# Convection-enhanced delivery of Topotecan

Convection-enhanced delivery of topotecan into diffuse intrinsic brainstem tumor.

Convection-enhanced delivery of topotecan into high grade glioma.

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Intracerebral convection-enhanced delivery (CED) has been limited to short durations due to a reliance on externalized catheters. Preclinical studies investigating topotecan (TPT) CED for glioma have suggested that prolonged infusion improves survival. Internalized pump-catheter systems may facilitate chronic infusion.

D'Amico et al. described the safety and utility of long-term TPT CED in a porcine model and correlation of drug distribution through coinfusion of gadolinium.

Fully internalized CED pump-catheter systems were implanted in 12 pigs. Infusion algorithms featuring variable infusion schedules, flow rates, and concentrations of a mixture of TPT and gadolinium were characterized over increasing intervals from 4 to 32 days. Therapy distribution was measured using gadolinium signal on MRI as a surrogate. A 9-point neurobehavioral scale (NBS) was used to identify side effects.

All animals tolerated infusion without serious adverse events. The average NBS score was 8.99. The average maximum volume of distribution (Vdmax) in chronically infused animals was 11.30 mL and represented 32.73% of the ipsilateral cerebral hemispheric volume. Vdmax was achieved early during infusions and remained relatively stable despite a slight decline as the infusion reached steady state. Novel tissue TPT concentrations measured by liquid chromatography mass spectroscopy correlated with gadolinium signal intensity on MRI ($p = 0.0078$).

Prolonged TPT-gadolinium CED via an internalized system is safe and well tolerated and can achieve a large Vdmax, as well as maintain a stable Vd for up to 32 days. Gadolinium provides an identifiable surrogate for measuring drug distribution. Extended CED is potentially a broadly applicable and safe therapeutic option in select patients [1)].

## References

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D'Amico RS, Neira JA, Yun J, Alexiades NG, Banu M, Englander ZK, Kennedy BC, Ung TH, Rothrock RJ, Romanov A, Guo X, Zhao B, Sonabend AM, Canoll P, Bruce JN. Validation of an effective implantable pump-infusion system for chronic convection-enhanced delivery of intracerebral topotecan in a large animal model. J Neurosurg. 2019 Aug 2:1-10. doi: 10.3171/2019.3.JNS1963. [Epub ahead of print] PubMed PMID: 31374547.