# Assessing Gamma-Knife Treatment Response in Human Brain Metastasis with CEST MRI

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**INTRODUCTION:** Gamma-Knife Stereotactic Radiosurgery (SRS) represents a significant advancement in the targeted treatment of brain metastases by administering high doses of radiation in a conformal manner to ensure that the concentration of radiation is confined mainly to the tumor area, preserving the surrounding healthy tissue. Hence, there is a pressing clinical need for reliable biomarkers for quick and accurate evaluation of Gamma-Knife SRS treatment response. Chemical Exchange Saturation Transfer (CEST) Magnetic resonance Imaging (MRI) emerged as a novel and promising technique that is sensitive to various pathophysiological conditions, potentially serving as an imaging biomarker for tumor response in Gamma-Knife SRS[1].

**METHODS:** Two patients diagnosed with brain metastasis were included. Imaging assessments were carried out at two critical junctures: the first scan was acquired before the initiation of Gamma-Knife SRS treatment to establish a baseline, and the second scan was acquired two weeks following the treatment to gauge early treatment response. Patients were scanned on a 3T MRI (Verio, Siemens) for routine scans such as 3D spin-echo $T_1$-weighted imaging and $T_2$-weighted imaging and CEST data was collected using a 2D spin-echo echo-planar sequence at 61 frequency offsets with repeated sampling at ±3.5 ppm, and off-resonance scans at ±100 ppm were acquired for signal normalization.

$MTR_{asym}$ analysis was performed voxel-wise to obtain an amide proton transfer (APT) value at 3.5 ppm. The Region of Interest (ROI) was manually delineated in the pre-treatment $T_1$-weighted image and then transformed to the pre-treatment and post-treatment CEST space. The mean APT value within the ROI of pre- and post-treatment were compared, and the difference was assessed using the Student's paired t-test (p=0.05).

**RESULTS:** Fig. 1 presents a representative imaging analysis for Patient 1. Visually, the tumor size for pre-treatment and post-treatment remained stable in the anatomical images, while CEST $MTR_{asym}$ analysis exhibited a marked reduction in APT signal within the tumor ROI. Patient 2 showed minimal visual changes in both anatomical and CEST $MTR_{asym}$ analysis (Fig.2). The observation is supported by box plot analysis (Fig. 3), where the changes in Patient 1 were statistically significant while changes in Patient 2 were not significant.

**DISCUSSION:** This proof-of-concept study underscores the potential of CEST MRI in providing early indicators of treatment response to Gamma-Knife SRS in brain metastasis, showcasing its detection abilities within a mere two-week period. While $T_1$ and $T_2$-weighted imaging still did not show obvious changes, CEST MRI in Patient 1 showed significant changes, which signifies the response to Gamma-Knife treatment within two weeks. The reduction in tumor cell density might be one of the possible reasons for the lower CEST signal observed. The insignificant changes in Patient 2 may suggest that the tumor has a limited response to the treatment, indicating a possible need for additional treatment strategies to enhance therapeutic outcomes.

**CONCLUSION:** CEST MRI has demonstrated its ability to detect changes before and after Gamma-Knife treatment, with significant findings observed as early as 2 weeks post-treatment.

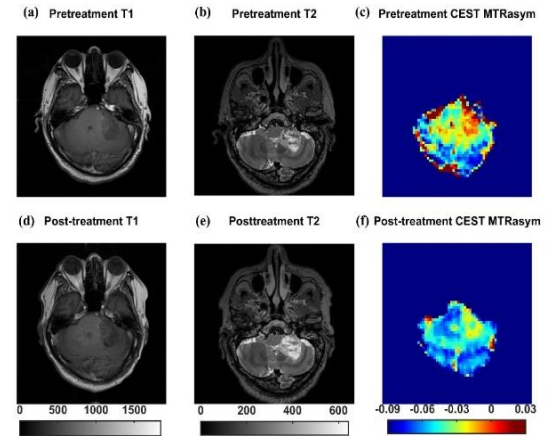**REFERENCES:** 1. Zhou, et al. Magn Reson Med 2022; 88(2):546-574

Fig. 1 Representative brain MRI images from Patient 1. Pre- and post-treatment of (a,d) $T_1$-weighted imaging, (b,e) $T_2$-weighted imaging, and (c,f) CEST $MTR_{asym}$ (3.5 ppm).
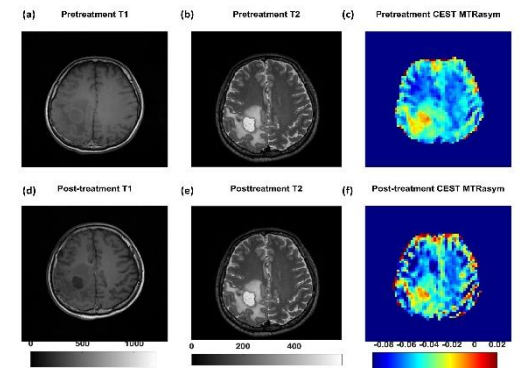


Fig. 2 Representative brain MRI images from Patient 2. Pre- and post-treatment of (a,d) $T_1$-weighted imaging, (b,e) $T_2$-weighted imaging, and (c,f) CEST $MTR_{asym}$ (3.5 ppm)



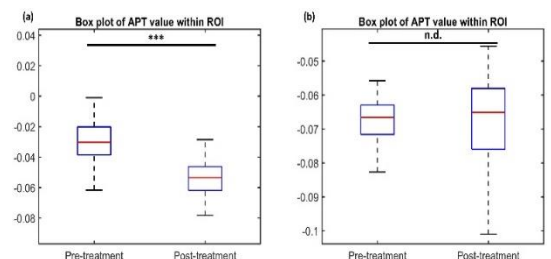Fig. 3 Box-and-whisker plot of pre- and post-treatment APT values within ROI for (a) Patient 1 (p-value < 0.001, *** - significantly different) and (b) Patient 2 (p-value > 0.05, n.d. - not significantly different).