AIUM/QIBA
Ultrasound Volume Blood Flow
Biomarker

CALL SUMMARY 4-May-2020

Action Items in RED.

Attendance:

Brian Fowlkes, Oliver Kripfgans, Mark Lockhart, Jin Gao, David Dubberstein, Cristel Baiu, Paul Carson, Matthew Bruce, Jon Rubin, Shiram Sethuraman, Ron Leichner,

1. Review of Previous Call Summary
   1.1. Reviewed with no changes.
2. Discussion regarding the revised *Radiology* manuscript for VF
   2.1. Oliver updated the group that we are waiting for final acceptance of the manuscript.
3. Profile and protocol discussion
   3.1. Subsections need to be worked on

   3.1.1. A doodle poll will be scheduled to strategize conquering sections

   3.2. Brian Fowlkes presented an overview on profile development (Slide deck "ProfileOverview_04May2020"

- Clinical
  - Determine conditions under which reproducibility is achieved
  - Determination of accuracy
- Review of test results using QIBA phantom
  - Establish accuracy of methods in controlled conditions (using phantoms sent to different institutions)
    - Three Systems Tested; Canon, GE Logiq LE9; Philips Epiq7
      - Gain dependence
      - Flow range dependence
      - Depth range dependence
    - Summary of phantom results (differences still being examined)
      - Accuracy: 11.5% mean bias
      - Reproducibility: 10.4% mean within-subject CV (wCV)
      - Mean bias is probably too high due to one system
        - Performance improvements being investigated
- Two studies in umbilical venous flow
  - Pinters et al (JUM 2017)
    - Reproducibility : Intrapatient relative SD (CV) = 20.3+/-10.1% (wCV)

- o Rubin et al (Abstract for 2020 AIUM meeting and manuscript submitted)
    - ▪ Mean within-subject coefficient of variation (wCV)
        - Spectral Doppler method : 46 ± 17%
        - Gaussian surface method : 18 ± 14%

- Potential Profile Claims
    - o 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%.
    - o Claim 2 (technical performance claim): The volume flow measurement has a within-subject coefficient of variation (wCV) < 20%.
- Discussion of Claims
    - o We discussed how these as compare to those of the SWS Profile
        - ▪ Claim 1
            - Consider depth range over which the claims would apply
            - Consider velocity range over which the claims would apply
            - Consider is there are any distinction for constant vs. pulsatile flow
            - Tim Hall suggested that one might consider criteria based on PSF/vessel diameter
        - ▪ Claim 2
            - Any subclaims that might be application specific
            - Current claim seems aligned with experience with umbilical cord.
            - Consider other applications
                - o Dialysis Grafts: Average COV 9.89 ± 8.02% based on 2D spectral Doppler – Based on analysis of UAB data
    - o Brian F. pointed out the QIBA Profile Claim Guidance document
- https://qibawiki.rsna.org/images/a/a1/QIBAProfileClaimGuidance-2017_02_17.pdf

QIBA Volume Flow Profile Info

May 4, 2020

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Clinical Objectives

- Provide an accurate and reproducible measurement of volumetric blood flow
  - Determine conditions under which reproducibility is achieved
    - Standard scanning procedures
    - Range of vessel sizes
    - Range of depths
  - Determination of accuracy
    - Identify possible conditions where reference standard exist

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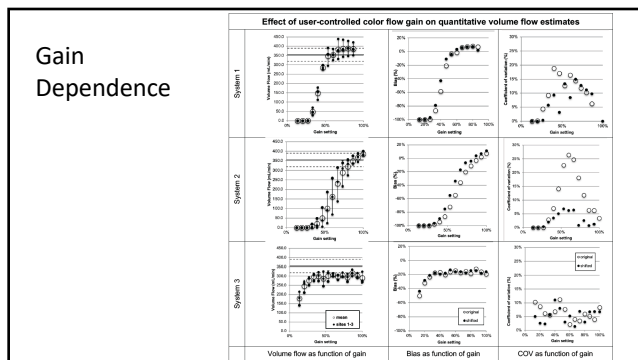## Testing Objectives Achieved

