Poster #69

QUANTIFYING FASTER HEMOSTASIS IN NONCOMPRESSIBLE TORSO HEMORRHAGE

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Introduction: Rapid surgical hemostasis is a critical component of trauma care and is associated with improved survival. However, little is known about the time spent in the various phases of care prior to achieving definitive hemostasis. We hypothesized that time to hemostasis varies based on different management strategies and prolonged hemostasis is associated with worse outcomes.
Methods: A prospective, observational study was performed at 6 level 1 trauma centers 2017-18. Adults with hemorrhage below the diaphragm requiring intervention within 60min were included. Patients were grouped by interventions required for hemostasis: interventional radiology only (IR), laparotomy and IR (Lap+IR), laparotomy only (Lap), REBOA and Lap (REBOA+Lap), and thoracotomy and Lap (Thor+Lap). Outcomes included time spent in 4 hospital segments, time to hemostasis, death, and complications. Univariate, multivariable, and Cox regression for time to hemostasis, censored for death, were performed.
Results: Of 398 included patients, hemostasis was obtained in 86%. Patients had a median age of 34 (IQR 25-50), and ISS of 26 (17-38). Death or complications occurred in 71% of patients, with a 24% mortality rate. The median time from ED arrival to definitive hemostasis was 117 mins (Figure 1). ED time was longer in the IR group than other groups ($p<0.001$) while procedural time was shorter in the Lap and Thor+Lap groups ($p<0.02$). On Cox regression, the Lap group had the shortest time to hemostasis (Figure 2). Above-average hemostasis time was associated with increased odds of death or complications (OR 1.8, IQR 1.1-2.9, $p=0.02$).
Conclusion: Time to hemostasis varied widely among severely injured patients with noncompressible torso hemorrhage requiring emergent intervention. Definitive hemostasis was obtained fastest in the Lap patients, after adjustment for death. Procedure start was nearly 60 minutes later in the IR group than others. Prolonged time to hemostasis was associated with worse outcomes. These detailed time data will allow targeted interventions to improve time to hemostasis.

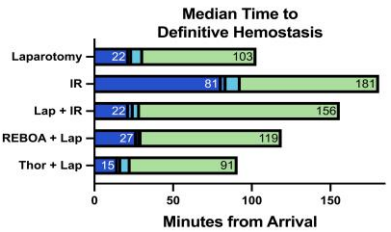

Figure 1

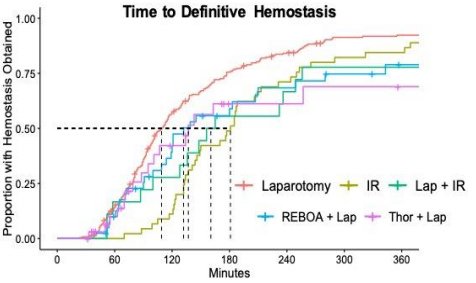

Figure 2

Poster #70

A NOVEL SILICON-BASED POLYMER- UNIVERSAL COMBAT MATRIX SUPPORTS LIVER VIABILITY OUT TO 72 HOURS IN PORCINE MODEL OF HEPATIC LACERATION

