INHIBITION OF THE MEK/ERK PATHWAY IN Glioblastoma Multiforme CANcer STEM CELLS WITH U0126 INHIBITS PROLIFERATION AND MIGRATION.

Correia JA, Park TIH, Rustenhoven J, Monzo H, Curtis MA, Mee E, Faull RLM, Dragunow M. Centre for Brain Research, Faculty of Medical and Health Sciences, The University of Auckland, Auckland New, Zealand. Department of Neurosurgery, Auckland City Hospital, Park Road, Grafton, Auckland, New Zealand.

Introduction: Glioblastoma Multiforme is the most malignant intrinsic brain tumour. Recent literature implicates the proliferation and migration of chemo-radiotherapy resistant glioma-stem cells (GSCs) as a key mechanism in GBM recurrence. The MEK/ERK pathway has been implicated in the self renewal of GSC’s. We sought to investigate the effect of inhibition of this pathway on GSC proliferation and migration.

Methods: Following institutional ethics board and patient consent, tissue from patients undergoing resection of confirmed Glioblastoma Multiforme at Auckland City Hospital was transported to the laboratory and GCS’s were cultured as free floating tumour-spheres, embedded in extracellular matrix and allowed to migrate away from the tumour-spheres. 10 μM of U0126, a highly selective, non-competitive MEK1/2 inhibitor was then applied to cells for a 96 hour duration and the effects quantified.

Results: Under normal culture conditions, GSCs continue to proliferate and migrate out from their spheres. However, when 10 μM U0126 is applied for 96 hours, it reduced the total cell count by 37 ± 3%, ki67 positive immunopositivity by 60 ± 6%, and the number of GSC’s migrating away from tumour-spheres by 67 ± 3%. In addition, U0126 treatment significantly increased the appearance of cleaved-caspase 3, an apoptotic marker. This confirms the MEK/ERK pathway as an appropriate candidate for targeting both proliferation and migration of the GSCs and also provides a model to further investigate the mechanisms of GSC migration and survival.

Conclusion: Inhibition of the MEK/ERK pathway reduces proliferation and migration of Glioma cancer stem cells. This represents a mechanism by which Glioblastoma Multiforme could be additionally targeted with novel therapeutic agents.

CROSSBAT (COMBINED RANDOMIZED AND OBSERVATIONAL STUDY OF SURGERY FOR TYPE B ANKLE FRACTURE TREATMENT):
RESULTS OF A MULTI-CENTRE RCT

Mittal R On Behalf Of The CROSSBAT Study Group
Orthopaedic Department, Liverpool Hospital

University of New South Wales

Introduction: Isolated type B ankle fractures are common. Treatments vary as there is no strong evidence informing optimal management. This study aims to determine if surgical management for the treatment of type B ankle fractures with minimal talar shift is superior to non-surgical management.

Methods: Participants from 22 hospitals were randomized to either surgical or non-surgical management. Eligible participants unwilling to be randomized formed an observational cohort. The primary outcomes were patient-reported ankle function using the American Academy of Orthopaedic Surgeons Foot and Ankle Outcomes Questionnaire (FAOQ) and health-related quality of life using the physical component score (PCS) of the Short-Form General Health Survey (SF-12v2) at 12 months post-injury.

Results: 436 participants were enrolled in the study; 160 and 276 participants formed the randomized and observational cohorts, respectively. The two cohorts were analyzed separately. Intention-to-treat analysis showed the surgical group was not superior to the non-surgical group for the FAOQ (mean difference 3.2, favouring the non-surgical group; 95% CI: 0.4 to 5.9; p=0.028) or the PCS (mean difference 0.6, favouring the non-surgical group; 95% CI: -2.9 to 1.8; p=0.63). The proportion of participants with adverse events was significantly higher in the surgical group (32% vs. 14%; p=0.009). Results of the observational cohort reflected those of the randomized cohort.

Conclusion: Surgical management is not superior to non-surgical management for treating type B ankle fractures with minimal talar shift. Given the higher costs and adverse events associated with surgery, non-surgical management is recommended for this common fracture.

