# Intelligent image repository for MRI brain clinical trials

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**Introduction:** Serial brain MRI examinations are increasingly used to assess change over time in clinical trials or for diagnosis. This use of MRI requires information to be recalled from data storage and relies on correct identification of scans that were acquired from the same subject. Errors in entering patient information are relatively common. The result can be that images to be compared are wrongly identified thereby confounding clinical trial results or delaying patient management. However, the images themselves contain a wealth of information that can be used to verify the subject's identity. In this work we developed a system called ISIDB for subject identification that uses intelligent text recognition and Image-based Subject Identification (ISI) based on volumetric brain MRI.

**Design**: The ISIDB is an integrated system that stores both subject metadata (i.e. name, date of birth, sex) and the scan data and verifies the subject identity independently from human typed-in information. Scans can be imported directly from the scanner console to the ISIDB which is recognised as a Picture Archiving and Communications System (PACS). In order to achieve robust subject identification, the ISIDB runs a completely automated algorithm to generate for each subject a subject unique identifier (SUID). The SUID is confirmed by analysing the scan data using the ISI algorithm. When a subject is scanned for a clinical trial, their scans can thus be sent to the ISIDB directly from any scanner console. The ISIDB will extract and store the subject metadata. It will rebuild and store all the volumetric images. Then it will perform a fuzzy search (based on the edit distance [1]) on previously scanned subjects that have similar metadata and a confirmed SUID. If a list of fuzzy matches is returned, then it will run the ISI algorithm on the selected candidates until a match is found. This will result in conferring to the new scan the same SUID as the match. When no fuzzy matches are found, the subject is given a new SUID. Since the subject metadata could be completely wrongly typed-in, one scan from the new SUID subject is then compared using ISI to 1 scan from each subject that have a confirmed SUID. If a match is found than the SUID is adjusted to the matched SUID, whereas if no match is found than the new SUID is tagged as confirmed (the subject is genuinely new).

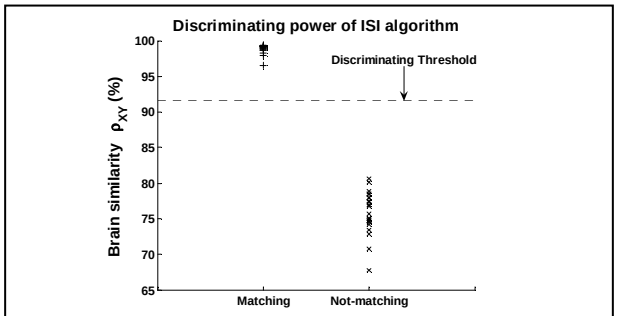


Figure 1. A plot of the brain similarity figures for *matching* pairs and the closest-to-threshold *not-matching* pairs from the test set. The minimum separation between the 2 classes is roughly 26 times the standard deviation of the matching pairs' figures.

