

CTSA Imaging Working Group Clinical Trials Committee

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***(on behalf of the CTSA Imaging Working Group,
Clinical Trials Committee)***

Clinical Trial Committee:

Deliverables

- Uniform Protocols for Imaging in Clinical Trials
- “Best practices” library, e.g.,
 - Imaging protocol development and review at CTSA
 - “How to do it” guide to rapid protocol site activation
 - Methods to facilitate imaging protocol conduct
- Demonstration inter-CTSA clinical trial(s)
 - Primary imaging endpoint
 - Validation / qualification of imaging biomarker(s)

UPICT Concept:

To facilitate the development and maintenance of widely acceptable, consistent imaging protocols (including imaging quality control procedures) for use in clinical trials across a range of disease states, anatomic sites, and imaging modalities

- to “improve” the contribution of imaging data in clinical trials, including improved statistical power
- while supporting robust case accrual
- and decreasing time to study initiation / site activation
- to facilitate image data aggregation across trials
- to allow the development, optimization, and validation of imaging biomarkers
- through the participation of imaging scientists and clinical trialists drawn from the broad range of interested constituencies

UPICT Goals (in part):

- Reduce variance related to imaging in the conduct of clinical trials (early and late phase so as to support both translation and clinical indications)
 - to allow the detection of differences that are a consequence of the intervention under study, not an artifact of the manner in which the imaging is conducted
 - to support optimization and validation of imaging biomarkers (platforms, agents, algorithms, etc.)
- Improve the likelihood that
 - clinical imaging studies obtained will comply with clinical trial protocol expectations
 - clinical trial imaging protocols will “fit” with practice
- Potentially provide a subtle impetus to improve standard of care (thereby increasing the chances that pre-enrollment imaging might be used as “baseline” study)

UPICT Objectives (in part):

- Short term
 - standard imaging protocol template(s)
 - a web-based workspace and supporting infrastructure to facilitate the submission, vetting, and annotation of Proffered Protocols in a transparent and inclusive manner
 - a web-based resource library of annotated Proffered Protocols that have been used to support clinical trials within institutions, cooperative groups, and trials consortia that meet some (tbd) minimum set of criteria
 - a web-based workspace and infrastructure to facilitate the iterative authoring and periodic review of Consensus Protocols (see below) in a transparent and inclusive manner
 - a web-based environment to facilitate the interaction among clinical trialists and imaging scientists within academia, industry, and agencies
- Long(er) term
 - a web-based resource library of Consensus Protocols that have been subjected to rigorous, transparent, inclusive (yet expert) review and approval that will be updated through an ongoing (tbd) process

UPICT Work Plan:

- Monthly calls of the Clinical Trials Committee – open participation (CTSA, IRAT, PhRMA, CROs, NEMA, FDA, etc.)
 - First Thursday of the month from 12 – 1 PM ET
- Accomplishments to date
 - Draft template, vetted at this meeting
 - Infrastructure in progress
 - Draft vetting and annotation criteria for comment
 - IT (discussion with RSNA, meeting for follow up)
 - Workflows in progress
 - Proffered Protocols from:
 - ACRIN, CALGB, ACOSOG, ADNI, CROs
 - Test template with proffered protocols, began at this meeting (ACRIN, Netherlands, ADNI)
 - Coordinating with “allied processes” e.g., QIBA

Draft Template

X. Imaging

X.1. Utilities and Endpoints of Imaging Tests within the Clinical Trial:

X.2. Pre-enrollment Imaging Tests:

X.3. Timing of Imaging Tests within the Clinical Trial Calendar:

X.4. Off-protocol and Off-schedule but On-protocol Imaging:

X.5. Imaging-related Selection Criteria (*mainly exclusionary in nature*):

X.6. Subject Preparation for Imaging Testing

X.6.1. Interval Timing (e.g., since)

Specific Interventions (e.g., Surgery, IGI, XRT, Therapeutic / Diagnostic Rx)

Oral and/or IV Intake

Vigorous Physical Activity

Etc.

X.6.2. Specific Pre-imaging Instructions

X.6.2.1. Prior to Arrival for Imaging

X.6.2.2. Upon Arrival for Imaging (*Including Ancillary Testing Associated with the Imaging and Downstream Actions Relative to Such Testing*)

X.6.3. Subject Preparation Documentation

Draft Template

X.7. Image Procedure

X.7.1. Quality Control Associated with Individual Subject Imaging

X.7.1.1. Phantom Imaging and/or Calibration (*Performed in Association with Subject Imaging and/or per routine during the trial for QC Purposes*)

X.7.1.2. Phantom Imaging and Calibration Documentation

X.7.1.3. Quality Control of the Subject Image and Image Data

X.7.2. Imaging Agent Specification / Preparation (*Contrast agent or radiopharmaceutical*)

X.7.2.1. Agent Dose Calculation and/or Dose Schedule

X.7.2.2. Imaging Agent Dose Calculation Documentation

X.7.3. Imaging Agent Administration (*Contrast agent or radiopharmaceutical*)

X.7.3.1. Timing of Agent Administration, Subject Activity Level, and Other Factors Relative to Initiation of Image Data Acquisition

X.7.3.2. Rate and Related Apparatus / Parameters

X.7.3.3. Route

X.7.3.4. Quality Control / Management and Reporting of Adverse Events Associated with Agent Administration

