Evaluating the Effect of Alzheimer's Disease Status on Co-Registration Accuracy of PET and MRI Brain Scans

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Abstract

Does the clinical status of patients with either Alzheimer's disease or mild cognitive impairment when compared with the normal healthy status of control subjects have an effect on the co-registration accuracy of the participants' PET and MRI brain scans? An initial evaluation reveals that a statistically significant difference may exist in co-registration accuracy with some popular algorithms for the different groups of participants' brain scans. These differences suggest that investigators should use appropriate caution when reviewing fusion studies of co-registered PET and MRI brain scans.

Objectives

A variety of registration algorithms are available in clinical and research software to create fusion displays of PET and MRI brain scans. Accurate image registration remains an important concern for scientists and physicians when analyzing brain scans in clinical trials aimed at better understanding and treating dementias such as Alzheimer's Disease (AD). There have been a variety of papers comparing the accuracy of different PET-MRI registration algorithms. However, there has been no study about the effect of brain degeneration caused by AD on PET-MRI registration accuracy. We seek to determine whether a significant difference exists for PET- MRI registration accuracy between various levels of progression of AD. As alternative to null hypothesis of no association, we hypothesize that differences may arise as a result of different rates of progression detected by PET and MRI as a linear correlation, or first a linear and then inverse correlation, ie, first worsening then improving co-registration accuracy.

Methods

MRI and PET brain image data were acquired through 78 brain scan pairs from 27 patients in the AIBL dataset. Each time point of a patient was classified as healthy normal controls (HNC), mild cognitive impairment (MCI), or AD. Each MRI brain scan was registered to the PET scan using six different registration algorithms; SPM 12, SPM 8, SPM 5, Freesurfer, FLIRT, and elastix. Joint entropy (JE) and mean squared error (MSE) were the quantitative metrics used to evaluate the registration accuracy, and a custom-built PET-MRI registration viewer was used to qualitatively evaluate the registration (Figure 1 and 2).

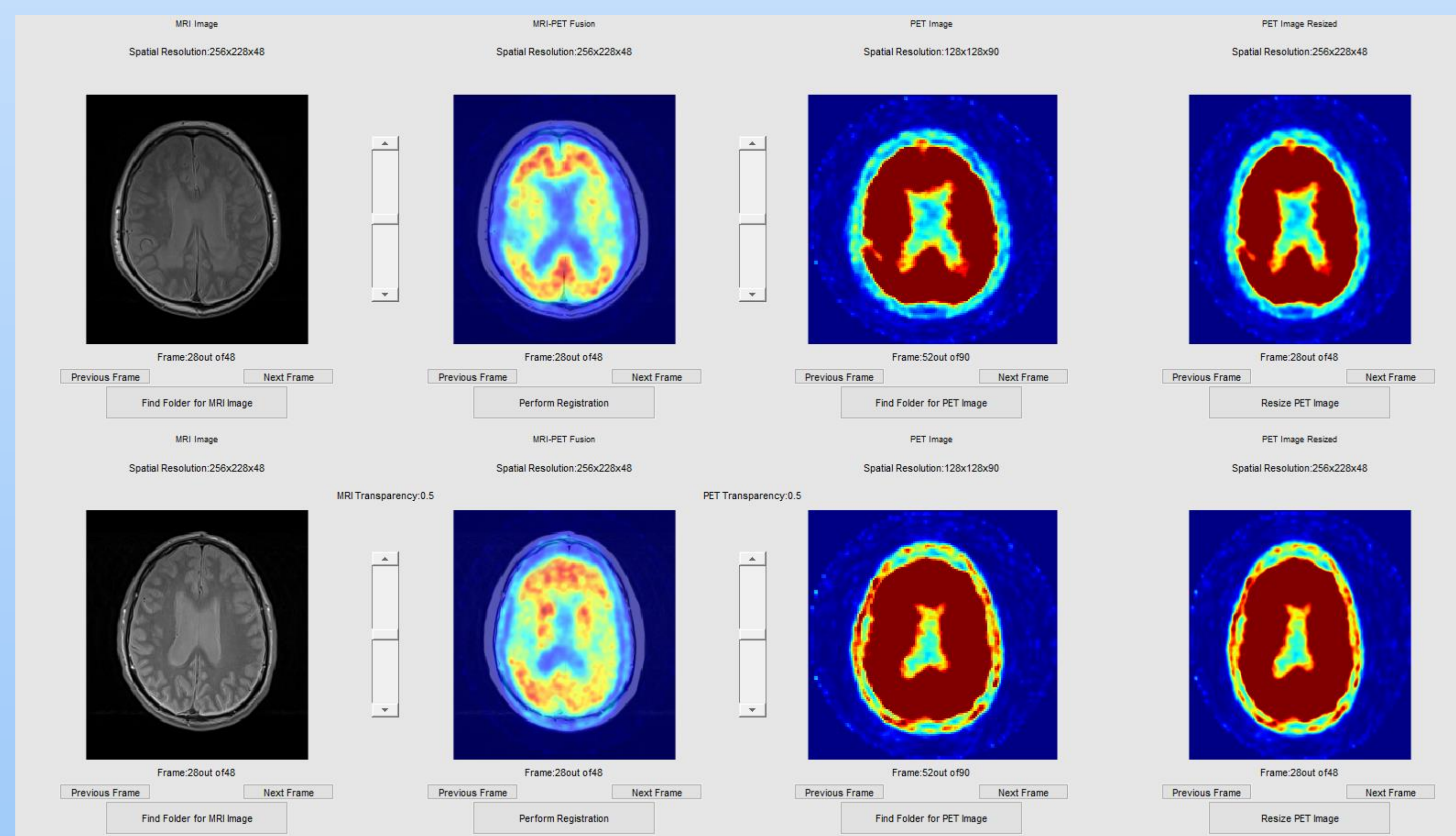### Figure 1: PET-MRI Scan Viewer in Dual Comparison Mode

