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Poster Title: Biofabrication of ultrasound responsive tPA loaded microbubbles with narrow size distribution and enhanced stability for the treatment of acute ischemic stroke

Abstract: Stroke is the second leading cause of death worldwide with permanent disability in surviving patients. In 2015, a study conducted in Singapore reported that 67,289 stroke cases are rising in number with the growing population. Most stroke occurrences are in people over the age of 60 and with Singapore's aging population, the stroke cases are predicted to increase further. Current treatment options for acute ischemic stroke are limited to the FDA-approved thrombolytic drug tissue plasminogen activator (tPA) but its usage is limited due to: narrow therapeutic window, short in vivo half-life, haemorrhagic complications, selective efficacy and its neurotoxicity. This work is founded on the novel technology of tPA-loaded microbubbles (tPA-MBs) that would serve both as ultrasound contrast agents as well as therapeutic agents to preserve ischemic penumbra after stroke. We have fabricated tPA loaded microbubbles coated with 1,2-dibehenoyl-sn-glycero-3-phosphocholine (DBPC) and 1,2-distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (DSPE-PEG2000) with sulfur hexafluoride (SF6) as the gas core using coaxial electrohydrodynamic atomization (CEHDA). The microbubbles prepared by CEHDA provides a narrow size distribution of 3-4 μm, therefore CEHDA can serve as a one-step fabrication method as opposed to conventional microbubble preparation techniques such as sonication and agitation, which provides a wide size distribution and requires an additional step of size sorting. For the first time, we have prepared tPA loaded microbubbles with enhanced stability of almost 64 hours which is 64 times greater than the stability of the previously prepared microbubbles using CEHDA. We would directly build on and expand on these results to evaluate the thrombolytic efficiency of tPA-MBs over tPA alone, tPA + US, tPA + US + MBs using an in-vitro model and a reperfusible rat stroke model.