Endothelial Cell-Adhesive Injectable Hydrogel as Endovascular Embolizing Agent

By

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Abstract

Vascular diseases such as cerebral aneurysms and arteriovenous malformations (AVMs) remain the most common causes of death around the world. In this study, an adhesive material that binds to the innermost layer of the blood vessel walls was developed. This material, synthesized from biocompatible polymer, forms an in situ three-dimensional crosslinked network via Michael addition reaction between vinyl sulfone modified dextran (Dextran-VS) and thiolated dextran (Dextran-SH). It demonstrates favorable swelling ratio and mechanical strengths, making it applicable as an endovascular embolizing agent. Certain formulations of hydrogels with 10-20% concentrations have swelling ratios around 1, indicating that they will neither shrink nor swell considerably in aqueous environment. The storage modulus of the hydrogel obtained from oscillation ranges from 12.9 to 19.5 kPa, which is greater than the maximum wall shear stress predicted from computational aneurysm rupture models (0.39 to 42.7 Pa); and the yielding stress of the hydrogel, varying from 413.8 to 854.2 kPa, is larger than the normal pressure obtained from the models (43 to 310 kPa), thus the hydrogel will not fall apart while keeping its shape. The adhesiveness is achieved by further modifying the polymer precursor Dextran-VS with N,N'-disuccinimidyl carbonate (DSC) into NHS esters, which can form stable carbamate linkage with amines under physiological conditions, and at the same time being hydrolyzed within hours. The adhesion strength of the hydrogel modified with NHS esters is 1770 Pa, which is more than eight times higher than that of the hydrogel without NHS modification (210 Pa). The material also demonstrates low cytotoxicity on human umbilical vein endothelial cells (HUVECs). Our findings suggest that this in situ hydrogel modified with NHS esters can be a promising endovascular embolizing agent, with low cytotoxicity and improved performance in mechanical properties and material-vessel interaction compared with current liquid embolizing agents.

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Examination Committee:
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