Blood-Brain Barrier Disruptions

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Conflicts of Interest

No conflicts of interest reported.
Blood-Brain Barrier Disruption (BBBD)

- BBBD transiently opens the vasculature throughout the mannitol-infused hemisphere
- Safely enhances delivery of chemotherapy, antibodies and nanoparticles in animals and patients

Evans blue dye

Dog brain

CT scan

Rat brain quantitative autoradiography

BBBD

IV

IA/BBBD

PCNSL
Gadolinium and BBBD

Animal Studies

- In dogs, dose-dependent delayed seizures with increasing (0.05, 0.1, 0.2 mmol) doses of gadopentate dimeglumine (Roman-Goldstein, AJNR 1991)
- Seizures not seen in rats given gadolinium with BBBD (Roman-Goldstein, J Comput Assist Tomogr, 1994)

Human Studies

- To date 4,018 BBBD procedures (unpublished data from OHSU 1995 to 2017)
- Very low incidence of seizures without methotrexate (~2%)
- Incidence is higher in patients receiving methotrexate (~9%)
- Repetitive doses of gadolinium may show analogous results to methotrexate following BBBD
Conclusions

• Bottom line:
  • BBBD alone rarely causes seizures, even in brain tumor patients who are prone to seizures.

• Hypothesis:
  • Repetitive doses of gadolinium may show analogous results to methotrexate following BBBD.

• Next step:
  • Primate study: standard IV dose of GBCAs (linear vs. macrocyclic) after BBBD.
  • Epidemiologic study assessing seizures and serial EEGs in patients exposed to repetitive doses of GBCA with different chemical characteristics.