- Establish accuracy of methods in controlled conditions (phantom)
  - Measure bias and variance
    - Range of flow rates
      - 1 to 12 mL/s
    - Range of depths
      - 2.5 to 7 cm
    - Range of Gains
      - 0-100%
    - Constant and Pulsatile Flows
    - Stenotic flow
    - Range of vessel sizes
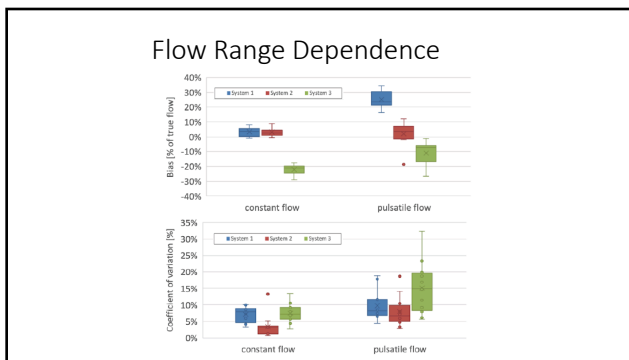   - Only 5mm diameter but with stenosis

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Testing To Be Published

- Three systems
  - Canon Aplio 500 (Canon Medical Systems Inc., Tustin, CA) with a mechanically swept 9CV2 probe
  - GE LOGIQ LE9 (GE Healthcare, Milwaukee, WI) with a mechanically swept RSP6-16 probe
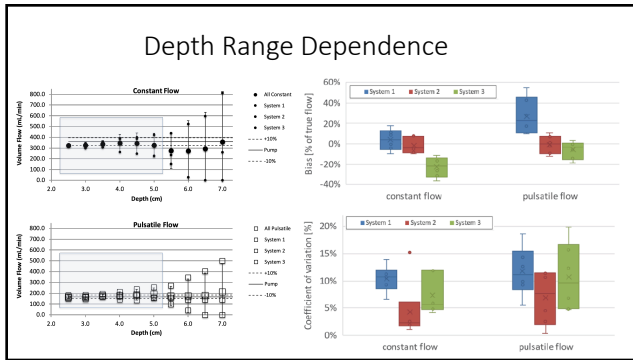 - Philips EPIQ 7 (Philips Healthcare, Bothell, WA) with an X6-1 2D matrix array
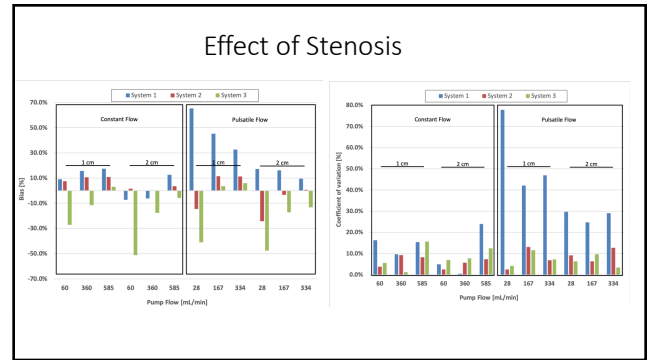
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Gain Dependence

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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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Summary of Phantom Results

- Volume flow estimated by 3D color flow ultrasound was
  - Accurate (11.5% mean bias)
  - Reproducible (10.4% mean within-subject COV)
- There were differences among systems that are still being examined.
- There are changes being made to systems expecting to improve performance.

