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In Vivo Characterization of the Kinetics of Clot Initiator Termination

Abstract

Blood clotting is an important biological process that prevents excessive blood loss from injured blood vessels. Following heart surgery, some patients experience continuous, difficult-to-manage bleeding that does not appear to have a distinct surgical cause. This can lead to increased risk of death or serious complications, increased costs and operating room time, and increased utilization of blood products which are a limited resource. In order for blood to clot, the injured blood vessel must send a signal to blood components to start the clotting process. These signals are known as clot initiators. In most of these patients, all clinical tests of their blood components are normal, suggesting that the cause of bleeding is due to impairment in the clot initiator signal. In this proposal, we will use a new, powerful microscopic technique to study clot initiator signals in live animals. We will evaluate the processes by which these signals terminate their function, as we think that early termination may cause bleeding. We will also study these signals in the context of the powerful blood thinning medications used during heart surgery to determine if these medications affect the duration of these signals. Together, this work will provide the foundation to develop targeted therapies to decrease or even eliminate dangerous postoperative bleeding.