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**INTRODUCTION:** The fusion of multiple medical imaging modalities has to potential to enhance and complement the lack of sensitivity, spatial information or resolution. The image content and contrast of magnetic resonance imaging (MRI) and positron emission tomography (PET) have entirely different meanings. Automatic and accurate image registration is therefore not trivial [1]. Although combined PET-MRI scanners are likely to become more available, most centers have separate imaging systems, often in different rooms [2]. Hence, PET-MRI registration is an important problem that can provide a cost-effective alternative to combined PET-MRI scanners. MRI-MRI or PET-PET registration can exploit spatial information and intensity values only but this is rarely satisfactory for automatic PET-MRI registration. An initial segmentation is often needed for good alignment of images and convergence of the registration solution [1, 3]. Since the image intensity content of PET and MRI images is highly uncorrelated, initialization is a crucial step for a successful and automated PET-MR registration. In this work, we propose an initialization based on principal component analysis (PCA) [4, 5]. PCA is introduced to incorporate spatial information of images as an initial coarse transformation. PCA automatically finds a coarse alignment of the PET and MR images and accelerates convergence. Then, the registration algorithm can exploit numerous strategies to find the best transformation parameters, such as the parzen-windows [6], a Gaussian analysis of overlapping regions, or an histogram comparisons using statistical information [3, 7, 8, 9]. In fact, statistically-based measures, such as mutual information (MI) [10] and correlation ratio (CR) [10, 8], were shown to be effective for PET-MRI registration. In this work, we also use MI and CR as similarity measures in the registration algorithm, and we propose 2 novel elements 1) we introduce a multi-resolution similarity measure combining the intensity histograms at 3 resolution levels simultaneously and 2) we add a PCA initialization to obtain fast, fully automatic accurate registration. These novelties are highlighted for accurate automatic registration of 8 rats in a femur bone tumor study.

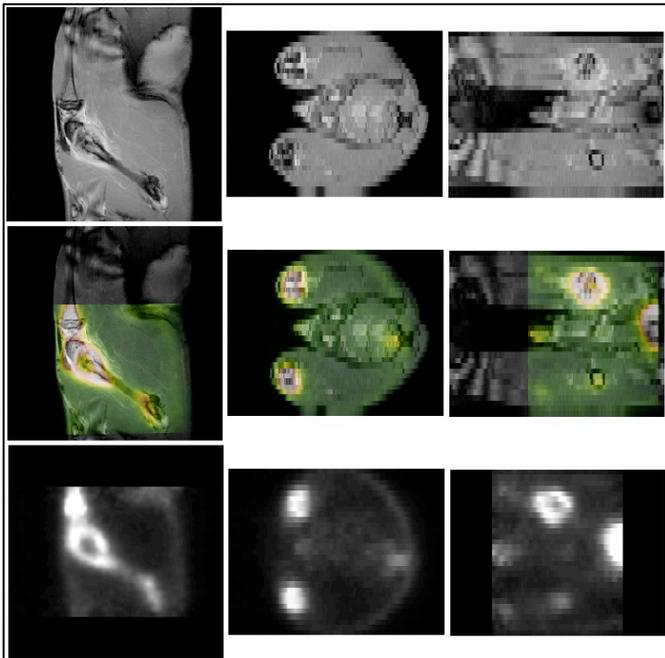


FIG.1 Example of successful PET-MRI registration using MRBIH and PCA initialization

**RESULTS:** The performance of our new registration algorithm was tested

with a PET-MRI femur bone tumor study with 8 rats. The dimensions of the PET images are  $160 \times 31 \times 160$  with a resolution of  $0.5 \times 1.175 \times 0.5$  mm<sup>3</sup>, whereas the MRI matrix dimensions are  $256 \times 256 \times 31$  with a  $0.23 \times 0.23 \times 1.5$  mm<sup>3</sup> resolution. We tested our technique with and without 3 level multi-resolution, with and without PCA initialization, combining results from NMI or SCR measures. For comparison, we also asked an expert to perform the usual manual registration, which we used as our gold standard. Fig.1 shows an example of image registration (3 multi-resolution levels and PCA initialization). Table 1 shows that using multi-resolution facilitates convergence of the DHS as seen by the reduced average number of iterations needed to converge, hence reducing computation time. It also shows that the average of the registration results, where an higher quality results is a statistically better alignment, is improved with the multi-resolution approach. In addition, it appears that the quality of the registration is higher for our automatic registration compared to the manual (gold standard) registration. In 4 of 8 rats, a PCA initialization was not required to converge to an optimal registration. For the 4 other cases, when omitted, results converged to false positives or had an increased distance error from the gold standard solution. Hence, the PCA initialization is not necessarily required when the two volumes are near from the registration solution. The last row of Table 1 shows a decreased mean of maximum translation error (in mm) between the gold standard position and our multi-resolution approach. Finally, using more than 3 levels of multi-resolution did not further improve the quality of the registration.

