
Intrapatient relative SE, %	12.1 ± 5.9
Intrameasurement relative SE, %	5.6 ± 1.9

Data are presented as mean ± SD. CV indicates coefficient of variation.

wCV

Pinter SZ, *et al* , J Ultrasound Med, 2017.

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Rubin et al. Umbilical Venous Study Results

- The true flow was unknown for these case (no reference standard)
- Mean within-subject coefficient of variation (wCV)
  - Spectral Doppler method : 46 ± 17%
  - 3D/4D Gaussian surface method : 18 ± 14%

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Clinical Objective – Umbilical Flow

THE JOURNAL OF MATERNAL-FETAL & NEONATAL MEDICINE
http://informahealthcare.com/jmf
ISSN: 1476-7058 (print), 1476-4954 (electronic)
J Matern Fetal Neonatal Med, 2016; 29(5): 701–706
 DOI: 10.3109/14767058.2015.1019855
informa healthcare

ORIGINAL ARTICLE

Modelling umbilical vein blood flow normograms at 14–40 weeks of gestation by quantile regression analysis

Giuseppe Rizzo[1], Ludovica Rizzo[2], Elisa Aiello[1], Eugenio Allegra[1], and Domenico Arduini[1]

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Review of Rizzo et al 2016

- Intra-observer study
  - Two sets of UV measurements were obtained in 50 fetuses at a time interval of approximately 30 minutes.
- Inter-observer study
  - Different group of 50 fetuses.
  - Second observer blind to the measurements obtained by the first
  - UV measurements obtained at the end of the ultrasound session.

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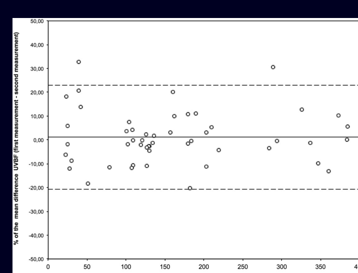
Intra-observer Results



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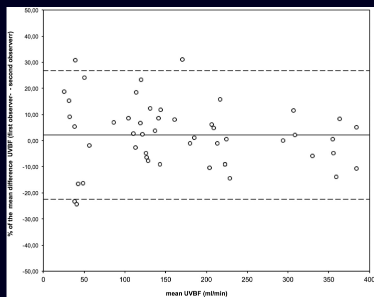
Inter-observer Results



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Potential Associated Claims

- **Claim 1: (cross-sectional) For a measured volume blood flow of *X* mL/min , a 95% confidence interval for the true flow is *X* mL/min ±15%.**
- **Claim 2 : (technical performance claim) The volume flow measurement has a within-subject coefficient of variation (wCV) < 20%.**

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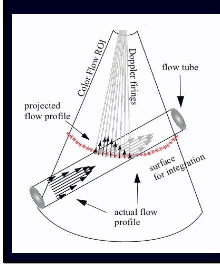
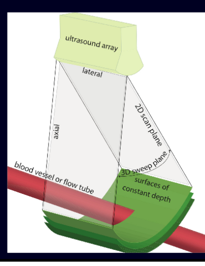
Thanks!

$$Q = \oint_S \vec{v} \cdot d\vec{A}$$





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