RADIATION INDUCED GENE EXPRESSION OF TISSUE FACTOR, THROMBOMODULIN, CADHERIN 5 AND CADHERIN 13 IN CEREBRAL MOUSE ENDOTHELIAL CELLS

Chen B, Raoufi-Rad N, Zhao Z, Grace M, Ukath J, Stoodley M
Australian School of Advanced Medicine, Marsfield, New South Wales, Australia

Introduction: Cerebral arteriovenous malformations (AVMs) are congenital vascular abnormalities associated with significant mortality and morbidity. Conventional treatment paradigms insufficiently address large deeply seated AVMs. We hypothesise that radiosurgery can induce unique molecule expression on the AVM endothelium, allowing vascular targeting to act more rapidly and selectively on the AVM vessels.
**Methods:** A murine brain endothelial cell line (bEnd.3) was treated with 25 Gray radiation using a linear accelerator. Non-irradiated cells were used as controls. Real-time quantitative polymerase chain reaction was used to determine the relative gene expression of bEnd.3 cells at 0, 6, 12, 24, 48, 72, 96, 120, 144, and 168 hours post-irradiation.

**Results:** Genes encoding for tissue factor (TF), thrombomodulin, cadherin 5, and cadherin 13 were found to be significantly upregulated post-irradiation at varying time points (p<0.05), with the maximum level of gene expression for TF being evident at 168 hours post-irradiation (over 24 fold increase in comparison with control samples). All molecules demonstrated significant upregulation at 96, 120, 144, and 168 hours post-irradiation.

**Conclusion:** The results of this study demonstrates that radiosurgery can significantly alter endothelial cell phenotype in vitro, potentially enabling the use of ligand-based molecular targeting therapies for AVM treatment.

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**THE LONG NONCODING RNA - PRINS AS A NOVEL TUMOUR SUPPRESSOR IN ADRENOCORTICAL CARCINOMA.**

Glover AR (1,2,3,4), Zhao JT (1,2,4), Joo LJS (1), Gill AJ (2,4), Robinson BG (1,2), Sidhu SB (1,2,3,4).

1 Cancer Genetics Laboratory, Kolling Institute, Northern Sydney Local Health District, St Leonards.
2 Sydney Medical School Northern, Royal North Shore Hospital, University of Sydney.
3 University of Sydney Endocrine Surgery Unit, Royal North Shore Hospital.
4 Sydney Vital Translational Research Unit, Northern Sydney Local Health District.

**Introduction:** Adrenocortical carcinoma (ACC) has high recurrence rates & poor outcomes. We have shown expression of PRINS, a long noncoding RNA (lncRNA) can predict ACC recurrence. In psoriasis, PRINS has shown expression of PRINS, a long noncoding RNA (lncRNA) can predict ACC recurrence. In psoriasis, PRINS has shown expression of PRINS, a long noncoding RNA (lncRNA) can predict ACC recurrence.

**Methods:** PRINS expression in ACC cells (NCI-H295R) was restored using the mammalian expression vector containing full length of PRINS cDNA transcript (pcDNA3.1[PRINS]). Cell phenotypes were compared to cells transfected with an empty vector (pcDNA3.1[Blank]). Transcriptome analysis was performed on clinical samples of ACC (n=10) and normal adrenal cortex (n=6) using the ArrayStar Human LncRNA V3.0 microarray.

**Results:** NCI-H295R cells have low expression of PRINS compared to normal adrenal cortex (Fold change [FC] 0.37, P<0.05). Restoring PRINS expression lead to increased rates of apoptosis (49.8%) by Annexin V assays (P<0.05) and reduced cell proliferation (30-40%) using MTS assays (P<0.05) in PRINS transfected cells. Using RNA FISH, PRINS was localised to the cell cytoplasm. Correlation of ~26,000 mRNA transcripts in clinical samples found PRINS expression to be correlated (>80%) with 48 mRNAs (P<0.05), including the anti-apoptotic TP53 related gene – TNFRSF11B. Following PRINS restoration, TP53 mRNA was increased (FC 1.5, P<0.001) and TNFRSF11B mRNA reduced (FC 0.6, P<0.05).

**Conclusion:** This first report of PRINS acting as a tumour suppressor in cancer supports the association with ACC outcomes. As PRINS is also under-expressed in many other cancers it offers further research opportunities into a novel mechanism of TP53 action in cancer.