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Introduction: Hemorrhage is the leading cause of death in trauma and control of non-compressible parenchymal bleeding remains challenging. Many hemostatic agents have been evaluated to minimize blood loss and improve survival. We compared a novel silicon dioxide-based universal combat matrix (UCM) to the recently FDA-approved QuikClot® Control+® (QCC+) in a hepatic laceration porcine model.
Methods: A 6cm full thickness left liver laceration was made sharply in 12 anesthetized swine and treated with UCM (n=6) or QCC+ (n=6). As many gauze applications required for hemostasis were used, and manual pressure held until hemostasis achieved. The animal was monitored for 1 hour and recovered for a 3-day period. Animal survival and number of applications were analyzed. Labs were drawn at baseline, end of hemorrhage, end of monitoring period, and daily for 3 days. The animal was euthanized, and liver tissue collected for histology and blinded histopathological evaluation.
Results: All UCM and QCC+ animals survived the 3-day period. On average, UCM required 3.1 applications to achieve hemostasis and QCC+ 2.2 ($p=0.54$). There was no significant difference in liver function tests (AST $p=0.29$, ALT $p=0.99$), white blood cell count ($p=0.94$), platelets ($p=0.89$), creatinine ($p=0.97$), hemoglobin ($p=0.99$) or hematocrit ($p=0.99$), between groups over the 3-days. On gross liver inspection, UCM livers were well perfused without necrosis or ischemia, while QCC+ livers showed early necrosis and discoloration. Blinded histopathology scoring demonstrated QCC+ had significantly more hepatic neutrophilic inflammation ($p=0.02$) and panlobular necrosis ($p=0.001$) compared to UCM.
Conclusions: UCM demonstrated comparable hemostatic efficacy to QCC+, without evidence of significant liver or kidney injury, blood loss, leukocytosis, or electrolyte derangement. While QCC+ was used in this model against product instructions (which recommend removal within 48 hours) histology examination indicates that UCM may be left in place for extended periods of time without appreciable inflammation and necrosis. This may have implications for improved post-treatment hepatic function if using UCM as a hemostatic agent for traumatic injury. Ongoing efforts include examining this product out to 30-day survival in this model.

Poster #71

BARRIERS TO ADOPTION OF AN ARTIFICIAL INTELLIGENCE CLINICAL DECISION SUPPORT SYSTEM FOR TRAUMA

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Introduction: Clinical decision support systems (CDSSs) can help trauma clinicians identify high-risk patients after injury. An artificial intelligence (AI) model that predicts trauma-induced coagulopathy (TIC) has been developed, validated, and embedded within a CDSS. However, barriers to adopting or implementing the AI CDSS may impede its effect on clinician decision-making or patient outcomes. We aimed to evaluate the potential barriers and facilitators influencing adoption of an AI CDSS in trauma care.
Methods: This prospective study was approved by the UK Health Research Authority (22/HRA/2324). Participants (trauma clinicians) used a prototype AI CDSS in a simulated environment using clinical vignettes, completed a validated questionnaire and a semi-structured interview. The 'non-adoption, abandonment, scale-up, spread and sustainability' (NASSS) framework – developed to identify complexity in healthcare technology interventions – informed the questionnaire and interview. Thematic analysis of interview transcripts was conducted on NVivi v12, achieving theme saturation.
Results: Participants (n=22) had a median age of 39 years (IQR 31-48), 73% were male, 77% were doctors, 18% nurses and 5% paramedics, with a median of 13.5 years (IQR 6.3-19.8) experience. The main potential barriers to adoption/implementation of AI CDSS were: 1) heterogeneous TIC mechanisms and treatments; 2) duplication of input unless connected to electronic patient records; 3) limited benefit to the decision-making process without treatment thresholds; 4) uptake is dependent on clinicians' seniority, specialism, and resistance to change; 5) organizational cost, 6) data governance and security; and 7) evidence of patient benefit for regulatory approval. The main potential facilitators were the system's: 1) usability (accessibility, efficiency, learnability, and ease of use); 2) usefulness (for treatment decisions, real-time prediction, triage, and confidence); 3) credibility (endorsement by key individuals, demonstration of patient benefit, and reinforcement of decision-making); and 4) dissemination (enthusiastic early adopters, and ensuring clinician awareness of the tool).
Conclusion: Reducing complexity will aid the successful adoption of our AI CDSS. This work has informed the design of future feasibility and randomized studies evaluating its impact on clinicians and patient outcomes.

