VALIDATION OF IOPAMIDOL-BASED MRI-CEST IMAGING TO DETECT AND VISUALIZE TUMOR AREA IN GLIOBLASTOMA MURINE MODELS

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INTRODUCTION: Glioblastoma is the most aggressive brain tumor with very poor prognosis. Gadolinium-based contrast agents are the gold standard for both detection and delineation of brain tumors, although the observed accumulation of these agents following repeated administration stimulated the quest for alternative agents [1,2]. Iodinated contrast media have recently been introduced as promising contrast agent within the MRI-CEST technique with good tumor detection capabilities [3]. In this study we investigated for the first time Iopamidol for tumor detection and delineation in murine brain tumors and validation was assessed by comparing tumor brain delineation with a conventional Gd-based contrast agent.

METHODS: The glioblastoma murine model was obtained upon stereotaxic injection of $2x10^5$ GL261 cells into 8-week-old male C57BL/6 mice. MR images were acquired with a microimaging Avance NEO (Bruker) 7T scanner equipped with a quadrature head coil with sequential intravenous injection of Iopamidol (dose 4 g I /kg) and of gadoteridol (dose 0.2 mmol Gd/kg) and acquisitions of CEST and T1w sequences, respectively. Qualitative and quantitative comparison between the two contrast agents was performed by evaluating contrast enhancement capabilities (in both difference images and post-contrast injection images), contrast to noise ratio (CNR) and tumor border delineation. Intra- and inter-observer variability was also assessed.

RESULTS: Iopamidol was well detectable inside the brain tumors and provided enough contrast enhancement to detect and delineate brain tumors in both difference image (ΔST at 4.2 ppm) or in post-injection images (ST% at 5.5 ppm) (Fig1a), although post-injection and contrast enhanced T1w images upon gadoteridol injection provided higher contrast enhancements than iopamidol. Evaluation of the Iopamidol tumor delineation capabilities in comparison with the Gd-based contrast agent showed moderate overlapping percentage, but high volume ratio and DICE values (Fig1c) between the ROIs drawn on iopamidol-based images and those drawn on Gd-based images. Low intra- and inter-observer variability was observed for both contrast agents.

DISCUSSION: Iopamidol showed good capability for detecting and contouring the tumor region, with good spatial correlation of contrast enhancement values across tumor regions. Although the Gd-based contrast agent still provides superior contrast and higher enhancement in poor vascularized tumors, Iopamidol bears a high potential for brain tumor detection.

CONCLUSION: Our study demonstrated that iopamidol is a promising alternative to Gd-based contrast agents for detecting and delineating brain tumors.

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REFERENCES: 1. van der Molen AJ *et al.* Eur J Radiol 2008;66:168; 2. Gulani V *et al.* Lancet Neurol 2017;16:564-570; 3. Anemone A *et al.* Eur Radiol 2017;27:2170-2179

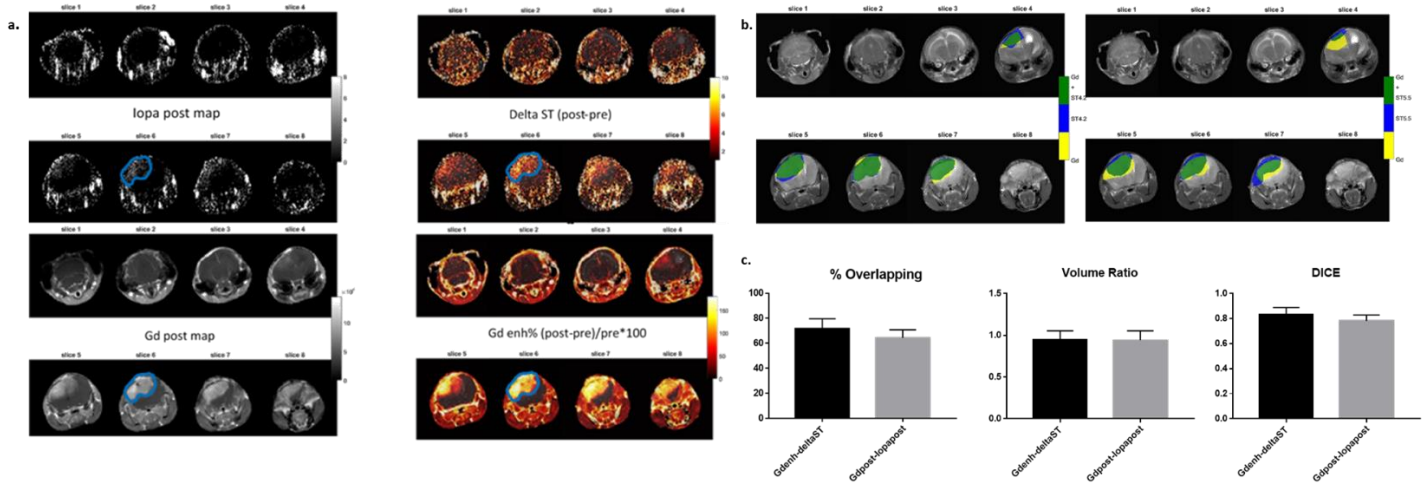

Figure 1. Representative post-inj. and deltaST images for Iopamidol and post-inj. and contrast enhanced images for Gadoteridol (right) with corresponding masks delineating tumor regions in the GL261 glioblastoma murine model (a). Overlapping between masks drawn on CEST and on Gadolinium-based images (b) and graphs showing calculated overlapping, volume ratio and DICE metrics (c).