

# Blood-Brain Barrier Disruptions

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# Conflicts of Interest

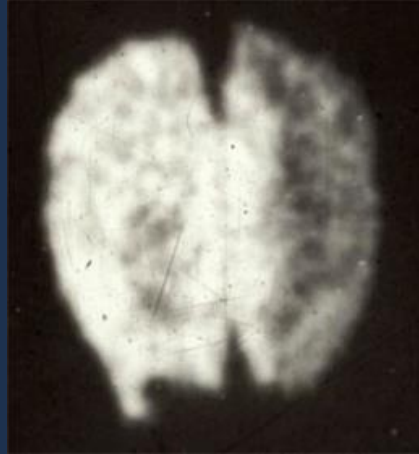
No conflicts of interest reported.

# Blood-Brain Barrier Disruption (BBBD)

Dog brain



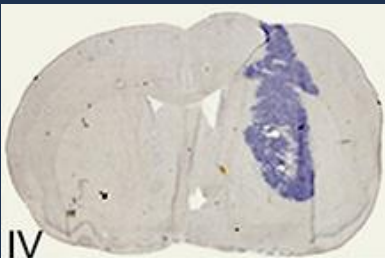
Evans blue dye



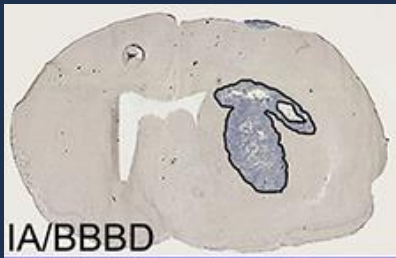
CT scan

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

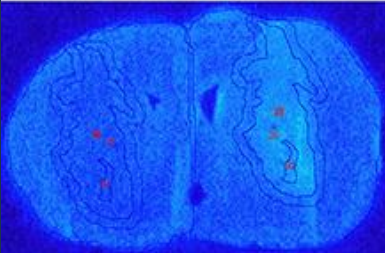
Rat brain quantitative autoradiography



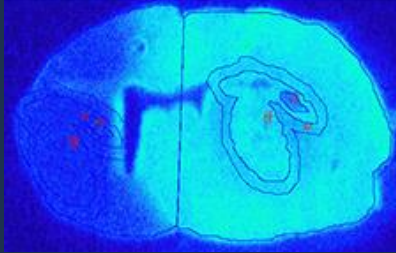
IV



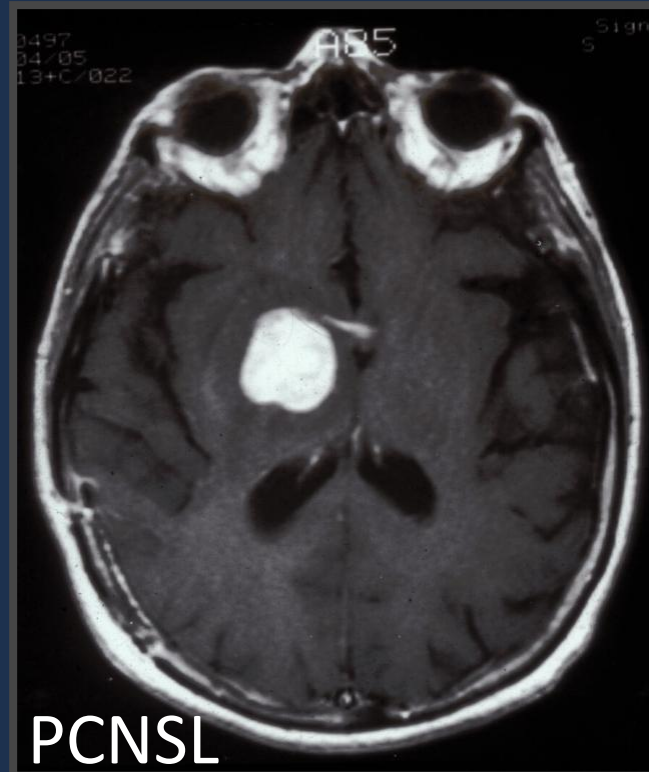
IA/BBBD



IV



BBBD



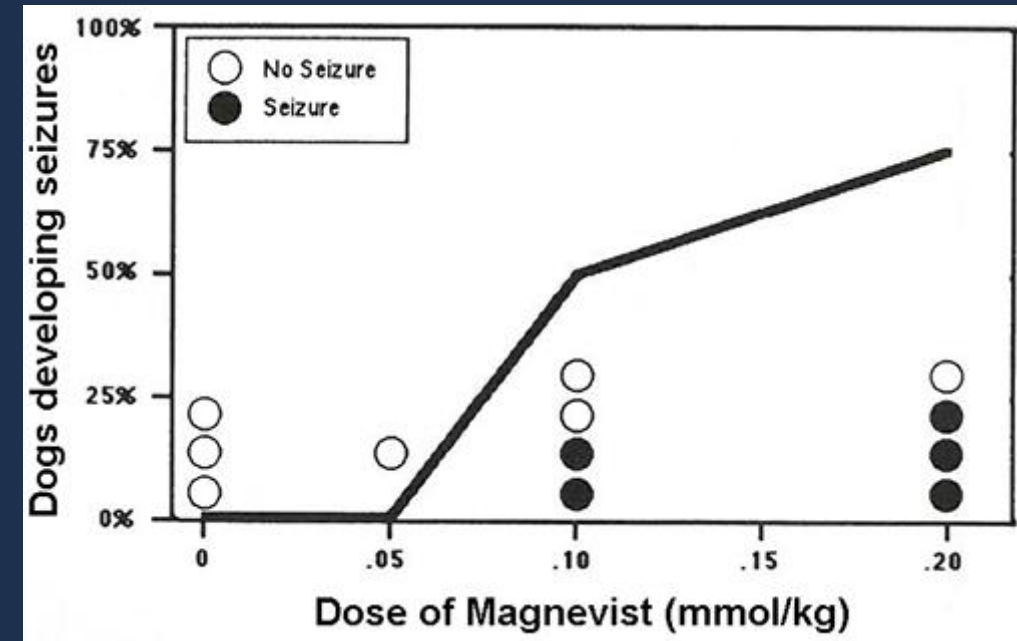
PCNSL



# 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)



(Roman-Goldstein, AJNR 1991)

## 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.