BACKGROUND

- Numerous multicenter clinical trials in Alzheimer’s disease use amyloid PET as a quantitative biomarker for patient enrichment during screening, and to derive longitudinal efficacy endpoints.

In this context, phantom imaging studies are crucial for reducing quantitative variability due to differences in acquisition settings and intrinsic imaging characteristics.

Phantom studies must also be used to verify that each scanner is properly calibrated and has adequate capabilities to support brain imaging.

Standards for phantom studies validating tumor imaging requirements have been well-described, and generally are focused on quantitative accuracy for uptake “hot spots” at tumor locations.

The task for amyloid PET imaging is quite different: rather than hot spots, correct interpretation of uptake differences between adjacent grey and white matter regions is the goal.

Although metrics for tumor imaging such as image uniformity and resolution recovery are still important for amyloid imaging, use of a realistic anthropomorphic phantom can be helpful in ensuring that all scanners will provide acceptable images for the study, and that scatter and attenuation correction methods work as expected.

Unfortunately, the preparation and analysis of such phantoms is not trivial. We describe methods and pitfalls for PET center qualification using the anthropomorphic 3D Hoffman phantom.

Techniques have been developed to obtain both traditional imaging metrics typical of tumor imaging, and to verify adequate brain imaging quality using a single phantom scan.

METHODS

Phantom Description

- A digital dataset derived from the Data Spectrum 18-slice bitmap was developed to obtain a 160×160×90, 1.548×1.548×1.548 mm voxel gold standard reference volume modeling the individual sub-layers of the Hoffman phantom [1].

- Each slice of this 90-slice phantom represents either an all grey layer with values either 0.0 or 1.0, or a grey/white layer with values either 0.5 or 1.0. When smoothed with a Gaussian filter, this model simulates the \( \frac{4}{1} \) grey matter : white matter uptake pattern typically seen in patient FDG data (Fig 1).

- Amyloid images for negative subjects are nearly the inverse of FDG images, so the Hoffman also provides a realistic model for amyloid imaging.

Hoffman Preparation and Scanning

- Hoffman phantoms are prepared by thoroughly mixing 0.5-0.6 mCi \( ^{18} \text{F-FDG} \) solution in the phantom, and imaging immediately using the same acquisition and reconstruction protocol planned for use with patient imaging.

- Phantoms are positioned in the center of the scanner’s field of view in a standard orientation simulating supine patient brain imaging.

Analysis Methodology

- For phantom analysis, a 20 min portion of the scan is summed and co-registered to the digital gold standard.

- Because the physical Hoffman phantom slice thickness is slightly variable, a scaling term is used in the co-registration process.

- Once co-registered, effective spatial resolution is determined by fitting in-plane and axial Gaussian smoothing parameters to best match the digital model to the test phantom data [2].

- Intensity of the test data is normalized to the gold standard using a volume of interest (VOI) specified in regions of pure grey matter, which represent the highest signal intensity in the phantom.

- Once co-registered, smoothed and intensity normalized, a difference image is computed from which various quantitative and visual assessments can be made.

- Additionally, standard uptake value ratio (SUVR) values are computed and compared for the digital and test datasets using a modified AAL atlas to define regions in the frontal, temporal, cingulate, occipital, parietal, and precuneus areas, normalized to whole cerebellum.

- The data presented here have been applied to Hoffman scan data acquired as a part of the ADNI and other AD studies site qualification process.

DISCUSSION

- The difference image and normalized Hoffman data allow computation of visual and quantitative metrics such as scanner spatial resolution, axial uniformity, grey to white matter contrast and accuracy of SUVR calculations.

- Results also demonstrate potential pitfalls in use of the Hoffman phantom (Fig 2).

- Proper phantom preparation is crucial to remove air bubbles that create areas of hypointensity, and to avoid non-uniformities in phantom radiotracer concentration resulting from improper mixing of the \( ^{18} \text{F} \) solution. In such cases, it is often difficult to determine if image quality is degraded due to improper mixing, or to physical imaging issues with the scanner. Therefore, close examination of the data and in some cases a repeated Hoffman scan must be carried out to verify unacceptable results.

- Another pitfall is that the Hoffman phantom does not completely cover the axial field of view of many scanners. For these environments, it is important to verify performance of the outer imaging planes using auxiliary data, such as from daily and periodic QA procedures, or from a separate scan of a uniform phantom.

CONCLUSION

- Use of a standardized Hoffman phantom acquisition protocol, and comparison to a high-resolution digital gold standard, allows computation of quality metrics and calibration data to reduce inter-scanner variability in multi-center brain PET imaging studies.

REFERENCES


Figure 1 - Digital Hoffman Phantom
- a) 19-slice version supplied by Data Spectrum.
- b) 90-slice version modeling more accurately individual layers of each slice.
- c) smoothed version of the 90-slice digital phantom.
- d) sample real phantom data obtained from the high-resolution HRRT scanner.

Figure 2 - Preparation Pitfalls
- a) air bubbles
- b) point hot spot
- c) hot spot due to plane separation
- d) inadequate mixing (difference image shown)

Figure 3 - Hoffman Analysis Methods
- Test data from a 20min scan are co-registered, intensity normalized, and matched for spatial resolution. Both visual and quantitative analyses are performed on the input and difference image data.
- With this analysis framework, both SUVR accuracy as well as conventional scanner image metrics such as spatial resolution, axial uniformity and signal to noise, can be evaluated from a single phantom scan.

Figure 4 - Example Results
- Top - Typical passing results
- Middle - Failing results with hyperintensity in anterior regions
- Bottom - Failing results due to incorrect scatter correction method

Figure 5 - Summary data from 89 ADNI phantom scans
- Equivalent Hoffman spatial resolution ranged from 3.5 – 8.9 mm
- Other values seen are mean error calculated over the entire brain region, grey/white intensity level calculated within the grey/white ROIs, and the ratio of SUVR seen in one region between the digital standard and the test data.