

Introduction

The effective delivery of central nervous system (CNS) targeted therapies, particularly gene editing modalities, is often hindered by the restrictive nature of the blood-brain barrier (BBB). The strategic placement of intrathecal catheters allows for a tailored approach, accommodating drugs designed to target specific regions in the CNS. This approach enhances drug efficacy and reduces systemic exposure and potential side effects. Test articles delivered intrathecally are distributed through the CNS to multiple tissues. Placement of indwelling intrathecal catheters significantly enhances the diffusion and bioavailability of therapeutic agents across targeted regions of the brain, as evidenced by improved pharmacodynamic outcomes compared to traditional systemic administration routes.

Intrathecal delivery can be performed using different methods including direct dosing into the lateral ventricles, Percutaneous cisterna magna and lumbar punctures, open surgical visualization and puncture of the dura, temporary intrathecal catheterization, and what is quickly becoming the gold standard, intrathecal catheterization with indwelling port. This poster presents an overview of the different methods.

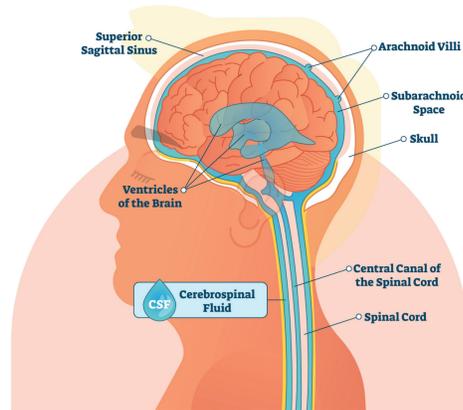


Figure 1: Illustration showing cerebrospinal fluid location in and around the brain.

Intracerebroventricular (ICV) Dosing

Intracerebroventricular administration represents a specialized technique for direct delivery of test article to the lateral ventricles of the brain. Stereotaxic coordinates provide precise anatomical guidance for bilateral ventricular targeting. Following proper positioning, a cranial burr hole is created, and the injection needle is advanced to the predetermined depth using established stereotaxic parameters.

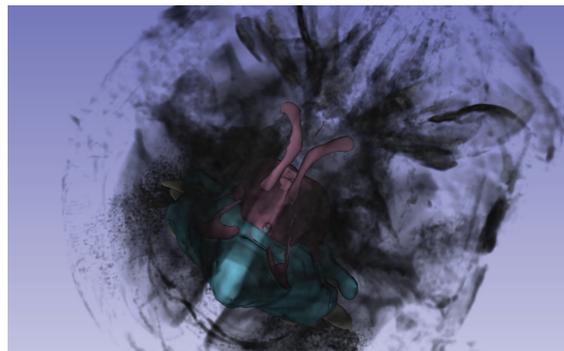


Figure 2: Axial view of segmented head MRI of cynomolgus monkey highlighting ventricles.

Percutaneous Intrathecal Dosing (Lumbar)

Percutaneous intrathecal dosing of the lumbar spine is a commonly employed method for introducing test articles into the central nervous system; however, this approach presents significant technical challenges due to the inability to directly visualize needle placement, as the image below illustrates:

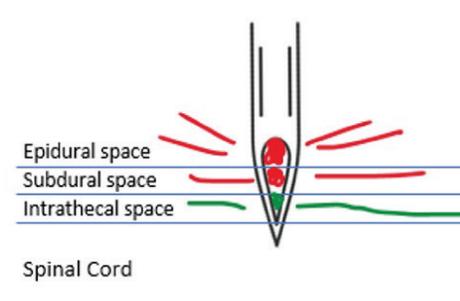


Figure 3: Illustration of needle lumen bridging multiple dural spaces.

The needle lumen may not be fully positioned within the intrathecal space, resulting in inadvertent subdural or epidural injection of the test article. Such misplacement can lead to inconsistent drug distribution, reduced efficacy, and potential complications that may compromise study integrity.

