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Coulomb nanoradiator-mediated, site-specific thrombolytic proton treatment with fucoidan-conjugated magnetite

Key words: Coulomb nanoradiator, iron oxide nanoparticle, arterial thrombosis

Traversing proton beam-irradiated, mid/high-Z nanoparticles produce site-specific enhancement of X-ray photon-electron emission via the Coulomb nanoradiator (CNR) effect, resulting in a nano- to micro-scale therapeutic effect at the nanoparticle-uptake target site. Here, we demonstrate the uptake of iron oxide nanoparticles (IONs) and nanoradiator-mediated, site-specific thrombolysis without damaging the vascular endothelium in an arterial thrombosis mouse model. The enhancement of low energy electron (LEE) emission and reactive oxygen species (ROS) production from traversing proton beam-irradiated IONs was examined. Flow recovery was only observed in CNR-treated mice, and greater than 50% removal of the thrombus was achieved. A 2.5-fold greater reduction in the thrombus enabled flow recovery was observed in the CNR group compared with that observed in the untreated ION-only and proton-only control groups (p <0.01).

Algal fucoidan is known to bind specifically with P-selectin from activated platelet. Prior study demonstrated fucoidan spontaneously exhibit thrombolysis by inhibiting plasma tPA-PAI1 binding and effectively enhancing free tPA. Therefore, Fucoidan-conjugated magnetite may have specific binding with activated platelet that was expressed in thrombosis initiation. We discuss various advantage of CNR thrombolysis with fucoidan-conjugated magnetite.

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