Breakout Session 1: Image Acquisition

General Themes

- You need to trust your data.
- You need a plan to ensure your data are acquired in a trustworthy fashion
- This plan must be adapted to your particular task.
- The plan must ensure data are usable, but cannot be so burdensome no one can undertake it.
- A lot of groups have been down this road before.
- We are breaking new ground.

Question 1

- 1) Are there specific prescriptive tests that should be conducted to standardize the image acquisition and imaging equipment performance?
- A. Are physical tests with phantoms, or clinical protocol specifics such as subject positioning and timing of images necessary in order to standardize across multiple sites?

Some Purposes of Phantoms & Qualification Scans

- Screen out sites who cannot follow the protocol
- Ensure that the equipment's results are acceptable
- Establish ongoing equipment performance and compliance by sites (by repeat phantom studies) to reduce amount of non-evaluable data.
- Enable multisite data aggregation

Additional Observations

- It is not safe to assume performance sites know what they are doing or are willing to follow a protocol, especially regarding timing, etc., which can be crucial.
- It is not safe to assume that performance sites are still following the protocol or that they will know if their machines have changed.
- People make even more mistakes than machines.
- Remember to mentally separate the “biomarker” (that is, the biological phenomenon) from the “assay” (that is, the equipment or scan procedure)

Phantoms

- There may be no such thing as the “universal phantom.” Each should be task-specific and modality-specific. “Fit for purpose.”
  - Examples: humans could be a phantom, such as to measure fMRI activity. Or an internal control could act as a phantom, such as liver uptake on PET which should be constant over serial studies.
- We are early in “the science of phantoms.” This is a new field with relatively little past experience to draw on.

Question 2

- 2) How do you select the appropriate imaging modality?
- A. How do the imaging goals of the trial drive the choice of specific modality? (Detection of an abnormality? Measurement of some anatomical and functional property? Assessment of response to therapy in terms of some measured value – diameter, volume, density or some other measure of morphology, some measure of function such as perfusion?)

This question must be answered by the sponsor.

- The sponsor must know the problem statement.
- Read the literature.
- Talk to experts in the field.

  (The goal is to become aware of strengths & weaknesses of various methods.)
- Cite both.
- Repeat.

What about experimental imaging modalities?

- The rapid innovation in imaging is both a strength and a weakness.
- Investigational methods can be used in clinical trials of investigational drugs/devices, but it adds complexity.
- Sometimes, large studies are needed simply to understand quantitatively the performance (e.g., sensitivity/specificity) of imaging tests (e.g., ADNI).
- In general, same drill: Read; Talk; Cite; Repeat.

Question 3

- 3) How can we ensure that clinical trials (as a whole) perform all of the necessary testing to ensure consistency and standardization of image acquisition?
- A. Focus on a certification/accreditation/attestation/audit process, with these groups ensuring adherence to protocol?
- B. Focus on actual physical tests (which phantom and how it relates to clinical task, equipment quality control)
- C. Standardization of the entire clinical protocol, subject positioning, geometry, timing of tests
- D. All of these, some of these?

3A: Some sort of process of attestation / certification / accreditation / auditing is required.

- Outside body accreditation is rarely the right way to do this. (DEXA is the only concrete example.)
- The process must be both “fit for purpose” and practical.
- Remember: it is not safe to assume anything about the sites.

3B: Equipment QC: “Clinical routine” is rarely appropriate

- Daily clinical routine QC of PET, CT, MRI or US is not useful for clinical trial imaging purposes. (The shining exception: DEXA.)
- Example: ACR accreditation for MRI (perhaps the most widespread example) does not assure any sort of performance relevant to clinical trial imaging.

3C: Standardization is Essential

- Focus on the important things to standardize, not on unimportant things.
- Example: timing of PET scans is important.
- If you do not check / audit, it probably won’t happen.

3D: “All of the above”?

- Practicality is crucial!
- Remember that many clinical trials use the screening exam -- which cannot be done per protocol, as it is a clinical scan -- in the data. So, aligning with clinical practice can have dual payoff.
- Timing of repeat phantom scans / repeat QC checks / etc., must be carefully considered.
- Balance all the various issues: performance, availability, feasibility, cost, etc.

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