Intra Cisterna Magna (ICM) Dosing

Percutaneous cisterna magna test article delivery offers reliable access to the central nervous system while minimizing the risk of the needle's lumen emptying into multiple cavities. The image below illustrates angle and location. Care must be taken during test article delivery to ensure the needle remains stable and is not advanced into the brain stem. It is also important to not over pressurize the thecal sac during dosing, as this can lead to serious neurological complications.

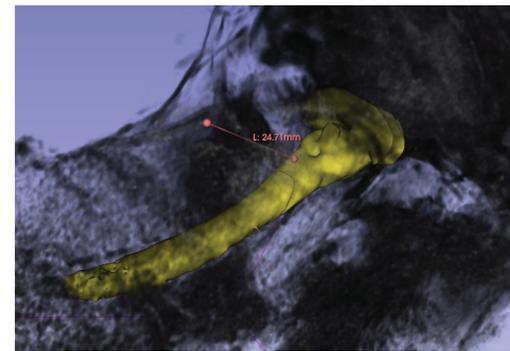


Figure 4: Oblique MRI view of basiocciput, highlighting brain stem and needle angle for entrance into the cisterna magna.

Surgical Intrathecal Dosing

To ensure precise needle placement and accurate dosing, a surgical cutdown is performed to directly visualize the dura mater. This approach provides complete control over needle insertion angle and depth, allowing for confident verification that the needle tip has penetrated the dural membrane and is properly positioned within the intrathecal space before test article administration.

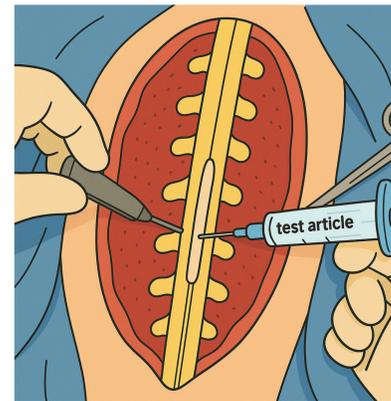


Figure 5: Illustration of test article delivered surgically via lumbar direct dural puncture.

Temporary Intrathecal Catheter

Following surgical exposure, a temporary catheter is advanced 30 to 40 millimeters into the intrathecal space along the spine to ensure optimal distribution of test article. After confirming proper catheter placement and completing the dosing procedure, the catheter is immediately removed, dural sealant is used, and the surgical site is closed in layers, minimizing tissue trauma while maintaining sterile technique throughout the procedure.

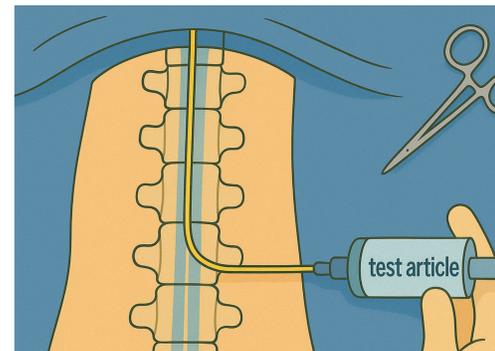


Figure 6: Illustration of test article delivered via temporary intrathecal catheter.

Intrathecal Catheter with Port

This preferred technique involves performing a surgical cutdown, followed by introduction of a catheter into the intrathecal space, with the catheter tip positioned at the L1 vertebral level for optimal cerebrospinal fluid distribution.

Alternatively, when enhanced precision is required, we utilize fluoroscopic guidance to terminate the catheter tip at the level of the cisterna magna, ensuring maximal distribution throughout the CNS for comprehensive transduction of test article.



Figure 7: Plain film radiograph of Cynomolgus monkey, showing port and catheter.

Summary

Biomere's indwelling porting method represents a sophisticated approach to CNS drug delivery that allows for both serial dosing of test article and serial sampling of cerebrospinal fluid throughout extended study periods. We utilize advanced human-grade catheter and porting systems to ensure the highest level of catheter patency and reliability. These premium systems are designed to significantly reduce complication rates while minimizing common technical challenges including catheter tip fibroses, catheter kinking, and catheter tip migration that can compromise study integrity.

Learn more about our Surgical Services at – <https://biomere.com/surgical-services/>