Quantitative Imaging Biomarkers Alliance RSNA

Definitions and Descriptions for QIBA Protocols and Profiles

Protocol

Generically, an image acquisition **protocol** is a description of a process to create medical images.

A Uniform Protocol for Imaging in Clinical Trials **(UPICT) Protocol** is a more comprehensive and detailed, consensus-derived imaging protocol intended to reduce variation related to imaging in the conduct of clinical trials:

- to allow the detection of differences that are a consequence of the pathophysiology and/or intervention under study, and not an artifact of the manner in which the imaging is conducted (i.e., not due to the variance of the imaging method),
- to support optimization and validation of imaging biomarkers (platforms, agents, algorithms, etc.), and
- to improve the likelihood that clinical imaging studies obtained will comply with clinical trial protocol expectations.

A UPICT protocol describes not only image acquisition, but also the use of medical images and the associated underlying quantitative data by providing specifications for reconstruction, post-processing, analysis and interpretation.

- Acquisition, reconstruction and post-processing refer to the collection and structuring of new data from the subject.
- Analysis refers to the computational steps that transform the data into information, extracting important values.
- Interpretation refers to the judgment that transforms the information into knowledge.

In addition, the UPICT template suggests a hierarchy or tiered levels of Compliance. This reflects the recognition that there are valid reasons to perform trials at different levels of rigor, even for the same disease/intervention combination. For example, a high level of image measurement precision may be needed in small, early-phase trials whereas a less rigorous level of precision may be acceptable in large, late-phase trials of the same drug in the same disease setting. Three levels of compliance are defined:

- ACCEPTABLE: failing to meet this specification will result in data that is likely unacceptable for the intended use of this protocol.
- TARGET: meeting this specification is considered to be achievable with reasonable effort and equipment and is expected to provide better results than meeting the ACCEPTABLE specification.
- IDEAL: meeting this specification may require unusual effort or equipment, but is expected to provide better results than meeting the TARGET.

ACCEPTABLE values are always provided for each parameter in a UPICT Protocol. When there is no reason to expect better results (e.g. in terms of higher image quality, greater consistency, lower dose, etc.), TARGET and IDEAL values are not provided.

A **QIBA* Protocol** is an imaging protocol developed in conjunction with a QIBA Profile, and which follows the UPICT template and conventions. QIBA Protocols describe how clinical trial subjects or patients should be imaged so as to achieve reproducible quantitative endpoints when those tests are performed utilizing systems that meet the specific performance claims stated in the QIBA Profiles.

It is hoped that the standardization introduced through the use of UPICT Protocols in clinical trials will

- improve the contribution of imaging data in clinical trials, including improved statistical power
- decrease time to study initiation and site activation
- facilitate image data aggregation across trials
- enhance the development, optimization, and validation of imaging biomarkers.

QIBA Profiles

A QIBA* Profile is a document that describes a specific performance Claim and how it can be achieved.

A Profile consists of one or more Claims and associated Details.

- Claims: tell a user what can be accomplished by following the Profile.
- Details:
  - tell a vendor what must be implemented in their product; and
  - tell a user what procedures are necessary.

QIBA organizes and records relevant information from the published literature as well as results of the collaborative work by QIBA participants when drafting a Profile. This is referred to as Groundwork. The Profile establishes a written standard procedure for obtaining an accurate and reproducible measurement that reflects an imaging biomarker of clinical interest. For example, a CT Volumetry Profile describes how to obtain measurements that reflect tumor volume with an accuracy and reproducibility as stated in the Claim. An oncologic FDG-PET SUV Profile describes how to obtain SUV measurements that reflect tumor FDG-avidity with an accuracy and reproducibility as stated in the Claim.

The Profile specifies each Activity which may have a significant effect on the accuracy and reproducibility, e.g. FDG dose preparation, image acquisition, image reconstruction, tumor segmentation, etc. If the vendor products and user procedures in each Activity are compliant with the Profile specifications, the user can expect the Claim(s) to be achieved.

Profile Development:

- Ad-hoc committees of physicians with clinical and imaging expertise and medical physicists first define a clinical context (e.g., disease staging, therapy monitoring, etc.), determine what biomarkers to pursue, and then for each biomarker, determine what Profiles to pursue (i.e., what measurements from imaging would be clinically useful).
- Profile claims are then defined by QIBA Technical Committees, by adopting a statistically rigorous and evidence-based framework.

The organizational structure of a Profile document is similar to the UPICT template. Typically, targets (inanimate or living) are imaged under specific conditions (including, but not limited to, imaging system requirements and imaging protocols). The imaging protocols used for the living targets are the QIBA/UPICT Protocols. Where image acquisition details must be followed exactly to achieve the Profile Claim, the text in a Profile and in the corresponding Protocol will be identical. For other image acquisition details the text will indicate that latitude or operator discretion is permissible, subject to the protocol requirements of whatever clinical trial the Profile is being used in.

A Profile may also have tiered levels of Claims and associated tiered levels of Details for compliance, similar to a Protocol. For example, a CT Volumetry Profile might have an Acceptable Claim based on a measurement variability of +/- 20%, a Target Claim based on measurement variability of +/- 15%, and an Ideal Claim based on measurement variability of +/- 10%. Such tiered Claims and Details would be based on data showing that if one followed the Details specified in the Acceptable fields one could be confident that the tumor volume measurements would be accurate with a variability of +/- 20%; that data were also available showing that if one followed the Details specified in the Target fields one could be confident that the tumor volume measurements would be accurate with a variability of +/- 15%; and that data were also available showing that if one followed the Details specified in the Ideal fields one could be confident that the tumor volume measurements would be accurate with a variability of +/- 10%. Absent such data, a Profile would not state a Claim.

The goal of QIBA is to establish processes and Profiles (standards documents) that will lead to acceptance of quantitative imaging biomarkers by the imaging community, clinical trial industry, regulatory agencies, and clinicians as reliable evidence of biology and pathophysiology.

*QIBA = Quantitative Imaging Biomarkers Alliance http://rsna.org/QIBA.aspx