Two cell lines, J3T-1 and J3T-2, were derived from the same parental canine glioma cell line, J3T. These cells were inoculated to establish brain tumors in athymic mice and rats. Pathologic samples of these animal gliomas were examined to analyze invasive patterns in relation to angiogenesis and were compared with human glioblastoma samples. The molecular profiles of these cell lines were also shown.

Histologically, J3T-1 and J3T-2 tumors exhibited different invasive patterns. J3T-1 cells clustered around newly developed vessels at tumor borders, whereas J3T-2 cells showed diffuse single-cell infiltration into surrounding healthy parenchyma. In human malignant glioma samples, both types of invasion were observed concomitantly. Molecular profiles of these cell lines were analyzed by immunocytochemistry and with a quantitative reverse transcription-polymerase chain reaction. Vascular endothelial growth factor, matrix metalloproteinase-9, hypoxia-inducible factor-1 and platelet-derived growth factor were overexpressed in J3T-1 cells rather than in J3T-2 cells, whereas integrin αvβ3, matrix metalloproteinase-2, nestin, and secreted protein acidic and rich in cysteine were overexpressed in J3T-2 cells rather than in J3T-1 cells.

These animal models histologically recapitulated two invasive and angiogenic phenotypes, namely angiogenesis-dependent and angiogenesis-independent invasion, also observed in human glioblastoma. These cell lines provided a reproducible in vitro and in vivo system to analyze the mechanisms of invasion and angiogenesis in glioma progression [1)].

The canine glioblastoma cell line J3T-1 was subcutaneously injected into a 6-week-old female BALB/c nude mice to obtain tumour fragments. Tumor fragments were implanted into adult male mongrel dog brains through surgery. Multiparametric MRI was performed with conventional MRI, diffusion-weighted imaging, and dynamic susceptibility contrast-enhanced perfusion-weighted imaging at one week and two weeks after surgery in a total of 15 surgical success cases. The presence of tumor cells, the necrotic area fraction, and the microvessel density (MVD) of the tumour on the histologic specimen were assessed. Tumor volume, diffusion, and perfusion parameters were compared at each time point using Wilcoxon signed-rank tests, and the differences between tumor and normal parenchyma were compared using unpaired t-tests. Spearman correlation analysis was performed between the imaging and histologic parameters.

All animals showed a peripheral enhancing lesion on MRI and confirmed the presence of a tumor through histologic analysis (92.3%). The normalized perfusion values did not show significant decreases through at least 2 weeks after the surgery ($P > 0.05$). There was greater cerebral blood volume and flow in the Glioblastoma than in the normal-appearing white matter (1.46 ± 0.25 vs. 1.13 ± 0.16 and 1.30 ± 0.22 vs. 1.02 ± 0.14; $P < 0.001$ and $P < 0.001$, respectively). The MVD in the histologic specimens was correlated with the cerebral blood volume in the Glioblastoma tissue ($r = 0.850$, $P = 0.004$).

The results suggest that the canine Glioblastoma model showed perfusion imaging characteristics similar to those of humans, and it might have the potential as a model to assess novel technical developments for glioblastoma treatment [2)].

1)
Inoue S, Ichikawa T, Kurozumi K, Maruo T, Onishi M, Yoshida K, Fujii K, Kambara H, Chiocca EA, Date I. Novel animal glioma models that separately exhibit two different invasive and angiogenic phenotypes of human glioblastomas. World Neurosurg. 2012 Dec;78(6):670-82. doi: 10.1016/j.wneu.2011.09.005. Epub 2011 Nov 7. PMID: 22120277.
2)

Lee S, Choi SH, Cho HR, Koh J, Park CK, Ichikawa T. Multiparametric magnetic resonance imaging features of a canine glioblastoma model. PLoS One. 2021 Jul 9;16(7):e0254448. doi: 10.1371/journal.pone.0254448. PMID: 34242365.