Orthopaedic patients are at risk for developing a hypercoagulable state. Complications from developing a hypercoagulable state include: deep venous thrombosis (DVT), pulmonary embolus (PE), systemic inflammatory response syndrome (SIRS), and acute respiratory distress syndrome (ARDS). Because of the severity of these potential complications, it is standard practice to prophylactically treat these patients with anticoagulants. However, anticoagulants negatively affect the wound healing as they cause wound hematoma and inhibit coagulation proteases that have been shown to play a critical role in skin and bone wound healing. Thus a critical balance must be achieved.

Thrombin generation assays (TGAs) are thought to provide a more global measure of hemostasis and thrombosis. These assays are based on monitoring cleavage of a slow-reacting fluorogenic substrate by the coagulation protease thrombin, and thus serves as a marker of thrombin activity. In regards to orthopedics, the greatest advantage of TGA over traditional coagulation tests is its ability to detect hypercoagulability. The overall goal of this study was to establish a reliable and sensitive basis for detecting changes in the pro- and anti-coagulant status of patient plasma in orthopaedic clinical settings in order to optimally individualize prophylactic anti-coagulant protocols. We have refined published methods for assessing the rate of thrombin generation as a tool to evaluate the endogenous coagulation status of patient plasma. The benefit of this assay is that it provides an inclusive glimpse at the sum of the pro- and anti-coagulant mechanisms in play at the time of sample collection and can detect both hypo- and hypercoagulability.

The thrombin generation assay can detect increases in hypercoagulability with clinical post-operative complications and provide a real-time coagulation monitoring strategy

One post-operative complication of particular concern for orthopaedic surgeons is pulmonary embolus, due to a hypercoagulable post-operative state. As shown below, our thrombin generation assay identified an elevated procoagulant status on post-operative day 2 following hip arthroplasty, despite treatment of this individual with the standard Coumadin protocol. This increased procoagulant status detected in our thrombin generation assay (procoagulant capacity of 1.3; above the normal range defined as ~ 1.0 in our assay) coincided with pulmonary embolus; immediate addition of treatment with low molecular weight heparin in addition to the Coumadin resulted in a decrease in pro-coagulant capacity still detected at post-operative day 4.

Impact of co-morbidities on thrombin generation capacity and hypercoagulable status of post-operative patient plasmas

A number of clinical states are associated with changes in the coagulation status of patient plasmas and the TGA provides a means of more closely monitoring these patients and even screening for hypercoagulable conditions. Interestingly, in diabetes mellitus and lupus erythematosis, these conditions result in a hypercoagulable state primarily due to a dramatically diminished anti-coagulant capacity in parallel with a detectable but lesser increase in pro-coagulant capacity. Genetic diseases also serve as co-morbidities increasing the probability of a hypercoagulable state post-operatively. Factor V-Leiden individuals are known to have a decreased capability to cleave Factor V, yielding active Xa, or prothrombinase activity. However, these individuals also possess a diminished sensitivity to activated Protein C-mediated suppression of activated V activity (Va). Overall, then, Factor V-Leiden patients would be expected to manifest an increased rate of thrombin generation in their plasma, because their diminished activation of prothrombinase is coupled with a diminished anti-coagulant cascade. As shown below, a patient homozygous for Factor V-Leiden was observed to show a significant increase in pro-coagulant capacity day 2 following spinal surgery post-trauma. Most dramatic, however, was the diminished anti-coagulant capacity in this individual, at days 2 following trauma spine surgery.