Poster #72

EXTRAVASCULAR FACTOR IX IN A RAT MODEL OF PENETRATING TRAUMA

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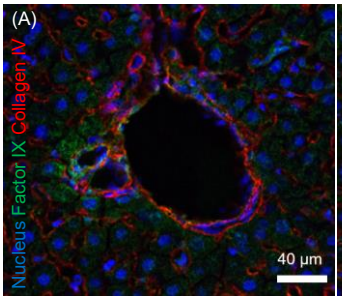
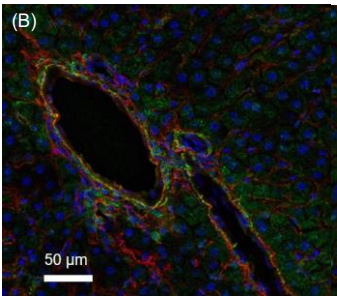
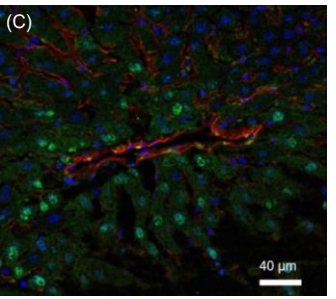
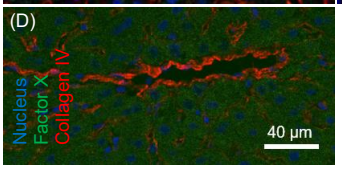
Introduction: Through its unique binding to collagen IV in the basement membrane of blood vessels, Factor IX forms a hemostatic reservoir outside of circulation that may be a target for augmentation or anticoagulation. Factor IX and collagen IV have never been studied in trauma.
Methods: Adult rats were anesthetized and subjected to laparotomy with penetrating injury to the liver. Injured and uninjured liver lobe specimens were fixed, frozen, and sectioned for confocal microscopy. Sections were stained with antibodies against Factor IX (variable), Factor X (control), and collagen IV (basement membrane protein). Confocal microscopy was used to colocalize Factors IX or X and the basement membrane, and to compare their spatial association with penetrating injury and the vasculature.
Results: Factor IX was associated with portal triad structures and colocalized with the basement membrane as evidenced by yellow overlap in merge images of uninjured and injured livers (A, B). Interestingly, cell nuclei around areas of injury but not in uninjured regions showed dense anti-Factor IX staining (C). Factor X had a more usual disseminated staining pattern consistent with known hepatocyte synthesis (D).
Conclusion: Unlike the prototype coagulation protein Factor X, Factor IX co-localizes with collagen IV in the basement membrane of liver tissue and has unique patterns of recruitment in the regions surrounding penetrating tissue injury. This extravascular reservoir makes Factor IX an exciting target for augmentation or anticoagulation in patients with penetrating injuries.









Poster #73

FINALLY, A USE FOR BALLOONS: AUTOMATED ENDOVASCULAR SUPPORT ENHANCES CLOSED LOOP DRUG AND FLUID DELIVERY IN A PORCINE MODEL OF SEVERE SHOCK

