Proposed Imaging Biomarker Roadmap
For QIBA Profiles

1. Image analysis infrastructure

2. Technical Characteristics and Standards Groundwork:
   - 2.1. Systems engineering analysis of sources of variability, including consideration for co-variates
   - 2.2. Phantom development:
     - 2.2.1. Maintain inventory of currently available phantoms
     - 2.2.2. Assess applicability of existing phantoms
     - 2.2.3. If new one is required, pursue development as defined by the Technical Committee
   - 2.3. Assessment of intrinsic scanner variability – same scanner, scanners from same manufacturer, scanners from different manufacturers
     - 2.3.1. Prospective Single- and multi-center phantom studies
   - 2.4. Assessment of intra- and inter-reader bias and variance of measurements on phantom and clinical images
     - 2.4.1. Phantom images from prospective single- and multi-center studies
     - 2.4.2. Clinical images from no-change (“coffee break”) conditions on patients
     - 2.4.3. Clinical images from retrospective clinical serial studies

3. Document Profile Details to include explicit coverage of:
   - 3.1. Quality Control and Covariates
   - 3.2. Acquisition protocols
   - 3.3. ROI definition
   - 3.4. Quantification computation
   - 3.5. Data transfer and storage issues
   - 3.6. Longitudinal measurements
   - 3.7. Establish and implement a system for software version tracking / mitigation so as to accommodate changes in software version during clinical trial period

4. Synthetic digital reference object (i.e., pseudo-data created to facilitate performance assessment for candidate implementations of the biomarker)
   - 4.1. Create synthetic digital reference object to support algorithm performance testing and certification activities

5. Clinical Performance Groundwork
   - 5.1. Begin with a single expert per software package (or method) working under ideal conditions, and use data obtained from clinical trials that used the QIBA Profile:
     - 5.1.1. For each new imaging biomarker and its reference standard, determine the sensitivity and specificity for individual expert readers using appropriate outcome measure, such as prediction of survival at relevant established time-point (e.g., 6 month survival for advanced lung cancer).
     - 5.1.2. Compare correlations between new and standard biomarkers with outcome measures.
   - 5.2. Progress to multiple image analysts for each software package (or method).

6. Clinical Efficacy Groundwork (not part of this funding request, but anticipated)

6.1. Progress previous analysis to "real world" imaging conditions across heterogeneous centers.
6.2. Formal estimate of the value from new imaging biomarker versus latent standard in terms of:
    6.2.1. Increased analytical power per subject,
    6.2.2. Cycle time required to make critical GO or NO-GO decisions based on group differences between treatment arms in clinical trials.

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