AIUM/QIBA
Ultrasound Volume Blood Flow Biomarker

MINUTES 2015-12-02

Attendance:

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I. Project overview

- Timeline: 6-9 months phantom design, 12 months round robin, 15-18 months *in vivo*
- Characteristics: biomarker transportable between various systems and manufacturers
- In the QIBA structure measuring renal flow and carotid flow are two different biomarkers

II. Profile and Protocol

Profile:

1. Two classes
   1.1 A Profile that describes a point measure (*i.e.* addressing bias in a formal way) and
   1.2 A type measuring changes over time

   Renal transplant has both phases, point measure at time of intervention and long-term measure for follow-up of organ acceptance over time. This committee will focus on the point measure as a direct gold standard is only available for that.

   Gray area: Point measurement of flow estimation at time of surgery versus serial measurement during follow-up. QIBA might see them currently as the same biomarker, but one could argue that these are different methods with different Profiles and Protocols.

2. Need to set %-errors for the anticipated clinical measurement to be significant:
   2.1 Ideal error, bias and variance,
   2.2 Working error, bias and variance,
   2.3 Acceptable error, bias and variance.
3. How large a change is clinically significant? What are the implications of a 30%, 50% 100% increase or decrease and how accurate is our estimate of such? Need to specify how an x-% change in volume flow will be reflected in the measurement, ideally, 1:1. While we can make statements on x% error with respect to flow meter, exact y mL/min for predicting failure is not possible at this point in time (need to talk to nephrology expert)
4. Need to incorporate statistical approach as presented in recent QIBA/RSNA publication, two “papers”, one being a summary of a 5-paper series, the other, the 5-paper series.

5. Profile is going to make a claim about how well we can make the measurement given that one follows the Protocol.
6. Profile is likely to change over time as one becomes better at making the measurement. One may be better in classifying clinical conditions because as one learns more about, sources of bias and variance. We are anticipating that the Profile is a living document for a long time.

There will exist a process by which one closes down a biomarker because at some point maybe a new biomarker is developed that will supersede something that has been developed previously. Superseding for a specific application, *i.e.* for example shear wave estimation for liver fibrosis, but it might continue to exist for breast masses.

Protocol: This document specifies how volume blood flow should be measured for the particular clinical application, renal blood flow, in transplants. That technique may vary depending on what one is measuring; however we need to make a clear statement for exactly how we think the measurement should be done clinically to reduce clinical sources of bias and variance as well as system configurations and those sorts of things that introduce system error sources, bias and variance.

- Standalone document and can accompany the Profile document
- Written before the Profile.

Notes: Manufacturer can conform to Profile N, even if N+1 is released but not stable yet. N=1 is expected to be draft.

III. Long term action path

- Stay highly focused
    - Avoid a shot gun approach
    - Will otherwise spread the biomaker committee thin and result in too many subtasks for RSNA staff
    - Stay focused until people can be using and demonstrating the value of the QIBA effort
- Continue with the single measure end – blood flow for renal transplants
- until we have
    - Technically validated Profile
        - Drafted
        - Out for public comment
        - Responded
        - Gone out again
        - Fully accepted
- Subcommittee
    - Creates Profile
    - Follows Profile and Protocol (called the Technical Validation)
        - Demonstrate meeting claims of Profile and
        - Level of performance
- Certification by steering committee
- Release into clinical pool that aren't familiar with that Profile and they're going to try to implement it and then we get a second reality check.

IV. Short term action path

1. Establish subcommittees
    a. Profile/Protocol subcommittee (lead by Brian Fowlkes, UM)
        i. Need literature review for levels of acceptable blood flow accuracy
    b. Phantom subcommittee (lead by Oliver Kripfgans, UM)
        i. Parameters for kidney transplant may be broad enough to give insight into other potential applications
        ii. Need to define ranges of
            1. Lumen diameter (3 to 9 mm)
            2. Lumen radius of bend
            3. Flow rate
        iii. Identify commercial partners willing to provide flow phantoms (#?)
        iv. Identify
            1. Number of sites willing to test a phantom
            2. Number of commercial partners providing scanners (#?)
        v. Phantom needs to be calibrated and is expected to be stable and reliable.
            1. Check actual flow in mL/s with stop watch and graduated cylinder
            2. Measure weight of flow phantom to check for dehydration
        vi. A cross imaging modality phantom would be great but it is not essential nor is it expected in the QIBA process.

1.1 Profile and phantom cross-feed to meet at the same geometry, flow rate, etc.

1.2 Contact other experts and perform literature search

2. Funding
    a. QIBA awards funding, activities must be pre-clinical
    b. NIH/NIBIB will need to be approached for clinical activities; well advised to include letters of support from QIBA officials
    c. AIUM might provide funding for clinical activities

    Note: This biomarker committee is co-funded by QIBA *and* AIUM.

V. Previous minutes

Approved by Dave Dubberstein (GE)