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Title : New Generation Liquid Embolic Material for the use of Endovascular Treatment: An organic polymer composite activated by the Ca2+ in the blood

Abstract

Liquid embolic material is an important treatment tool used in the field of endovascular treatment. In neurosurgery, it plays a key role particularly for the treatment of arteriovenous malformation (AVM), dural Arteriovenous malformation (dAVF) and intracranial tumors. Onyx embolic system® was approved by FDA in 2003 as the first non-adhesive liquid embolic agent. The development goal was to overcome the major limitation of a widely used liquid embolic agent e.g. NBCA, which is a strong adhesive and occasionally causes catheter-entrapment in the treated site. The Onyx, along with similar products with same composition, remains the only FDA approved non-adhesive liquid embolic material as of 2018.

However, the main component of the Onyx, Ethylene Vinyl Alcohol (EVOH), is resolved in the organic solvent "DMSO", which is known to have a cytotoxicity from the multiple previous reports. Recent reports of the adverse effect associated with Onyx include acute respiratory distress syndrome (ARDS), epileptic seizure and tissue necrosis. Recently FDA issued a safety alert after receiving reports of more than 100 adverse events, including 9 patient deaths, that may have been cause by the Onyx. In at least 54 of these cases, it was not possible to remove the catheter, so part of the catheter and the implanted Onyx material remained implanted in the patient.

To overcome these limitations, we developed a new generation liquid embolic material (NGLEM), which is made of multiple organic polymers. The NGLEM is a clear liquid that immediately forms a solid hydrogel cast once exposed to the $Ca2^{+}$ in the blood stream. Since it does not have the adhesive effect, catheter-entrapment can be avoided. In addition, it does not require the use of organic solvent such as DMSO. The main components of the NGLEM have been widely used in the medical and food industries with large evidence of biocompatibility.

The goal of this proposal is to evaluate the efficacy and biocompatibility of this new embolic material, "NGLEM", using a large animal model.

Our preliminary data using in vitro models showed non-adhesive characteristics and sufficient radiopacity of the NGLEM. The in-vivo experiment using rat model showed complete occlusion of the target artery without catheter-entrapment. To extend these findings to a preclinical evaluation using large animal model, the first Aim of this project is to evaluate mechanical property and visibility of the NGLEM under fluoroscopy using a swine AVM model. Because little is known about the mechanism of tissue reactions induced by the DMSO and EVOH in the Onyx, our second Aim is to perform thorough histologic investigations on the tissue samples treated with Onyx by performing immunohistochemical analysis. The third Aim is to evaluate tissue reactions and persistent efficacy of the target tissue treated with NGLEM.

Together these experiments will establish efficacy and biocompatibility of the NGLEM, providing proof-of-concept to support future clinical trials in the field of neuro-endovascular surgery.