X.7.3.5. Imaging Agent-related Documentation

X.7.4. Imaging Enhancer(s)

X.7.5. Imaging Procedure

X.7.5.1. Subject Positioning

X.7.5.2. Instructions to Subject During Image Data Acquisition (*e.g., breathing*)

X.7.5.3. Timing of Image Data Acquisition (*Relative to Previously Administered Imaging Agents / Enhancers; Inter-timepoint standardization*)

X.7.5.4. Anatomic Coverage

X.7.5.5. General Parameters (*that May Be Stated in a Vendor, Platform, Version Independent Manner*)

X.7.5.5.1. Hardware and Set-up

X.7.5.5.2. Software Parameters (*Provide as electronic file for direct implementation on to the imaging platform if appropriate*)

X.7.5.6. Specific Parameters (*that Should Be Stated in a Vendor, Platform, Version Dependent Manner May Be Contained in Associated Tables*)

X.7.5.6.1. Hardware and Set-up

X.7.5.6.2. Software Parameters (*Provide as electronic file for direct implementation on to the imaging platform if appropriate*)

X.7.5.7. Quality Control / Management and Reporting of Adverse Events Associated with Image Data Acquisition

X.7.5.8. Image Data Acquisition-related Documentation

Draft Template

X.7.6. Inherent Image Data Reconstruction / Processing (*Data Correction, Smoothing, etc.*)

X.7.6.1. General Parameters (*that May Be Stated in a Vendor, Platform, Version Independent Manner*)

X.7.6.2. Specific Parameters (*that Should Be Stated in a Vendor, Platform, Version Dependent Manner May Be Contained in Associated Tables*)

X.7.6.3. Quality Control of Inherent Image Data Reconstruction / Processing

X.7.6.3.1. General

X.7.6.3.2. Vendor, Platform, Version Specific

X.7.6.4. Documentation of Inherent Image Data Reconstruction / Processing

X.7.7. Primary Source Data Archival Requirements for Imaging Data

X.8. Post-processing (*Anything not done on acquisition platform that affects DICOM image data and/or pixel / voxel values*)

X.9. Image Analysis and Interpretation

X.9.1. Data to Be Used (*i.e., Raw or Processed or Both*)

X.9.1.1. Target Level

X.9.1.2. Subject Level

X.9.2. Methods of Analysis to Be Employed, e.g.,

X.9.2.1 Measurements

X.9.2.2. Annotations

X.9.2.3. Etc.

X.9.3. Types of Platforms / Versions to Be Employed

X.9.3.1. Include All Platform / Version-specific Instructions – Platform 1

X.9.3.2. Include All Platform / Version-specific Instructions – Platform 2

X.9.3.3. Include All Platform / Version-specific Instructions – Platform etc.

X.9.4. The Use of Categorical Interpretation Schema(s) (*e.g., RECIST*)

X.9.4.1. Definitions

X.9.4.2. Training of Readers

X.9.5. Central and/or Site Interpretations and How They Will Be Managed

X.9.6. Quality Control of Image Analysis and Interpretation

X.9.7. Documentation Related to Image Analysis and Interpretation

Draft Template

X.10. Image Data Archival and Transmission

X.10.1. Transmittal of Imaging Data from Sites to Central Archive

X.10.2. De-identification / Anonymization Schema(s)

X.10.3. Requirements for Local Retention of Imaging Data

X.10.4. Requirements for Central Management of Imaging Data

X.10.4.1. Primary Source Imaging Data

X.10.4.2. Post-processed Imaging Data

X.10.4.3. Secondary Imaging Data (*e.g., Derived Values, Interpretations, etc.*)

X.11. Imaging-associated Risks and Risk Management

X.11.1. Radiation Dose and Safety Considerations

X.11.2. Imaging Agent Dose and Safety Considerations

X.11.3. Platform Specific Safety Considerations

X.12. Imaging Site Selection, Qualification and Protocol-specific Training:

X.12.1. Site Characteristics: (*e.g., Support Infrastructure, Internet capability, Image De-identification and transmission capability, etc.*)

X.12.2. Personnel

X.12.2.1. Qualifications

X.12.2.2. Training relative to specific protocol

X.12.3. Imaging Equipment (*Pertinent to the Clinical Trial*)

X.12.4. Modality Quality Control (*Pertinent to the Clinical Trial*)

Mandatory to Demonstrate Suitability as an Imaging Site

Mandatory to Submit for Review Prior to First Use

Mandatory to Submit Periodically During the Trial

X.12.5. Site Selection and Quality Control Documentation

X.13. Summary of Documentation

UPICT Next Steps:

- Utilize Wiki for rapid turnaround of template to completion
 - Targeted WebEx interactions
 - Goals:
 - Complete template to “final” state
 - Extract Proffered Protocols for posting
 - Netherlands FDG-PET
 - ACRIN 6678 FDG-PET
 - ACRIN 6678 Volumetric CT
 - ADNI MRI
 - Refine vetting criteria, annotations, etc.
 - Present work products to PhRMA Extended Imaging Committee and FDA (10/8 and 9/2009)
- Work with RSNA (RadLEX, Playbook, etc.) & Informatics Committee on IT infrastructure