

MRI-based guidance for predictable and precise intra-arterial delivery of therapeutic agents to the central nervous system

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Neurological disorders constitute one of the biggest medical challenges. Although there has been rapid progress in the treatment of peripheral malignancies over the last 20 years, the prognosis for brain tumors is imperturbably grim. However, many drugs, including melphalan, are highly effective *in vitro*. Moreover, intra-arterial delivery of high-dose melphalan radically changed the treatment of retinoblastoma, with a frequent cure rate, without the need for eye removal. However, melphalan, as well as many other antineoplastic agents, cannot effectively cross the blood-brain barrier, thus limiting their efficacy for the treatment of brain tumors. The opening of the blood brain barrier (BBB) to facilitate tumor penetration by drugs has been attempted for many years. Intra-arterial administration of hyperosmotic agents (IAHA) has been shown safe, but high variability of results was discouraging and the method has been almost abandoned. We have found that MRI contrast agents are sufficiently sensitive to report on the brain territory supplied by a catheter thus MRI is critically needed to guide the intra-arterial delivery of therapeutic agents to the brain. Superparamagnetic iron oxide nanoparticles (SPIO) are very attractive as contrast agents due to their very strong signal, which allows for a very short MRI acquisition time, e.g., two to three seconds, using a GE-EPI pulse sequence. This actually enables real-time monitoring of the territory supplied by the catheter. In addition, the SPIO clears rapidly after infusion discontinuation, which, in turn, allows for precise adjustments of the territory supplied by the catheter through manipulation of the speed of infusion and the catheter tip position. Moreover, we have shown that the delineation of the brain territory supplied by the catheter also allows for precise prediction of the subsequent BBB opening area, which, in turn, overcomes the previously reported problems with the variability of the BBB opening territory after IAHA. This then, allows for a new era of predictable and precise intra-arterial drug delivery to the brain ([Janowski et al. 2015](#)). Thus, in our opinion, the intra-arterial delivery of therapeutic agents through a predictable and precise blood brain barrier opening should always be attempted before the agent is deemed ineffective. Our method can also be potentially useful for other neurological disorders, such as neuroinflammatory and neurodegenerative conditions.

1. **Janowski M, Walczak P and Pearl MS (2015).** Predicting and optimizing the territory of blood-brain barrier opening by superselective intra-arterial cerebral infusion under dynamic susceptibility contrast MRI guidance. **J Cereb Blood Flow Metab.**2016 Mar;36(3):569-75

Biography:

Dr Janowski completed residency in neurosurgery at the Medical University of Warsaw, Poland and then moved to Department of Radiology at the Johns Hopkins University, USA where he holds a position of Associate Professor. His research is focused on the development of the precise methods to deliver high doses of therapeutic agents including drugs and stem cells to the desired areas of the brain. He has published over 40 papers in peer reviewed journals, edited a book on experimental neurosurgery, served as a program chair for workshop, chaired multiple sessions at international conferences and gave over 15 invited talks worldwide. His research is funded by NIH, DoD and Maryland Stem Cell Research Fund.