INTRODUCTION
Low molecular weight heparins (LMWH) such as enoxaparin are anticoagulants that are known to inhibit coagulation by inactivation of Factor Xa via activation of Antithrombin. They are often used and preferred to unfractionated heparin in thrombus prophylaxis due to improved bioavailability leading to once-daily dosing and a decrease in adverse reactions such as heparin induced thrombocytopenia. The question of reliable Low Molecular Weight Heparin (LMWH) reversal, especially in the case of emergency pediatric surgery, has been discussed in the literature in brief. Protamine sulfate is the only FDA approved LMWH antidote. Protamine, however, does not fully or reliably reverse the effects of LMWHs due to the variable sulphate content. The efficacy of other antidotes such as rFVIIa have been illustrated in some cases, however, a reliable method for full reversal of LMWHs has not yet been established, especially in the pediatric population.

CASE REPORT
A 17 month old female patient, with a past medical history of a suprasellar glioneuronal tumor and corresponding hydrocephalus status post debulking and ventriculoperitoneal shunt placement, on enoxaparin (1mg/kg Q12 hours) following the development of a sagittal sinus thrombosis, presented with a subdural bleed following a three foot fall from a bed. Upon examination, patient presented with altered mental status and concerns for seizure like activity. On physical exam patient was found to be irritable, tachycardic, but otherwise had stable vital signs. Pupils were constricted bilaterally at about 2 mm, but were equally round and reactive to light. Increasing weakness of the left upper extremity was also noted on examination. Laboratory results revealed a hemoglobin and hematocrit of 8.7 and 24.8, respectively, with a PT/INR of 12.4/38.2 and 1.12. CT of the head illustrated a large heterogeneous subdural hematoma overlying the right cerebral convexity and along the right aspect of the faix and right tentorium cerebelli. The presence of a functional VPS, precluded the development of Cushing’s triad. Last Enoxaprin dose was 6 hours ago. Patient was resuscitated in the emergency department, given 0.1 mg/kg of protamine sulphate for LMWH reversal, and then taken to the OR for emergency craniectomy and evacuation of subdural bleed. Intra-operatively the patient was bleeding profusely and coagulation was only noted after the administration of 10 ml/kg of FFP. Following the procedure, Patient was extubated uneventfully and transported to the PICU in a stable condition.

DISCUSSION
Enoxaprin, with a molecular weight range of 3,800 - 5,000 daltons (versus 15,000 daltons for heparin) acts via an anti-thrombin dependent mechanism. It accelerates the rate of the neutralization of certain activated coagulation factors by antithrombin.

Enoxaparin cannot be measured directly in the bloodstream, rather the effect on clotting mechanisms is measured. aPTT may not be significantly prolonged relative to unfractionated heparin at prophylactic doses, and at therapeutic doses aPTT prolongation is not used to measure the therapeutic effect. Potency is described in international anti-Xa units (e.g., 1 mg of enoxaparin is equivalent to 100 IU of anti-Xa). The anti-Xa activity, further anti-thrombin-, and anti-inflammatory properties of enoxaparin have been identified including ATIII-dependent inhibition of other coagulation factors like factor VIIa, induction of endogenous Tissue Factor Pathway Inhibitor (TFPI) release as well as a reduced release of von Willebrand factor (vWF). These factors are known to contribute to the overall anti-thrombotic effect of enoxaparin.

A major difference between UFH and LMWH is in their relative inhibitory activity against factor Xa and factor IIa. Any pentasaccharide-containing heparin chain can inactivate factor Xa, but a minimum number of saccharide units is required to exert an inhibitory effect on factor IIa. Therefore, LMWH has a greater ratio of factor Xa to factor IIa inhibitory activity when compared with UFH, which has equivalent activity against these factors.

Reliable reversal of LMWHs in the setting of acute trauma is essential. Although commonly used, protamine sulfate alone does not fully reverse the anticoagulant effects of LMWHs. The literature has shown this is due to nearly full reversal of anti-IIa activity of LMWHs, but only partial reversal to non-reversal of anti-Xa activity. While guidelines and several case reports have suggested different reversal strategies, here we used a combination of protamine sulfate and FFP to effectively reverse the anticoagulation of enoxaparin. We believe this is the most effective method of reversal as it addresses the deficiency of protamine reversal, primarily by adding vitamin K-dependent clotting factors, including Factor X, the factor that is not completely reversed by protamine.

CONCLUSION
We suggest further investigation into the combination of protamine at FDA recommended doses with FFP in reversal of LMWHs in the acute setting, as a reliable and effective reversal of LMWH is needed in the setting of acute pediatric trauma.