APPIAN: Automated Pipeline for PET Image analysis

Thomas Funck[1,2], Kevin Larcher[2], Paule-Joanne Toussaint[2], Rick Hoge[2], Alain Dagher[2], Alan C. Evans[2], Alexander Thiel[1,*]

1) Lady Davis Institute, Jewish General Hospital, McGill University; 2) McConnel Brain Imaging Center, Montreal Neurological Institute, McGill University.

*Author for correspondence : alexander.thiel@mcgill.ca

1. Introduction

The increasing availability of large brain imaging data sets makes automated analysis essential. Not only is automated analysis important for saving time, but it also facilitates reproducible research. We therefore present **APPIAN** (**A**utomated **P**ipeline for **P**ET **I**mage **A**nalysis), a new open-source pipeline based on NiPype [1] for performing automated PET analysis. APPIAN begins with reconstructed PET images and performs all the processing steps necessary to extract measures from the PET images and perform statistical analysis (Fig.1). Automation requires rigorous quality control (QC) to ensure that each processing step has been performed as expected. To this end, results from APPIAN are displayed in an internet browser-based dashboard with integrated 3D/4D image viewer for easy visual QC (Fig.2). In addition to visual QC, we have implemented a **novel technique for automated groupwise QC** to detect images that may have failed a processing step. We present a simulation study to assess the sensitivity and specificity of this outlier detection algorithm for detecting errors in co-registration.

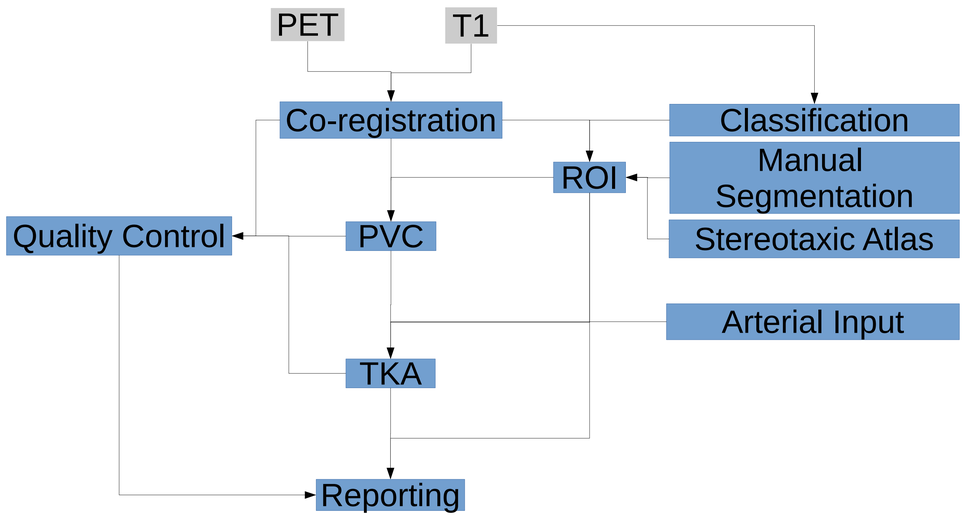

Fig 1. APPIAN performs 1) PET-T1 co-registration, 2) define regions of interest (ROI) for later processing steps, 3) partial-volume correction (PVC), 4) tracer kinetic analysis (TKA), 5) reporting of results for subsequent statistical analysis and 6) quality control (QC).

2. Methods

Three sets of PET images with corresponding T1 MRI were acquired:

- **46 [18-F]-flumazenil (FMZ)**
- **31 [18-F]-fluoro-deoxyglucose (FDG)**
- **26 [11-C]-raclopride (RCL)**

All scans were acquired with the ECAT HRRT scanner in list mode and reconstructed with FBP [2]. PET images were co-registered to T1 images by performing hierarchical co-registration at progressively finer spatial scales [3]. This set of correctly co-registered PET and MRI images formed a set of paired control images.

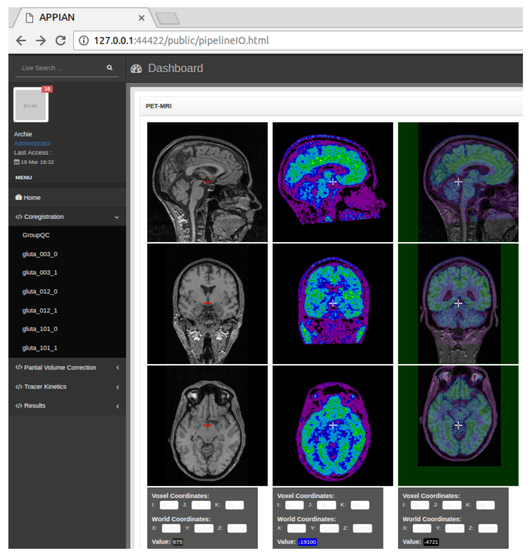

Fig 2. APPIAN uses a browser-based dashboard for visual QC.

For each of the PET images a series of transformations were applied to the correctly registered image to systematically misalign it relative to the T1 MRI:

- **rotations (degrees): 2, 4, 8, 16, 32, 64**
- **translations (mm): 2, 4, 8, 10, 12, 14**

Three similarity metrics were used to were used to measure the correspondence between the co-registered PET and T1 MRI: **mutual information (MI), feature-space entropy (FSE)**, **cross-correlation (CC)** [4]. A synthetic similarity metric (All) was defined as the magnitude of the vector of the normalized values each of the three individual metrics. Outlier detection was performed by approximating the empirical distribution for each similarity metric using gaussian kernel density estimation and calculating the cumulative probability of observing a similarity metric less than or equal to the actual value. The area under the curve (AUC) of the ROC curves for each condition was calculated to compare the performance of the outlier detection at various levels of misregistration.

3. Results

The results from the simulation indicated that the automated outlier detection was able to detect misaligned PET images with good sensitivity. The effect of progressively larger misregistration on the similarity metrics and outlier measure is illustrated in Fig.3.

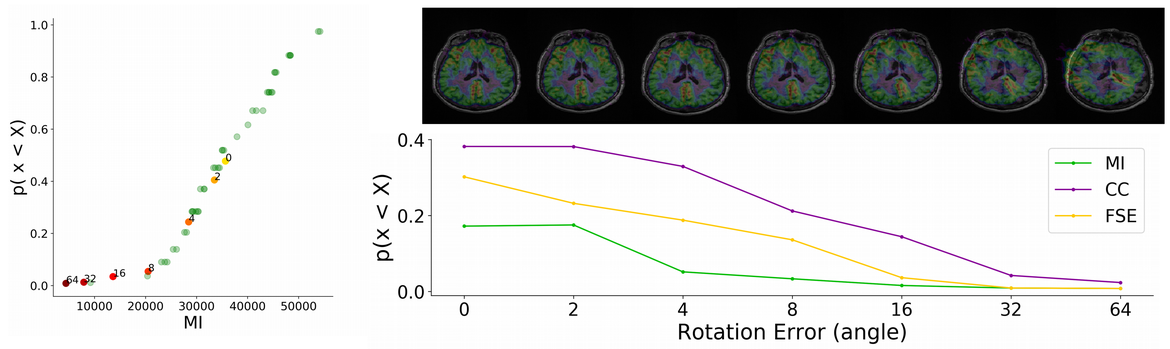

Fig 3. Increasing the misalignment between the FMZ PET and T1 image decreases the similarity, making it easier to identify this PET-T1 pair as an outlier compared to successfully co-registered images.

While the groupwise QC algorithm only performs slightly better than chance (AUC 0.6) for small errors (2° rotation or 2mm offset), this increases quickly to 0.7-0.8 AUC for moderate errors. The sensitivity of the automated outlier detection was generally worse for translation versus rotation errors. Similarly, the optimal similarity metric depended both on the error type and on the radiotracer. For example, CC was very sensitive to outliers for rotated FDG and FMZ PET images, but performed poorly for translated FDG and raclopride images.

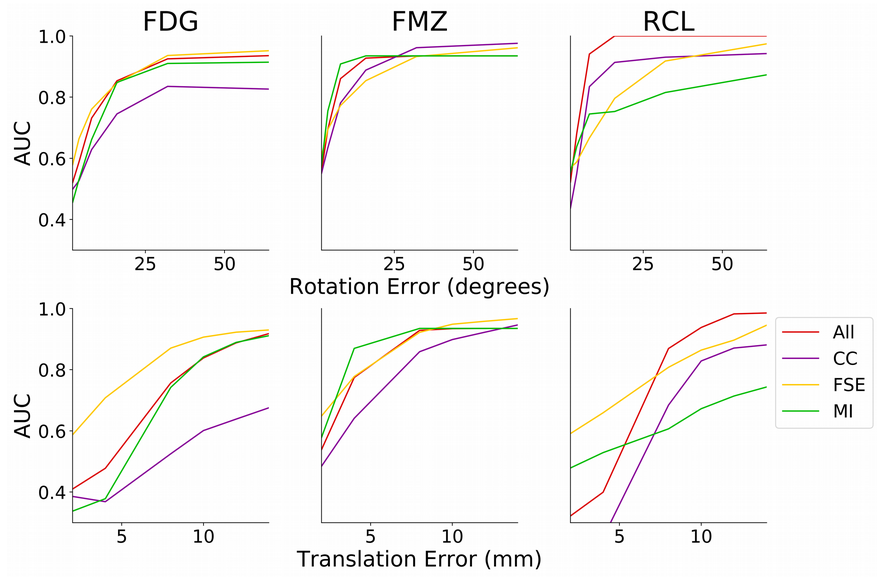

Figure 4. AUC curves show that optimal similarity metric varies for each condition. While small errors are difficult to detect, groupwise QC is able to reliably detect medium to large errors.

4. Conclusion

Rigorous QC is an essential component of any pipeline aimed analyzing big data. We have implemented a new pipeline that includes both a GUI for easy visual QC and an automated groupwise QC algorithm to assist the user in identifying failed processing steps. We tested the groupwise QC algorithm on the co-registration step of the APPIAN algorithm. The results showed that groupwise quality control is able to detect moderate to large errors in co-registration with high sensitivity and selectivity (AUC 0.7-0.9), especially for errors in rotation. While the optimal similarity metric for outlier detection depends on the error type and radiotracer, FSE provides the most reliable outlier detection.

Although the groupwise outlier detection method presented here has been demonstrated in the context of co-registration, future work will extend it to detect failures in TKA and PVC. Future work will also include the incorporation of multiple outlier measures and more similarity metrics (e.g., stochastic sign change).

5. Installation

Github: https://github.com/APPIAN-PET/APPIAN

Docker: docker pull tffunck/tka:latest

References:

[1] Gorgolewski, K. et al. 2011. Front. Neuroinform. 5, 13.; [2] Wienhard, et al. IEEE Trans. Nucl. Sci. 49, 104–110. [3] Collins, et al. 1994. J. Comput. Assist. Tomogr. 18(2), 192–205; [4] Studholme, et al. 1998. Medical Physics. 24(1), 23-25.

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