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Introduction: Endovascular Perfusion Augmentation for Critical Care (EPACC) is a method of dynamic aortic balloon catheter titration for precision hemodynamic support. EPACC has a potential role in augmenting hemodynamics in tandem with conventional resuscitation strategies. We have previously described that even short periods of EPACC in conjunction with an automated fluid and drug delivery system termed, Precision Automated Critical Care Management (PACC-MAN), can reduce resuscitation requirements over the first few hours after severe ischemia-reperfusion injury (IRI). We sought to understand if an initial 180 minutes of EPACC+PACC-MAN has sustained benefits over a 24-hr period compared to PACC-MAN alone in an established IRI model.
Methods: Twelve large swine underwent 30% hemorrhage, followed by 45 minutes of complete zone 1 aortic occlusion to induce IRI and a vasoplegic state. Animals were then transfused to euvolemia and randomized to a standardized critical care (SCC) algorithm with the PACC-MAN system, or EPACC+PACC-MAN (180 min of dynamic partial aortic balloon pressure augmentation that autonomously adjusted based on the animal's physiology). Fully autonomous, closed-loop resuscitation lasted for a total of 24 hrs in both groups. Primary outcomes included duration of hypotension (HYPO) (MAP <60mmHg) and hypertension (HTN) (MAP >70mmHg), and total crystalloid/norepinephrine (NE) volumes.
Results: Duration of HYPO for SCC vs EPACC [3.75% vs 3.10 % p=0.47) and HTN for SCC vs EPACC (5.58% vs 8.90% p=0.13) was equivalent. SCC required significantly more NE during the study period (1102.0 mcg/kg vs 210.77 mcg/kg p=0.045) than EPACC. Total volume trended higher for SCC vs EPACC (308.2 ml/kg vs 198.3 ml/kg p= 0.38).
Conclusion: Supporting hemodynamics with EPACC in the initial phases of resuscitation had a sustained effect on limiting overall vasopressor requirements in this 24-hour study without compromising physiologic or metabolic endpoints. Automation of endovascular devices may play an adjunctive role in the management of severe shock states and augment autonomous resuscitation system capabilities. Such systems may play an important role in resource-constrained care environments.

Poster #74

MICROBIAL NETWORKS, ANTIMICROBIAL RESISTANCE AND VIRULENCE FACTORS ARE ASSOCIATED WITH DIFFERENTIAL RECOVERY FOLLOWING ABDOMINAL INJURY

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Introduction: Alterations in microbiome diversity occur after injury, although the impact on clinical outcomes is unknown. We performed a pilot study to evaluate microbial features associated with complications after abdominal trauma.
Methods: Adult patients sustaining abdominal trauma (2014-2016) were clustered into four complication groups (Table). Genomic DNA was extracted from peritoneal lavage (PTL) specimens and sequenced. Sequences were classified via Centrifuge (NCBI nt database) and functionally annotated. Associations between complications and microbiome features were assessed via Multiple Correspondence Analysis (MCA).
Results: Eighty-five samples from 54 patients were analyzed. C4 samples had significantly lower Shannon entropy scores (microbial diversity) compared to C2 (Figure). Only C2 had increasing microbial diversity across days post-injury. C4 specimens had higher abundance of Bacteroides and Enterobacter species, and enrichment of tetracycline resistance genes compared to C2. MCA revealed correspondence of high Bacteroides bioburden with complications such as severe sepsis.
Conclusion: The highest bacterial burden, antimicrobial resistance, and morbidity was seen in patients with multiple systemic complications after abdominal injury. Such observations could facilitate the identification of microbial metagenomic determinants predictive of patient outcomes.

Cluster	Cluster description	no. of samples	no. of patients
1	Wound & infectious complications, organ dysfunction, escalation of care	10	5
2	No complications	29	25
3	Cardiovascular complications, organ dysfunction, escalation of care	14	8
4	Multiple complications	32	16

Table 1. Cluster descriptions for the patient cohort.

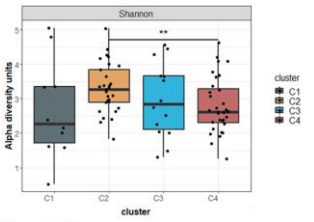

Figure 1. Shannon entropy scores across complication clusters (Wilcoxon test: **, p≤0.01).

