Uniform Protocols for Imaging in Clinical Trials – UPICT
Clinical and Translational Science Awards Imaging Working Group: Clinical Trials Committee

Background
Imaging is used in clinical trials for a variety of purposes, (e.g., determining eligibility, triage for subgroup analyses, response assessment, and endpoint measurements). Variance in imaging-derived data in clinical trials detracts from the value that imaging might contribute. Multiple factors other than biology contribute to this variance, such as differences in vendors, machine drift over time, and changes introduced by services calls and system upgrades.

Imaging biomarkers (quantitative whenever possible) could contribute to decreased sample size through enrichment of the accrued cohort and to shortening the clinical trial's duration through the use of imaging as an early predictive surrogate endpoint. In order for imaging to fulfill this promise, non-biologic variance (noise) must be reduced so that signal is 1) sufficiently conspicuous and 2) a consequence of the intervention under investigation in the trial rather than some artifact of the manner in which the imaging is conducted.

In order to improve the reliability of imaging in clinical trials, the CTSA Imaging Working Group (CTSA-IWG) promulgates Uniform Protocols for Imaging in Clinical Trials (UPICT).

UPICT Concept and Goals:
To facilitate the development and maintenance of consistent imaging protocols in clinical trials (including imaging quality control procedures) for use in clinical trials:

• to “improve” the contribution of imaging data, including increased statistical power,
• while supporting robust case accrual, and decreasing time to study initiation and site activation;
• while facilitating data aggregation across trials and supporting the development, optimization, validation, and quality of imaging biomarkers;
• through the participation of imaging scientists and clinical trialists drawn from the broad range of interested constituencies.

In addition, UPICT provides an impetus to improve the consistency of imaging performed during routine clinical care (thereby increasing the chances that pre-enrollment imaging might be used as the “baseline” study for clinical trials). Furthermore, as interventions translate from clinical trials to clinical care so too will the standardized imaging protocols translate from a supporting role in trials to clinical practice.

In order to actualize the UPICT concept and goals, the CTSA-IWG has established and implemented specific objectives, strategies, and activities (see next panel).

Objectives
UPICT has established the following objectives:

• Provide a standardized template to facilitate the authoring of, comparison among, and use of imaging protocols within the Clinical Trial Calendar
• Provide a searchable library of imaging protocols that have been used in single- and multi-site clinical trials
• Provide a searchable library of consensus protocols that are endorsed by pertinent experts and organizations
• Provide a forum for clinical trialists and imaging scientists to collaborate on improving the value of imaging protocols in clinical trials
• Ensure that UPICT is transparent and inclusive
• Avoid duplication of other clinical trial imaging protocol development efforts (but instead include their work products within the UPICT infrastructure)

Strategies / Activities
UPICT has implemented the following strategies and activities:

• Inclusion of CTSA and non-CTSA representation in all UPICT activities including monthly web-based meetings (i.e., imaging device industry, PhRMA, BIO, federal agencies, CROs, academia, and clinical imaging practices)
• Formal workflow for UPICT Processes
• Invite contributions of clinical trial imaging protocols from academia (single- and multi-site) and industry (device, PhRMA, BIO, CRO) trials (Proffered Protocols)
• Establishment of the UPICT Technical Committees which are also contributing Proffered Protocols
• Established UPICT web site / wiki under the CTSA-IWG with specific workspaces for the authoring, vetting, annotation, and editing of protocols – http://upictwiki.ctsa.org/index.php?title=Main_Page
• Finalized UPICT Template v1.0

Current extracting Proffered Protocols into the UPICT Template for posting in the Proffered Protocol Library:

| UPICT Template v1.0
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>6. Executive Summary</strong></td>
</tr>
<tr>
<td><strong>1. Context of the Imaging Protocol within the Clinical Trial</strong></td>
</tr>
<tr>
<td><strong>2. Site Selection, Qualification and Training</strong></td>
</tr>
<tr>
<td><strong>3. Subject Imaging Protocol</strong></td>
</tr>
<tr>
<td><strong>4. Subject Preparation</strong></td>
</tr>
<tr>
<td><strong>5. Imaging-related Substance Preparation and Administration</strong></td>
</tr>
<tr>
<td><strong>6. Image Procurement</strong></td>
</tr>
<tr>
<td><strong>7. Imaging-associated Risks and Risk Management</strong></td>
</tr>
</tbody>
</table>

Considerations
UPICT Consensus Protocols should 1) account for variations in current technology and 2) accommodate continued technological evolution 3) while maintaining protocol stability using versioning; 4) provide detail sufficient to ensure consistency and reproducibility while 5) incorporating placeholders for trial / disease-specific parameters; 6) accommodate standard of care imaging to the extent possible; 7) facilitate accrual; and 8) support the needs of academic, industry, and governmental agencies.

UPICT Proffered and Consensus Protocols recognize the variable capabilities of clinical trial imaging sites worldwide by incorporating Acceptable, Target, and ideal parameters to which participating sites adhere.