Predicting tumor pH from in-vivo CEST spectra by 31P informed deepCEST MRI

Jan-Rüdiger Schüre[1,2], Junaid Rajput[1], Eike Steidl[2], Manoj Shrestha[3], Ralf Deichmann[3], Elke Hattingen[2], Andreas Maier[4], Armin Nagel[5], Moritz Zaiss[1,4]

[1] *Institute of Neuroradiology, University Clinic Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany*
[2] *Institute of Neuroradiology, Goethe University Hospital Frankfurt, Goethe University, Germany*
[3] *Brain Imaging Center (BIC), Goethe University Frankfurt, Frankfurt am Main, Germany*
[4] *Department Artificial Intelligence in Biomedical Engineering, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany*
[5] *Institute of Radiology, University Clinic Erlangen, Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Germany*

INTRODUCTION: ^{1}H amide proton transfer (APTw) CEST imaging is known for its potential in pH-weighted imaging and overcomes several limitations of measuring pH with phosphorus spectroscopy while providing higher spatial resolution and SNR, reduced scan times and the possibility for its integration into clinical routine[1,2,3,4,5,6]. As the APTw-CEST signal intensity is influenced by MTC, rNOE, tissue liquidity, T1 relaxation or altered protein/peptide and metabolite concentrations, these factors hamper accurate prediction of pH in vivo in brain tumors. Deep learning approaches have demonstrated the ability to perform well in ill-posed situations, suggesting that they could potentially overcome the challenges currently encountered in this field. Therefore, we started to develop a voxel-wise neural network model that can derive the 31P-pHi map directly from APTw-CEST and quantitative measured T1 data (qT1).

METHODS: 15 tumor patients and 1 healthy subject underwent quantitative T1, APT-CEST and ^{31}P- spectroscopic imaging on a 3T PRISMA scanner. A feedforward neural network (FNN) with three hidden layers and a probabilistic output layer providing the mean and heteroscedastic uncertainty[7] was realized in Python. The training was performed voxel-wise, compromising 107786 spectra from 11 patients with co-registered ^{31}P-pH$_i$ as target and the CEST (B1=1µT), qT1 as input data:

(i) B_0-corrected Z-spectra (51 offsets, -8 to 8 ppm)
(ii) APT-weighted MTR_{asym} (3:0.1:4 ppm)
(iii) quantitative T1 values

RESULTS: All unseen patient test datasets provide a good match between the measured ^{31}P-pH$_i$ and down-sampled predictions, while the higher resolved prediction reveals new pH hotspots, as shown in Fig.1. To ensure the prediction does not only perform a T1 segmentation, we modified the healthy subject image (Fig.2a) by adding a tumor feature into the central WM (Fig.2e), which did not affect the pH prediction.

DISCUSSION: We herein show the general feasibility of predicting pH$_i$ from CEST data using a learning-based, 31P-informed approach. Although the down-sampled data match well the ^{31}P-pHi maps, the prediction shows slightly elevated pH$_i$ in WM. It could be further demonstrated that the predictive model does not simply perform a T1 segmentation. Consequently, the information for the pH prediction is likely hidden in the CEST data. Surprisingly, deepCEST shows different tumor features that can't be seen in qT1 or MPRAGE maps, which derive through the higher-resolved CEST data. It is therefore even more exciting to expand this approach in the future with additional B1 levels and CEST features such as amines or hydroxyl groups and thus get closer to a clinically accessible alternative for non-invasive pH determination.

CONCLUSION: High-resolution CEST–MRI–based pH$_i$ mapping in brain tumors seems possible at 3T, but needs further optimization such as the acquisition of B1 levels or better suited predictive network structures.

REFERENCES:

1.Zhou et al.,,Nat Med (2003), 2.Zaiss et al.,MRM (2017), 3.Tang et al., Front Oncol (2020), 4.Longi et al., J Am Chem Soc (2014), 5.Schuere et al., NMR in Biomedicine (2019), 6. Liepinsh and Otting,MRM(1996), 7. Glang et al., MRM (2019)

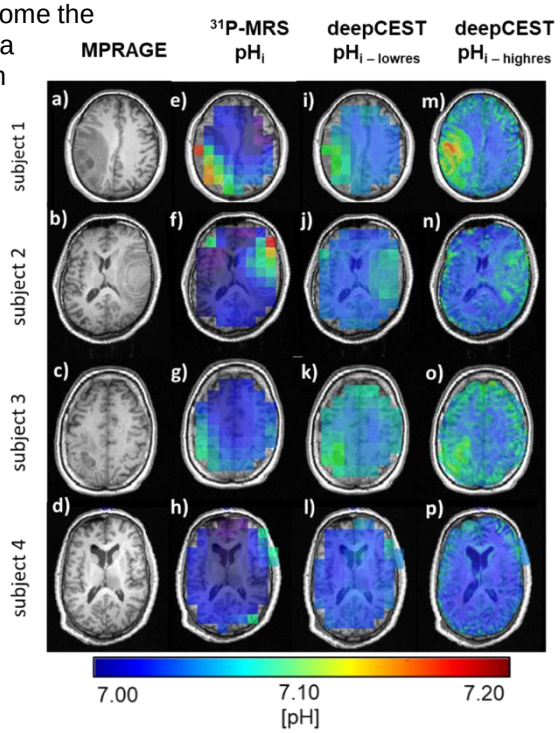

Fig.1: Unseen tumor patients (a-d) with phosphorus pH (e-h) and down-sampled (i-l) and higher resolved (m-p) prediction

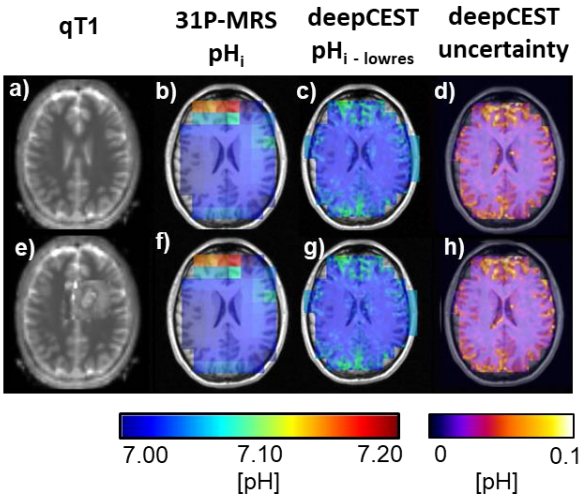

Fig 2: Illustrates the impact of a network attack on T1 data, both without (a) and with (e) tumor. Original 31P-pH data is presented in (b,f), while the predictions (c,g) and uncertainty (d,h) seem similar.