Table 1: Is there a significant difference between patient condition and registration accuracy?

Algorithm	JE 1	MSE 1	JE 2	MSE 2	JE 3	MSE 3
SPM 12	Yes	Yes	Yes	No	Yes	No
SPM 8	Yes	Yes	Yes	No	Yes	No
SPM 5	Yes	Yes	Yes	No	Yes	No
Elastix	No	No	No	No	No	No
FreeSurfer	Yes	Yes	Yes	No	Yes	Yes
FLIRT/FSL	No	No	No	No	No	Yes

Figure 2: Registration using SPM 12 algorithm (HNC time point on left, AD time point on right)
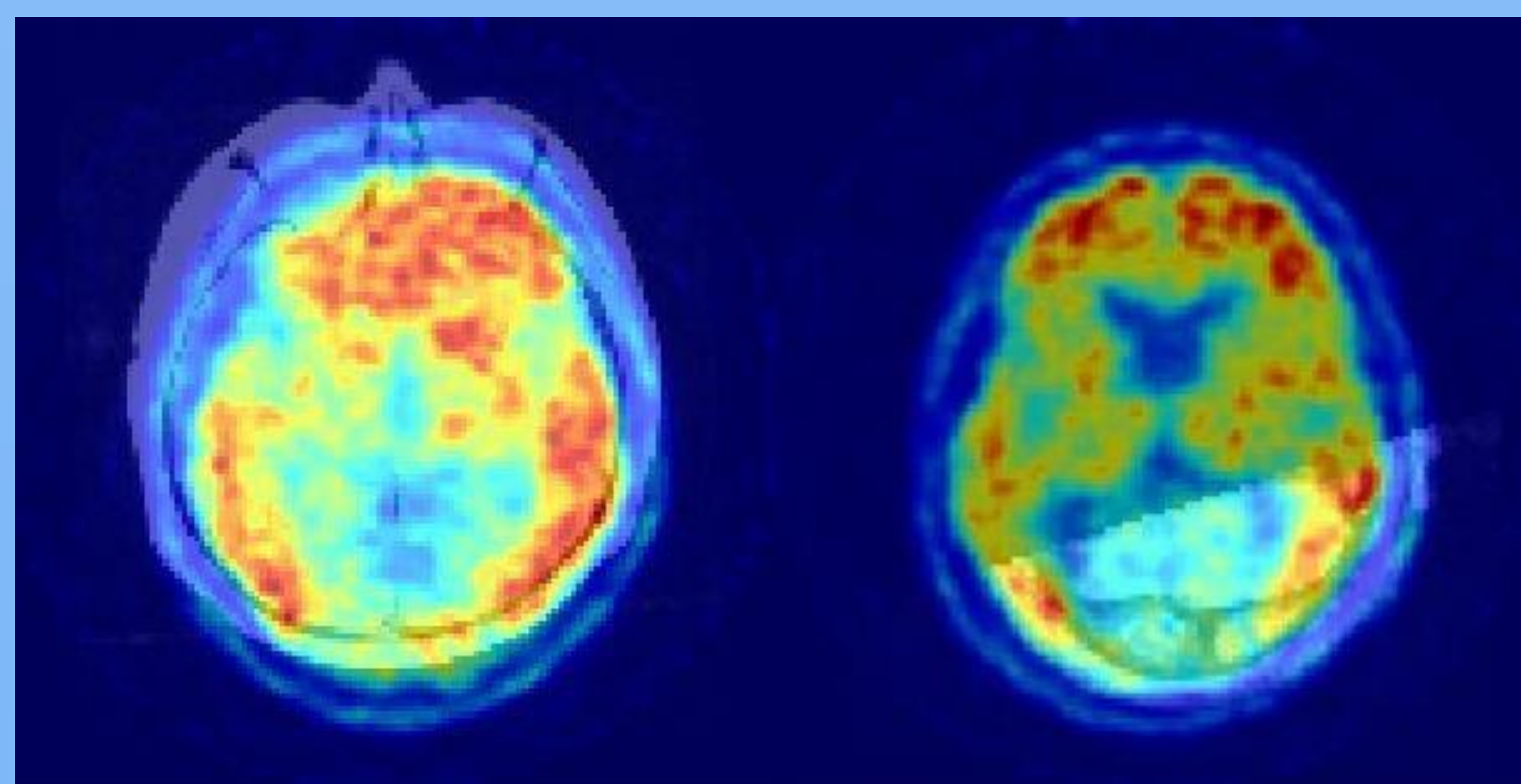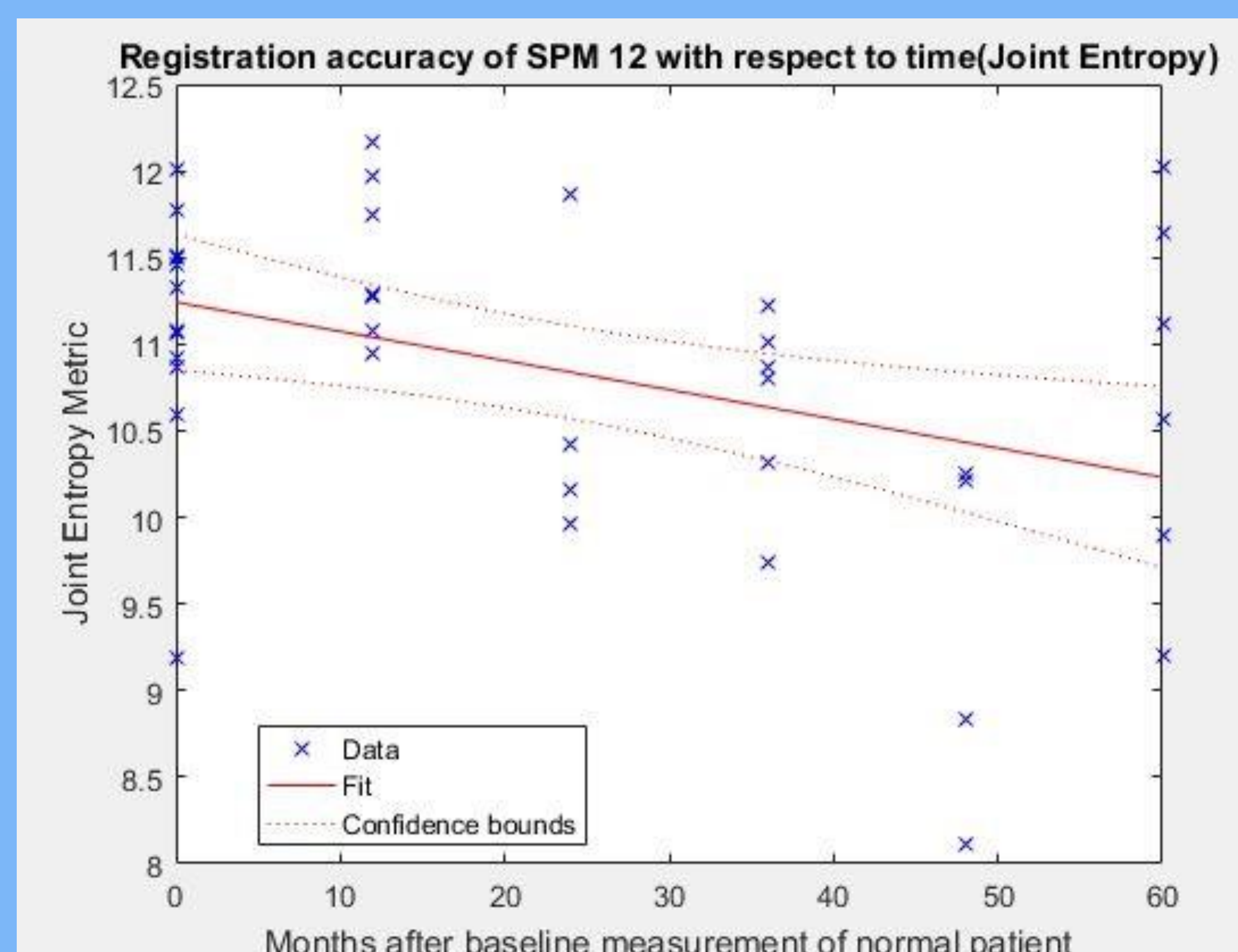

