Introduction
Advances in glioma imaging have made it possible to not just capture anatomy, but the biology of tumors. Besides well established techniques like DSC perfusion (measuring neangiogenesis), diffusion-tensor imaging (reflecting cellular architecture) and PET-FET (visualizing protein synthesis), amide-proton transfer imaging (APT) has recently been introduced. APT measure the amide concentration and has been shown to correlate strongly with cellular proliferation.

Purpose
Given that these sequences measure partially overlapping biological processes, we aimed to investigate the spatial overlap of biological imaging modalities in a series of patients with newly-diagnosed gliomas.

Methods
We analyzed the preoperative MRI of 18 glioma patients with APT, 32-direction diffusion-tensor (DTI) and perfusion-weighted imaging (PWI). In addition, patients underwent static FET-PET imaging. Post-processing encompassed calculating cerebral blood volume (nCBV) maps using AUC-based leakage correction (Hedderich et al., J. Neuroradial, 2018), and signal deconvolution of DTI data. For the latter, we have previously introduced. APT measure the amide concentration and has been shown to correlate strongly with cellular proliferation.

Results
Of the 18 patients, 12 were diagnosed with an IDH wild type glioblastoma, 2 with an IDH mutant astrocytoma, 3 with an 1p/19q codeleted oligodendroglioma and 1 patient with a BRAF mutant pilocytic astrocytoma.

As we expected from the similar biological processes measured, APT and FET showed the highest correlation (Spearman’s rho = 0.714, adj. p < 0.0001) in the FLAIR-hypointense tumor, nCBV and the tissue volume fraction also showed a high correlation (Spearman’s rho = 0.313, adj. p = 0.0002) in the FLAIR-hypointense tumor. FET and CBV were also positively correlated (Spearman’s rho = 0.309, adj. p = 0.0006). Interestingly, APT and tissue volume fraction were negatively correlated in contrast-enhancing tumor (Spearman’s rho = 0.238, adj. P = 0.009).

To investigate spatial overlap, we analyzed Dice scores between tumor areas defined through established cut-offs in the biological imaging modalities. In general, Dice scores were higher in contrast-enhancing than in FLAIR-hypointense tumor. However, for predicting tumor growth and recurrence, the latter region is most interesting. Here, nCBV and tissue volume fraction had the highest overlap (Dice score = 0.53), followed by FET and CBV (Dice score = 0.428). APT had good overlap with CBV (Dice score = 0.406) and FET (Dice score = 0.398). We observed low spatial overlap for fractional anisotropy and tissue volume (Dice score = 0.295), APT and fractional anisotropy (Dice score = 0.298) and FET and fractional anisotropy (0.270).

Conclusion & Outlook
Voxel-wise, the PET signal was most strongly correlated with APT, followed by nCBV. However, spatial analysis revealed that while there is relevant overlap between some sequences (like nCBV and tissue volume fraction or PET signal and nCBV), each modality also depicts unique areas within the tumor, as is expected from the different oncogenic processes they capture. This highlights the potential of combining imaging information from different sequences to more accurately visualize tumor growth and infiltration.

Figure 1: Examples of the imaging sequences analyzed:
(a) nCBV, (b) APT, (c) Fractional Anisotropy (FA) from DTI data (d) and FET-PET (d).

Reference: