Methodology for intrathecal dose administration and cerebrospinal fluid sampling in cynomolgus monkeys for advanced dose and sampling regimens

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Intrathecal (IT) implantation of catheters equipped with subcutaneous access ports provides the means for repeated access to cerebrospinal fluid (CSF) in the IT space around the spinal cord, without the need for chemical sedation. IT implantation of two catheters provides capability to dose and sample from separate lines, as well as backup in case of loss of patency in either of the lines. Ten Cynomolgus monkeys were implanted with two vascular access ports (VAPs) and catheters via the L3-4 and L4-5 vertebral spaces. The first catheter was advanced to the vicinity of the cervico-thoracic junction and the second to the thoraco-lumbar junction. Post-surgery catheter maintenance was performed once weekly to verify patency of the ports. VAPs were well tolerated by the animals. IT VAPs for CSF sampling were more prone to failure with loss of sampling patency being roughly 50% of animals within two weeks of catheter implantation. IT VAPs for dose administration appeared to be less prone to failure (roughly 10% of the animals within one month). The additional utility of having separate paths for dosing and sampling via two different locations within the IT space has been useful for short term studies (4 weeks). Alternatively, direct IT punctures (sedated) either administration or CSF collection at L3-5 using atraumatic needles was also evaluated. This technique is reliable for non-concurrent and non-frequent (e.g., once weekly) IT administrations and collections. Several approaches now exist for accessing the IT space, allowing for an expanded range of study conditions.