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Testing Objectives Achieved

- Two studies in human umbilical venous flow
  - Pinter et al. (JUM 2017)

  - Rubin et al. (Abstract for 2020 AIUM meeting and manuscript submitted)
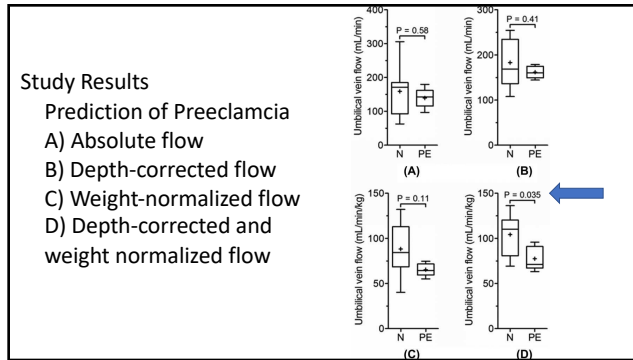
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Pinter et al.

- 35-patient cohort could be classified into 3 groups
  - 21 at-risk patients
  - 5 patients with preeclampsia
  - 9 patients with normal pregnancies
- LOGIQ E9 ultrasound system (GE Healthcare, Milwaukee, WI)
  - 2.0–8.0-MHz bandwidth convex array transducer (RAB6-D)
  - Mechanically- swept array
  - 30 volumes per data set
  - 5-10 minute acquisition time

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Pinter et al.

- Free cord loop imaged
  - Generally 3 different free loop positions along the length of the umbilical cord
    - 5 patient had only two positions
    - 1 patient had only one position
  - Imaging depth range
    - 3.3-11.0 cm

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Study Results

   Prediction of Preeclamcia

   A) Absolute flow

   B) Depth-corrected flow

   C) Weight-normalized flow

   D) Depth-corrected and

   weight normalized flow

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Study Results - Reproducibility

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

Statistic	Value
Intrapatient relative SD (CV), %	20.3 ± 10.1 ← wCV
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 $\pm$ SD. CV indicates coefficient of variation.

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Rubin et al.

- 12 subjects
  - High risk gestations
  - Hospitalized during pregnancy
  - Gestation
    - 24 to 35 5/7 weeks
    - Singleton
- Philips EPIQ 7 ultrasound scanner
  - 2D array transducer
  - X6-1 or XL14-3
    - Body habitus
    - Depth range
    - Availability

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Rubin et al.

- Free cord loop imaged
  - At least six separate volume flow measurements were made along the vein
    - Generally three each for 3D volume flow and 2D spectral Doppler method for comparison

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Slide 17

Study Results

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

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Slide 18

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 $\pm 15\%$.**

- **Claim 2 : (technical performance claim) The volume flow measurement has a within-subject coefficient of variation (wCV) < 20%.**

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Thoughts on Claim 1

- If we look at the results of the QIBA phantom study there can be additional restrictions considered.
  - 1) Depth range over which a given accuracy can be achieved.
  - 2) Velocity range over which it has been tested.
  - 3) Any difference in such specifications between pulsatile and constant flow.
- Need to define the range over which we will intend for the profile to apply.
  - What is the rationale?
- What can be stated from work done so far (QIBA round robin study, etc.)
- Reconsider in favor of defining a PSF/vessel diameter criteria

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Thoughts on Claim 2

- Add any application specific claim(s) (absolute or longitudinal).
- The term "**technical performance claim**" appears appropriate for a similar type of claim.
- This is based on the performance in umbilical venous flow.
  - Consider other sources such as dialysis grafts
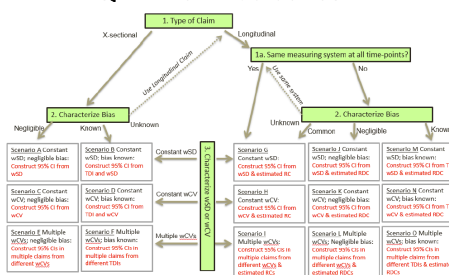   - Average COV 9.89 ± 8.02% based on 2D spectral Doppler

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Overall Considerations

- What is needed for the clinical purpose?
  - Accuracy
  - Reproducibility
- Claims construction process

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QIBA Claim Guidance

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