

#### Purpose:

Image registration is important for determining correlations of tumor phenotypes to assess and to modify biologically-guided therapies. Such correlations may vary significantly with different registration algorithms. The sensitivity of phenotype correlations to rigid versus deformable registrations was investigated.

#### Methods:

PET/CT images of ten canine patients with sinonasal cancer were acquired using [F-18]FDG, [F-18]FLT, and [Cu-61]Cu-ATSM prior to and 2-3 fractions into radiotherapy. Post-treatment FDG-PET/CT images were acquired 3 months after therapy. CT images were registered to the planning CT using rigid and fast-free-form deformable registrations. The resulting transformations/deformation fields were applied to corresponding PET images. Correlation coefficients between FDG, FLT, Cu-ATSM were calculated over the GTV at different imaging timepoints (pre:pre, pre:mid, and pre:post treatment). Paired t-test and the relative differences of Pearson's R were used to investigate the sensitivity of the phenotype correlations to rigid and deformable registrations.

#### Results:

The difference between rigid and deformable registrations for pre:pre (Diff=2%,  $p>0.05$ ) and pre:mid (Diff=-6%,  $p>0.05$ ) phenotype correlations was insignificant. However, pre:pre phenotype correlations were observed to be very sensitive in dogs with osteosarcoma (Diff=46%) or small tumors (Diff=-20%) due to errors in bony deformations and partial volume effects. Despite not reaching statistical significance, the relative difference in pre:post [18F]FDG correlation of more than -50% indicated that the correlation is very sensitive to registration algorithms.

#### Conclusions:

The study demonstrated that canine sinonasal tumors do not deform severely in the early treatment, while substantial variation between the registration algorithms was observed in pre:post phenotype correlation. Therefore, rigid registration is sufficient for determining the phenotype correlations in early treatment assessment. Deformable registration should be considered for correlations with the post-treatment imaging data. Future works include repeating the study on human patients and using different deformable registration algorithms to fully investigate the sensitivity of phenotype correlations.