Cerebral hypoperfusion-assisted intracarotid delivery of liposomes to normal and glioma-bearing brain

Shailendra Joshi MD; Rajinder Singh-Moon; Jason A. Ellis MD; Durba Chaudhuri; Mei _Wang; Jeffrey N. Bruce MD; Irving Bigio; Robert Straubinger

Columbia University Medical Center

Introduction

Optimizing liposomal vehicles for targeted delivery to the brain has important implications for the treatment of brain tumors. The promise of efficient, brain-specific delivery of chemotherapeutic compounds via liposomal vehicles has yet to be achieved in clinical practice. Thus we propose that intraarterial injection of specially designed liposomes may facilitate efficient delivery to the brain and to gliomas. In this report we test the hypothesis that cationic liposomes may be effectively delivered to both normal and glioma-bearing brain tissue utilizing a strategy of intraarterial injection during transient cerebral hypoperfusion.

Methods

Cationic, anionic, and neutral liposomes were separately injected via the internal carotid artery of normal Sprague Dawley rats during transient cerebral hypoperfusion. C6 glioma-bearing rats were similarly injected with cationic liposomes. Liposomal concentrations were measured using diffuse reflectance spectroscopy. Multi-spectral imaging and confocal microscopy was used to assess liposomal distribution.

Results

A robust uptake of cationic as compared to anionic and neutral liposomes into brain parenchyma was observed after intraarterial injection. High liposomal cationic charge was associated with more efficient delivery to the brain. Cationic liposomes were also readily observed within glioma tissue after intraarterial injection. However, over time, cationic liposomes were retained longer and at higher concentrations in the surrounding, peri-tumoral brain.

Learning Objectives

By the conclusion of this session, participants should be able to: 1) Appreciate the advantage conferred by using positive surface charge to enhance liposomal delivery during intraarterial flow arrest, 2) Understand that liposomes may be retained in both healthy and glioma-bearing brain tissue after intraarterial delivery, 3) Discuss a possible role for using liposomes to deliver chemotherapy to malignant brain tumors.

Conclusions

This study demonstrates the feasibility of cationic liposome delivery to brain and glioma tissue after intraarterial injection. Highly cationic liposomes directly delivered to the brain via an intracarotid route may represent an effective method for delivering anti-glioma agents.