**DISCUSSION AND CONCLUSION:** In this work, we have presented a new approach for PET-MRI registration, using a PCA initialization and a combined multi-resolution similarity measures ran in parallel. We have shown that a multi-resolution binarized intensity histogram representation used in conjunction with the NMI and SCR similarity measures across multi-resolution levels improves convergence speed and accuracy of the alignment. Our method differs from traditional multi-modality techniques, where only one resolution level is considered at a time [3]. Here, all 3 levels are run in parallel, thus gaining for the low noise sensitivity at coarse levels and higher contrast and details at higher levels. The PCA initialization also incorporates the initial spatial information omitted by statistical measures such as MI and CR [5]. Therefore, our multi-resolution approach with PCA initialization not only removes sensitivity to global noise, but it also guides the convergence by providing a coarse view of the transformation whenever it is needed. We expect our technique to work robustly on PET-MRI data from rat or human brain as these are less challenging than the rat femur presented here.

**REFERENCES:** [1] Herholz *et al* NeuroImage 2004. [2] Pichler *et al* Semin. Nucl. Med. 2008. [3] Liu & Tian IJBI 2007. [4] Schlen CNS vol, page, 2001. [5] Leiva-Murillo *et al* ICA 2004. [6] Xu *et al* IEICE 2008. [7] Roche *et al* U.Nice Ph.D. thesis, 1998. [8] Lau *et al* 2001 Phys. Med. Biol. [9] Milko CARS, 2009. [10] Malandini U.Nice, Ph.D. thesis 2006. [11] Hanh *et al* IEEE, 2010

**METHODS:** Given an MRI volume (fixed volume) and a Na<sup>18</sup>F PET volume (floating volume), we first construct a pyramid of 3 lower resolutions using smoothing and undersampling of the datasets. For each level of the multi-resolution pyramid, we compute a binarized histogram using 32 bins [11]. Hence, we name our technique MRBIH (Multi-Resolution Binarized Intensity Histogram). Then, we perform the PCA initialization to obtain a robust initial coarse transformation. Next, we input the fixed MRBIH and the PCA-transformed MRBIH into a Downhill Simplex (DHS) [5] to determine the 9 unknown affine transformation parameters [1]: translation, rotation and scaling in the axial, coronal and sagittal directions. In order to compare two MRBIH with a given set of transformation parameters, we use the normalized MI (NMI) and the symmetric CR (SCR) on each level of the MRBIH. During the first step of the DHS, each of the 10 initial transformations given around a near-neighbor of the PCA initialization are computed. For each of the 10 sets of parameters, the transformed 3-level-MRBIH are computed and, for each level, the resulting similarity measure is stored. Hence, for each MRBIH of the mobile volume, we have three resulting similarity measures (3 multi-resolution levels), which we combine in a single weighting factor. This factor gives more weight to coarse levels for the initial iterations of the DHS and more weight to the higher levels as the algorithm approaches the solution. This combined multi-resolution similarity measure is used as the quality score for a given set of transformation parameters. The DHS changes the 10 sets of parameters by maximizing their quality score until they all converge to the same set of parameters.

TABLE 1 Average of 8 rat femur bone tumor PET-MRI automatic registration results

	No multi-resolution	3 levels multi-resolution	Gold Standard
Avg Iterations:	46.67 ( $\sigma = 9.2664$ )	37 ( $\sigma = 12.64$ )	---
Quality result:	0.1871 ( $\sigma = 0.0121$ )	0.1906 ( $\sigma = 0.0143$ )	0.1851 ( $\sigma = 0.0150$ )
PCA required:	4 of 8 subjects	4 of 8 subjects	---
Avg error (mm):	2.667 ( $\sigma = 2.338$ )	1.250 ( $\sigma = 1.841$ )	---