The Clot Thickens: Autologous Fibrin Sealants Adhere to Articular Cartilage and Show Distinct Changes in Mechanics Based on Fibrinogen Concentration

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INTRODUCTION: Commercial, pooled human plasma fibrin sealants are commonly used for cartilage repair, but are expensive and carry the risk of adverse patient reactions. Alternatively, autologous fibrin sealants are easier and less expensive to obtain because they can be created using blood and plasma from individual patients. Fibrin sealants are formed via a dual-ejection syringe that combines thrombin and fibrinogen components to form a fibrin clot. Autologous fibrin sealants can be created from an individual patient’s blood and plasma and are commonly used. Two sources of fibrinogen are currently commercially available: Tisseel (Arthrex Inc.) and Thrombinator (Arthrex Inc.). However, it has been shown that different methods can be created from an individual patient’s blood and plasma to form a fibrin clot and to produce different mechanical properties. Some studies have shown that the mechanical properties of fibrin sealants are easier and less expensive to obtain because they can be created using blood and plasma from individual patients.

METHODS: All procedures were IRB approved. Human blood (n=10) was collected in 14% ACD anticoagulant and processed to PRP and PPP using the Angel System (Arthrex Inc.). Autologous thrombin was generated from PPP in the Thrombinator system (Arthrex Inc.). Blood, PRP, and PPP were analyzed for fibrinogen concentration and sealant strains were analyzed using two-way ANOVA. The mechanical properties of fibrin sealants were compared to those of PRP and PPP using pooled plasma sealants.

RESULTS: PPP fibrinogen concentration was significantly higher than PRP or blood (p<0.05), but all blood products were two orders of magnitude lower than the reported concentration for the Tisseel fibrinogen component (Fig 2A). Sealant toughness was equivalent between the commercially available autologous Tisseel thrombin (Tisseel fibrinogen) and Thrombinator thrombin (Thrombinator fibrinogen) (Fig 2B). Ultimate tensile stress was significantly higher in sealants created from Tisseel thrombin and pooled plasma Tisseel fibrinogen (Fig 2C). Thrombinator thrombin had a dose-response relationship between fibrinogen concentration and mechanical properties, while Tisseel thrombin showed a linear relationship (Fig 2D, toughness not shown). In the cartilage defect model, shear strains were highest at the surface of the tissue and were lower deeper in the tissue. The Tisseel thrombin and PRP fibrinogen sealant showed the highest shear strain and were significantly greater than Tisseel alone, Tisseel thrombin with PPP fibrinogen, and Thrombinator thrombin with PRP fibrinogen (p<0.001, p<0.05, and p<0.05, Fig 3A). The mechanical effect of all sealants was confined to a narrow region at the surface of the repair construct (~125µm). There was a negative correlation between sealant ultimate tensile stress and shear strain at the interface of repair (Fig 3B).

DISCUSSION: All sealants adhered to articular cartilage under tensile and shear loading, with higher concentrations of fibrinogen having stronger mechanical properties regardless of fibrinogen source (pooled plasma Tisseel or autologous). Autologous Thrombinator thrombin showed increasing ultimate tensile stress and toughness at lower concentrations of fibrinogen compared to that of Tisseel thrombin, suggesting that Thrombinator thrombin appears to have higher potency at enhancing mechanical adhesion. Results of bulk mechanical properties from tensile tests were mirrored in the defect model as sealants with higher ultimate tensile stress showed lower strains at the interface of repair. Understanding the adhesion strength of fibrin sealants provides insight to their ability to seal or adhere repair strategies in a cartilage defect during surgery.

SIGNIFICANCE: Regardless of source, fibrinogen concentration appears to be the dominant predictor of adhesive strength for fibrin sealants. Bulk behavior of sealants also predicted strains at the interface of repair, and this effect was confined to the cartilage surface. Autologous sealants show equivalent mechanical properties to pooled plasma sealants and could potentially aid in cartilage repair due to the known presence of autologous growth factors.