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**NEUTRALISATION OF HISTONES AND NEUTROPHIL EXTRACELLULAR TRAPS (NETS) PREVENTS SEPSIS-ASSOCIATED MORTALITY**

O’Meara C (1,2), Coupland L (2), Dulhunty A (3), Freeman C (2), Bezos A (2), Brown A (2), Mitchell L (4), Stephens R (6), Arnolda L (5), Parish C (2).

1 Dept of OHNS, The Canberra Hospital
2 Cancer & Vascular Biology Group, The John Curtin School of Medical Research (JCSMR), The Australian National University (ANU)
3 Dept of Molecular Bioscience, JCSMR, ANU
4 Intensive Care Unit, The Canberra Hospital
5 Dept of Cardiology, The Canberra Hospital
6 Dept of Applied Mathematics, ANU

**Introduction:** Histones (H), derived predominantly from neutrophil extracellular traps (NETs), play an integral role in the pathogenesis of sepsis. H cause endothelial injury, platelet activation and erythrocyte dysfunction precipitating end organ injury and increased mortality. In this study, novel polyanionic compounds (PACs) are tested in 3 models for their ability to attenuate sepsis-associated pathology.

**Methods:** (1) Human Microvascular Endothelial Cells (HMECs) were exposed to H and LPS-induced NETs with/without PACs and extent of cell injury was measured. (2) PACs were tested in a rat caecal-ligation and puncture (CLP) sepsis model with end organ injury and severe morbidity requiring euthanasia as outcome measures. (3) Blood plasma obtained from septic patients in ICU was added to HMECs with/without PACs and the extent of cell injury determined.

**Results:** (1) Histones and LPS-induced NETs are cytotoxic for HMECs in a concentration dependent manner yet PACs significantly attenuated this cytotoxicity. (2) Saline treated CLP rats had a
higher mortality (62.5% vs 0%) and significant renal and liver injury (creatinine 79 ± 18 vs 39 ± 2,
p=0.01; ALT 253 ± 44 vs 66 ± 12 p=0.0008) compared to rats treated with PACs, respectively. 
(3) The degree of HMEC cytotoxicity of plasma from septic patients correlated strongly with 
APACHE II mortality scores (p=0.0007). Importantly, this cytotoxicity was attenuated by 
DNAse, anti-H antibodies and PACs (p=0.002).

Conclusion: An uncontrolled immune reaction is responsible for much sepsis-associated pathology 
with NETs and histones causing cell damage and coagulation disturbances. Novel PACs tested in 
this study were shown to be highly effective at abrogating histone and NET-mediated damage in vitro and in vivo and thus hold great therapeutic promise as immunobiotics.

THE EFFECT OF ORAL SIMVASTATIN ON FIBRINOLYTIC PATHWAYS FOLLOWING MAJOR COLORECTAL SURGERY
Alexander ZE, Su’a BU, Singh PP, Hill CTG, Lyndon MP, Hill AG
South Auckland Clinical School, University of Auckland

Introduction: Studies have shown that statins reduce intra-abdominal adhesion formation in 
animal models by modulating the peritoneal fibrinolytic pathway. This randomised clinical trial 
investigated the effect of oral statins on the peritoneal fibrinolytic environment in patients 
following major colorectal surgery.

Methods: 144 patients undergoing elective colorectal resection for any indication, or reversal 
of Hartmann’s procedure, were randomised to receive either 40mg oral simvastatin or placebo 
once daily for 3-7 days before surgery till 14 days after surgery. Peritoneal drain fluid was collected 
for 24 hours postoperatively and analysed for active tissue plasminogen activator (tPA), total 
tPA, active plasminogen activator inhibitor (PAI-1), total PAI-1, and tPA/PAI-1 complex levels 
using the ELISA method.

Results: Only ninety five patients had sufficient peritoneal drain fluid suitable for the ELISA 
analysis. Forty six patients (48%) were from the oral simvastatin group. Active tPA levels were lower in the simvastatin group compared to the placebo group (P >0.05). Total tPA levels between the two groups were similar and insignificant (P >0.05). PAI-1 levels were higher in the statin group (P >0.05). Total PAI-1 levels were higher in the statin group (P >0.05). tPA/PAI-1 complex levels were higher in the placebo group (P >0.05)

Conclusion: Oral simvastatin has minimal effect on the intraperitoneal fibrinolytic pathway in the 
first 24 hours following major colorectal surgery.

