QIBA Contrast Enhanced Ultrasound (CEUS) Biomarker Committee (BC) Call

Friday, May 10, 2019; 11 AM CT

Call Summary

In attendance			**RSNA**
Mike Averkiou, PhD (Co-Chair)	Tim J. Hall, PhD	Reinhard Kubale, MD	Fiona Miller
Paul Carson, PhD	Ged Harrison, BS	Nancy Obuchowski, PhD	Julie Lisiecki
J. Brian Fowlkes, PhD	Luna Hilaire, PhD	Thierry Rognard	
Christian Greis, PhD	Eric Juang		

Moderator: Dr. Averkiou

QIBA Proposals for Pharma (Dr. Averkiou):

- Dr. Averkiou mentioned that his two pharma proposals have been submitted to US CC leadership and Dr. Zahlmann with some adjustments to make them more appealing to pharma
    - **Perfusion quantification of liver lesions—a QIBA/CEUS pilot study**
        - *The primary goal of this project is to evaluate CEUS perfusion quantification in a clinical setting and establish its reproducibility.*
    - **Method for calibrating the CEUS image intensity of ultrasound scanners in order to evaluate tumor vascular density in multicenter trials**
        - *The primary goal of this project is to calibrate all scanners and commercial image analysis software to a reference intensity that corresponds to a reference concentration, in order to be able to compare perfusion quantification results between different scanners.*
        - *This will lead to establishing an imaging biomarker for the absolute tumor vascular density, which will enable support of therapy monitoring trials and pharmaceutical research such as dose finding trials for new drug development.*
- Dr. Averkiou plans to publish results from the phantom variability study to add validity to the work and is also planning a future publication for work being done currently
- Some interesting results were as follows:
    - Time parameters varied no more than 10%
    - Amplitude parameters varied anywhere from 20 to 50%, though this was determined not to be unusually large, considering the logarithmically compressed images being used
- The phantom variability study is now considered to be complete, thought it may be interesting to consider additional studies using other microbubbles
- Available contrast agents and their applications were discussed
- For the purposes of the BC project, the Sonovue contrast agent will be the only one used, along with microbubbles that are readily available in most countries
- Dr. Carson mentioned that most clinical trials only use one contrast agent; so, considering other agents at this time would not be necessary, especially due to the challenges with value comparisons for the liver
- Some help is needed with work on a parameter for the amplitude standardization project that would allow for standardized calibration and standardized contrast agent measurement when using Bracco's VueBox software
    - Mr. Rognard will put Dr. Averkiou in touch with Bracco engineers who can advise him regarding this conversion value
    - Amplitude is an important parameter which is hard to control but carries much useful information

Other topics for consideration:

- Quantifying the tumor perfused absolute and fractional area as a new metric
- Consider other biomarkers that should have robust quantification
- With regarding to artificial intelligence (A.I.), look at additional values around parameters acquired from TIC analysis and inquire with Dr. Wilson regarding suggestions
- Identify other imaging biomarkers of tumor response to therapy
- Consider the use of color spectroscopy as a complementary study for amplitude standardization work
    - It might be useful to leverage frequency information from spectroscopy
- Backscatter of blood related to hematocrit may also be an interesting study
    - It might be the basis of normalization in a spectral-based approach for liver assessment
    - Canon and other manufacturers have the ability to measure backscatter and with the potential addition of 3D ultrasound; bolus may not be needed
- In general, measurements for clinical use that involve the standardization of parameters is what is under consideration

Next steps:

- Updates regarding amplitude standardization and news from Bracco engineers will be shared on the next call
- The process of drafting the CEUS Profile will begin
- Possible new clinical applications for quantification of time-intensity curves (TICs) will be discussed and how they may apply to claims in the Profile
- Dr. Averkiou to prepare a brief memo for RSNA staff to distribute for committee feedback regarding additional parameters for exploration

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The next scheduled QIBA ultrasound calls will be as follows at 11 am CT:

- **6/7/2019** SWS BC call
- **7/12/2019** CEUS BC call
- **8/2/2019** SWS BC call
- **8/9/2019** CEUS BC call
- **8/23/2019 - Q3 US Coordinating Committee call**

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