Figure 3: Registration accuracy with respect to time after baseline measurement of HNC (SPM 12 Joint Entropy)

Results

The null hypothesis was no significant difference in registration accuracy because of patient condition. Three tests were used to test this hypothesis for each pair of metric and algorithm; a one way, within subject, analysis of variance test, grouped linear regression analysis (Figure 3), and individual linear regression analysis (Table 1). For four or five of the six metrics (two metrics for the three tests) within the three SPM and FreeSurfer algorithms, at the 5% confidence level, the null hypothesis was rejected, indicating a significant difference in registration accuracy as a result of patient condition, ie, categorical group. For zero or one of the six metrics with the elastix and FLIRT algorithm, at the 5% confidence level, the null hypothesis could be rejected. The rejection of the null hypothesis was caused by the differences of registration accuracy occurring for all 3 patient groups.

Discussion

Because we remain concerned that significant differences may exist across different patient conditions when using certain PET-MRI registration algorithms, investigators should take appropriate care when choosing which algorithm to use for registration of PET and MRI brain scans for different patient conditions. Investigators should also use caution when comparing registration results between brain scans with different patient conditions as this can be inaccurate. These claims of differences in registration accuracy because of patient condition are further confirmed by the fact that independent metrics and tests returned the same result.

Conclusion

Significant differences exist in PET-MRI registration accuracy for some co-registration algorithms in association with a patient's neurodegenerative status within the AD spectrum. In order to investigate further our initial results, we plan to expand our study to include more patients. We also plan on using more types of serial sampling statistics to determine more carefully what type of correlation exists between patient condition and co-registration accuracy.

References

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