Purpose: Registration of micro-PET and micro-CT images is important for the interpretation of multi-modality images. Here we develop a voxel-based image registration method to facilitate the co-registration of multi-modality imaging of small animals.

Method: Rigid image registration (six degrees of freedom: three translational and three rotational parameters) was developed using an open-source ITK/VTK platform for coregistering micro-PET and micro-CT data. Modules importing/exporting DICOM data (binary mask files of contours and image sets) and the scanner specific proprietary microPET/CT/MRI data were also developed. Automated registration procedures based on the normal cross-correlation (NCC) metric and mutual information were implemented. To better “see” the bony landmarks in microPET, a strategy for enhancing the bone matrix uptake of radiotracer by adding a tracer amount of $^{18}$F during the FDG-microPET imaging was investigated. The convergence behavior of the voxel-based registration algorithms was analyzed and the global convergence of the calculation was demonstrated. The accuracy of the developed registration algorithm was assessed by measurements using dual-modality external fiducial line sources incorporated into the mouse cradle.

Results: A voxel-based registration technique has been established for in vivo molecular imaging study. Application of the technique to a number of mice micro-PET and micro-CT registrations indicated that an accuracy of better than 0.2 mm is achievable with the help of $^{18}$F injection. Without lighting-up of the bony structures, however, we found that it is difficult to obtain a registration better than 1mm for regular FDG-microPET. Computationally, the setup based on the NCC metric performs better in comparison with the mutual information approach.

Conclusion: A NCC metric coupled with the use of $^{18}$F injection allowed us to obtain sub-millimeter accuracy in microPET-microCT registration of mice. The robust registration procedure should be valuable for routine molecular imaging application.