Poster #75

PLASMA LIPIDOMICS IN BURN PATIENTS REVEAL ALTERATIONS IN OCTANOYL CARNITINE LEVELS

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Introduction: Severe burn patients demonstrate a pathological stress response characterized by a hypermetabolic state, which may produce alterations in the plasma lipid profile. Alterations in lipid metabolites may cause dysregulation in fatty acid oxidation (FAO) as the body attempts to meet increased energy requirements. We hypothesized that the plasma lipid metabolite profile would differ between burn patients and healthy subjects.
Methods: Plasma samples were collected from 8 patients who were admitted to an ABA-verified hospital for burn injuries and matched with 8 healthy individuals. Samples were collected using Telimmune DUO Plasma Separation Cards. Lipids were extracted with the 8:4:3 (CHCl3:MeOH:H2O) Folch ratio. Mass spectrometry was performed on each sample and used for quantification of each lipid species. Lipid profiles of burn and healthy subjects were analyzed pairwise using the Limma empirical Bayes t-statistics to detect differences in lipid levels between the two groups. Significantly different lipid species ($p<0.05$) were identified and matched by mass to known lipids catalogued in the LIPID MAPS® database.
Results: Mean age was 41.8 ± 16.0 years in the burn patients and 43.8 ± 12.1 years in the healthy subjects ($p=0.39$). The mean BMI was 26.1 ± 7.3 kg/m2 in the burn patients and 27.5 ± 6.7 kg/m2 in the healthy subjects ($p=0.34$). Of the burn patients, 88% were male, and of the healthy subjects, 63% were male ($p=0.25$). The mean percent of burned total body surface area (TBSA) was 12.7 ± 10.0% in the burn group. A total of 1008 peaks were identified by mass spectrometry in the plasma samples. Significant differences in plasma levels of 41 peaks were found between burn patients and healthy subjects. Of those peaks, 27 were identified as lipid species using the LIPID MAPS® database. Of interest, significantly decreased plasma levels of the fatty ester, O-octanoylcarnitine, were found in burn patients compared to healthy subjects ($p=0.03$).
Conclusion: L-carnitine transports fatty acids into the mitochondria for FAO. Therefore, downregulation of octanoyl carnitine in the plasma of burn patients may provide a mechanism behind the dysregulation of FAO in severe burns. Larger studies examining the relationship between octanoyl carnitine downregulation and burn injury are warranted.

Poster #76

QUANTUM ELECTROCHEMICAL SPECTROSCOPY (QES) ALLOWS FOR CLASSIFICATION OF TRAUMA PATIENT PHENOTYPES

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Introduction: Trauma patients have a complex milieu of circulating proteins and metabolites that contribute to thromboinflammation and consequential outcomes. Traditional assays such as mass spectrometry require complex parallel sample preparations and lengthy runtimes. Quantum electrochemical spectroscopy (QES) is a novel technique that allows for the measurement of numerous and diverse biomolecules in 30 minutes using only 2μL of plasma without reagents or sample preparation. The multidimensional data produced by QES is then processed with machine learning (ML) algorithms to allow for classification of samples into phenotypic cohorts. The aim of this study was to assess the ability of QES technology to discriminate clinically relevant phenotypes after trauma.
Methods: Plasma samples were collected from injured patients meeting trauma activation criteria on day of admission during two separate study protocols at two Level 1 trauma centers. Minimal injury (MI) was injury severity score (ISS) <15 and base deficit (BD) <6. Serious injury (SI) was ISS ≥15 and BD ≥6. Plasma samples were run in triplicate through QES. ML algorithm was trained and verified with 70% of data; the remaining 30% was then used for blinded classifier testing. Bootstrap resampling was implemented to enhance model robustness. Area under receiver operating characteristic (AUROC) curve was used to assess performance.
Results: There were 16 MI and 15 SI patients. The ML classifier demonstrated robust discrimination between MI and SI groups with a mean AUROC of 0.83 (max 0.95, min 0.72). The algorithm also effectively distinguished between cohorts from the two independent study locations with a mean AUROC of 0.78 (max 1.0, min 0.70).
Conclusion: QES allows for accurate classification of trauma patient phenotypes utilizing small sample volumes and one-step operation. Next steps will include improving the prediction model with more patient samples and quantifying relevant biomolecules from the multidimensional data. Future directions will also include expanding the classification methodology using the quantum signatures to predict complications such as respiratory failure, venous thromboembolism, and mortality. This will allow for targeted clinical care of the trauma patient.

