

#### Variations in Blood-Brain Barrier Disruption in Metastatic and Primary Brain Neoplasms

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Introduction

The effects of metastatic and primary brain neoplasms on the blood-brain barrier are poorly understood. To better understand this interaction, the morphology of the astrocytic component and blood brain barrier structural and functional proteins in the peritumoral region can be analyzed.

## **Methods**

9 patients that underwent resection of metastatic or primary brain neoplasms (5 metastases, 1 low grade astrocytoma, 2 anaplastic astrocytomas, 1 glioblastoma) were included in the study. Magnetic resonance (MR)imaging, histopathologic and immunohistochemical (glial fibrillary acidic protein [GFAP], CD31, tight junction protein zona-occludin 1 [ZO-1], and Pglycoprotein [C219]) findings were analyzed.

### Results

Metastases including melanoma and colorectal cancer, demonstrated lack of perivascular GFAP, Pglycoprotein, a n d discontinuous ZO-1 on CD31 positive intratumoral vessels. Low grade astrocytoma maintained integrity o f the neurovascular architecture while anaplastic astrocytoma a n d glioblastoma demonstrated reactive astrocytic architecture a n d discontinuous immunofluorescent staining for ZO-1 and the presence of P-glycoprotein. Neurovascular compromise in gliomas as seen by immunofluorescence was, however, less than that of metastatic lesions.



Fig. 1 Variations in blood-brain barrier and tumor cell interactions. A) Cervical cancer cells do not invade native astrocytes surrounding blood vessels. This is clinically apparent on MRI. B) Metastatic colorectal and melanoma cancer cells are better able to disrupt astrocyte foot processes and hence disrupt the BBB. This is clinically apparent by contrast enhacnedment on MRI.



Metastastic melanoma lesions also disrupt tight junction proteins (ZO-1) of blood vessels. B) Primary brain tumors such as low grade astrocytomas preserve ZO-1 integrity. These staining patterns correlate with increased contrast enhancment in metastatic lesions.

# Conclusions

Regions of MR-imaging enhancement in metastatic malignancies correspond to areas of structural (including the astrocytic component and tightjunction proteins) and functional (P-glycoprotein) disruption. Low grade gliomas of the brain maintain both structural and functional integrity while high grade gliomas do not. Structural and functional compromise of the blood-brain barrier is greatest in metastatic lesions.

#### References

Wilhelm I, et al. Int J Mol Sci. 2013 Jan
11;14(1):1383-411
Wolburg H, et al. Mol Aspects Med. 2012
Oct-Dec;33(5-6):579-89