**Methods**: The principle of ISI is simple – repeat scans of the same subject should show similar brain morphology so that when aligned there would be only small differences in brain structure in contrast to scans acquired from different individuals: the hypothesis we wished to test was that inter-subject differences were much greater than within-subject changes over time even in patients with neurodegenerative disease or with movement artefacts. If correct this should support the use of the ISIDB in checking subject identification. Key design criteria for ISI were that the method should be simple to use, robust and run quickly, so that it can be applied rapidly at the time of an individual examination. The ISI first extracts the brain from the images of any newly acquired subject (X), to exclude non-brain tissue using FSL BET (www.fmrib.ox.ac.uk/fsl/) in a recursive manner[2]. The new brain images are then aligned with a reference image from the archive using rigid body registration (www/doc.ic.ac.uk/~dr/software). Then the new brain X is aligned to each brain image Y from the fuzzy match result set using rigid body registration with the registrations to the reference image as a starting point (thus making each alignment extremely fast). Then a maximum intensity $I_M$ of each image is computed via the images' histogram. $I_M$ is the threshold which excludes 3% of the total brain volume. Any intensity above $I_M$ is set to $I_M$ and the image intensities are then rescaled to have a range of M = 4096. This allows robust normalisation of the image intensity without undue sensitivity to high signal outliers. The absolute difference image between the 2 normalised aligned brain images is then computed. All voxels that fall below a threshold $\delta$ are masked out from the latter image. Then the number $N_d$ of remaining voxels is computed. $N_d$ is then normalised by the total number of voxels in the intersection of the two masked brains to produce a relative difference figure $\rho'_{XY}$. The volumetric intensity-similarity is then measured by the figure $\rho_{XY}=1-\rho'_{XY}$.Two scans are identical when $\rho_{XY}$ is 1. Thus a scan can be matched to another when $\rho_{XY}$ is above a threshold $\rho_{ID}$. The two thresholds $\delta$ and $\rho_{ID}$ can be learned from an appropriate set of training images. In order to learn the 2 thresholds, a set of 54 T1 weighted head volumetric scans of 22 different subjects was used. The scans were acquired on a 1.5T GE Signa (Milwaukee, USA) with parameters (coronal): FOV 280x280x186cm, resolution 1.3x.1.3x1.3mm [TR/TE/Flip 5.82ms/2.42ms/20, TI 450ms]. Five subjects had Alzheimer's disease (AD) with progressive cerebral atrophy – each of whom had 3 scans: 2 of these were same-day scans and 1 was 1 year later (15 scans); 9 different subjects had very different image quality scans (9 scans of good quality and 10 corrupted ones). The last 20 scans were same-day good quality scans of 10 different subjects. From the 54 scans 15 candidate scans, that had at least another match, were selected as the training subset (TS). 5 of those scans were chosen because the subjects' brains were changing (AD subjects). 10 of the TS scans had poor image quality (due to patient motion). Thus this set would train the ISI to be tolerant to pathological changes in brain and to image quality deterioration. The training process was performed by comparing each scan in the TS to each other scan in the full set. $\rho_{XY}$ was computed for each comparison at several values of $\delta$. Then the minimum value $\rho_{min}(j, \delta)$ of $\rho_{XY}$ that would correctly match the right scans was recorded for each candidate scan $j$ and for each value of $\delta$. A threshold $\rho(\delta)$ on $\rho_{XY}$ was then set as $\rho(\delta)=\text{mean}_{j \text{ in TS}}(\rho_{min}(j, \delta)))-3x\ \text{std}_{j \text{ in TS}}(\rho_{min}(j, \delta))$. Then the threshold $\rho(\delta)$ was used on all comparisons to find the closest not-matching scan $\rho_{XY}$ figure for each value of $\delta$. The value $\delta_{MAX}$ of $\delta$ that gave the maximum relative separation between the previously computed closest not-matching $\rho_{XY}$ figure and $\rho(\delta)$ was chosen as the final image-intensity threshold $\delta_{ID}$, i.e. $\delta_{ID}=\text{argMax}_{\delta}|\text{Max}_{\text{not-matched}}(\rho_{XY}(\delta))-\rho(\delta)|/\text{Max}_{\text{not-matched}}(\rho_{XY}(\delta))$. The values of the thresholds learned from the TS were $\delta_{ID}$=20% and $\rho_{ID}=\rho(\delta_{ID})$=91.6%.

**Results:** To test the ISI we chose an independent set of 22 subjects with 47 scans acquired with a totally different acquisition: sagittal T1-weighted MP-RAGE data acquired at 3T from a Philips Intera scanner (Best, The Netherland) with parameters: FOV 24cmx24cmx18 cm, matrix 208x208x150 ( resolution 1.2mmx1.2mmx.1.2 mm), TR/TR/Flip 9.6ms/4.6ms/8.0, TI 1250ms, shot interval 2260ms. These 47 scans consisted of 8 subjects with 3 scans, 9 with 2 scans and 5 with 1 scan. We selected 22 scans, one from each subject, and compared each to all the other scans using the same thresholds learned from the TS for a total of 506 comparisons. We obtained 506 correct answers: that is a match for scan pairs of the same subject and a not-match for scan pairs from different ones. That implied that the null-hypothesis, i.e. the matching was caused by chance alone, was rejected. The probability of correct answer was thus between 0.993 and 1 with 95% confidence and p-value<<0.0001. Each comparison took 20s on a single core 2.4Ghz Intel computer. The number of comparisons was reduced to 43 when the fuzzy search on the subject name was used. Thus correct matches were found at a rate of 40s/match. Finally, the algorithm scales directly to multicore/cluster like computer systems, thus facilitating higher match rates.

**Discussion and conclusion:** A dedicated image repository for use in longitudinal studies has been developed in order to verify the identity of a newly examined subject. The ISIDB proved robust on T1 weighted data from healthy volunteers and AD patients and with variable quality scans. The ISI approach is a promising means of reducing errors in trials as part of on-site quality control at the time of scanning to allow errors to be detected when they can still be corrected. The method may also have application in clinical use in cases where multiple examinations are obtained.

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[1]V. I. Levenshtein, Soviet Physics Doklady 10 (1966):707–710); [2] Fagiolo et al, in press, British Journal of Radiology