Poster #77

POTENTIAL INVOLVEMENT OF PI-3 KINASE SIGNALING IN PERITONEAL MESOTHELIAL CELLS EXPOSED TO REACTIVE ASCITES: IMPLICATIONS FOR ADHESION FORMATION

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Introduction: Previous abdominal surgery (PAS) increases risk of abdominal adhesions that may cause small bowel obstruction (SBO). Trauma and peritoneal inflammation, e.g., acute appendicitis (AA), causes formation of peritoneal reactive ascites (rA) and activates peritoneum surface mesothelial cells (MCs) to form adhesions. MCs treated with reactive ascites (rA) collected during appendectomy (appy) or adhesiolysis for SBO may form adhesion-like fibers (FIB) and glycocalyx (GCX).
Methods: This is an ongoing prospective observational IRB-approved study at four level 1 trauma centers where rA is collected prior to surgical intervention for non-perforated AA or SBO. 44 appy and 10 SBO rA patient fluids were categorized into 6 groups by history of PAS (PAS/naïve) and by formation of FIB (high/no) and GCX (high/low/no) by rA-treated MCs. 71 cytokines/chemokines and 14 soluble receptors were quantified in rA and analyzed by Dunn's tests; adjusted $P<0.05$ was considered significant. Log2 fold-changes were calculated for each group compared to the PAS-highFIB-highGCX group and were analyzed by Ingenuity Pathway Analysis (IPA).
Results: PAS-FIB-GCX groups showed differences in the median concentration of 33 cytokines. IPA analysis showed that the naïve-noFIB-noGCX group was predicted to mobilize neutrophils, prime for activation phagocytes and myeloid cells, and increase epithelial tissue formation. Upstream analysis predicted that LY294002, a phosphoinositide 3-kinase inhibitor, would inhibit proteins of these associated pathways.
Conclusions: rA fluids collected from patients with naïve abdomens, which do not induce FIB or GCX formation in treated MCs, show predicted activation of pathways critical to the formation of abdominal adhesions. Future testing of PI-3 kinase inhibitors on MC formation of adhesion-like fibers and GCX is warranted.

Poster #78

THE STUDY OF EDUCATIONAL EFFECTS: 2D VS. VR RANDOMIZED CONTROLLED TRIAL

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Introduction: Virtual reality (VR) has potential for effective learning in medical education. There are increasing reports of simulation and procedures education using VR. Compared to conventional two-dimensional (2D) videos, however, the effects of VR in medical education are not clear. This study aims to compare VR and 2D videos on distance learning of live-action Focused Assessment with Sonography for Trauma (FAST) in initial trauma care and to examine psychological learning effects such as self-efficacy and comprehension.
Methods: We conducted a randomized controlled trial using distance learning. Eligible participants for inclusion were fourth- to sixth-year medical students and first- and second-year residents in five medical schools and university hospitals. We conducted stratified randomization by institution and participants were assigned to 2D and VR groups. Participants attended approximately 30 minutes of remote lectures on initial trauma care and watched live-action FAST practices in the emergency room in 2D or VR. Primary outcomes were self-efficacy, intrinsic value and emotional engagement to assess learning effectiveness. Multiple regression analysis was used to evaluate the association between VR use and outcomes.
Results: Sixty-four participants were eligible for analysis (2D, n = 33; VR, n = 31). There were no significant differences in participant characteristics; however, the median pre-test score for measuring medical knowledge differed by two points (2D, 20.0; VR, 18.0). In multiple regression analysis to evaluate the association between VR and outcomes, all outcomes showed no significant association (B, -0.62, 0.44, 0.98; 95% CI, -5.62 to 4.38, -2.72 to 3.59, -2.12, 4.08; p-value, 0.80, 0.78, 0.53, self-efficacy, endogenous value and emotional engagement, respectively).
Conclusion: We evaluated VR use and psychological learning effects in distance learning of FAST in initial trauma care. In this study, using VR was not significantly associated with learning effectiveness.