DEEP BRAIN STIMULATION TARGETING THE ZONA INCERTA MODULATES EYE MOVEMENTS IN HUMANS
Bangash OK 1,2, Dissanayake A 3, Knight S 3, Murray J 3, Thorburn M 2, Thani N FRACS 2, Bala A FRACS 2, Stell R FRACP 3, Lind CRP FRACS 1,2

Introduction: The posterior subthalamic area (PSA) centred on the zona incerta (ZI) is a 
promising experimental target for therapeutic deep brain stimulation (DBS). Animal evidence 
indicates the ZI may play a role in saccadic eye movements via a GABAergic incerto-collicular 
pathway. PSA DBS for Parkinson’s disease (PD) and essential tremor (ET) provided a rare 
opportunity to test this hypothesis in humans. The effects of PSA DBS on saccades have never 
been previously characterised.

Methods: Sixteen patients (PD=12, ET=4) underwent DBS using the magnetic resonance 
imaging (MRI) directed implantable guide tube technique. Active electrode positions were 
confirmed at the caudal ZI. Eye movements were tested using direct-current electro-oculography 
(EOG) in the medicated state pre and post-operatively on a horizontal predictive task 
subtending 30°. Post-operative assessments consisted of stimulation-off constituting a 
microlesion (ML) condition and high frequency stimulation (HFS: frequency = 130Hz) up to 3 
volts. REX/MARK software allowed for analysis of saccade amplitude, peak velocity, duration and latency. A two-way analysis of variance (ANOVA) was performed with α=0.05.

Results: PSA HFS leads to significant reduction in first saccade amplitude by 10.4% (P=0.0007) 
and essential tremor (ET) provided a rare opportunity to test this hypothesis in humans. The 
effects of PSA DBS on saccades have never been previously characterised.

Conclusion: Posterior subthalamic area DBS in 
patients with PD and ET leads to hypometric, slowed saccades with an increase in the number 
of steps taken to reach the target. Given the location of the active contacts the GABAergic 
(inhibitory) incerto-collicular pathway is likely to be responsible. This is the first evidence for its 
existence in humans. Our findings also suggest patients undergoing PSA DBS may have impaired 
saccadic performance which requires further investigation.
VASCULAR ANATOMY OF THE MEDIAL SURAL ARTERY PERFORATOR FLAP: A NEW CLASSIFICATION SYSTEM OF INTRAMUSCULAR BRANCHING PATTERNS

Dusseldorp JR, Gianoutsos M and Moradi P
Concord Clinical School, Sydney Medical School, University of Sydney
Department of Plastic & Reconstructive Surgery, Prince of Wales Hospital, Randwick

Introduction: The medial sural artery perforator (MSAP) flap is a versatile fasciocutaneous flap. The main difficulty encountered when raising the MSAP flap is in obtaining adequate pedicle length during intramuscular dissection. The objective of this study was to determine the pattern of intramuscular course of the MSAP flap pedicle.

Methods: 14 cadaveric specimens were dissected and CT angiograms of 84 legs were examined. The intra-muscular branching pattern and depths of the medial sural artery branches were analyzed. The number of perforators, position of the dominant perforator and both intra-muscular and total pedicle length were also recorded and compared to existing anatomical data.

Results: Three types of arterial branching pattern were identified within the medial gastrocnemius, demonstrating one (31%), two (59%) or three or more (10%) main branches. A dominant perforator from the medial sural artery was present in 92% of anatomical specimens (13/14). Vertically, the location of the perforator from the popliteal crease was on average 13cm (+/-2cm). Transversely, the perforator originated 2.5cm (+/-1cm) from the posterior midline. Using CT angiography it was possible in 10 consecutive patients to identify a more superficial intra-muscular branch and determine the leg with the optimal branching pattern type for flap harvest.

Conclusion: This study is the first to describe the variability of the intra-muscular arterial anatomy of the medial head of gastrocnemius muscle. Surgeons utilizing the MSAP flap option should be aware of the possible branching pattern types. Routine use of pre-operative CT angiogram may help determine which leg has the most favorable branching pattern type.

CENTRAL BRAIN RESPONSES FOLLOWING SACRAL NEUROMODULATION IN PATIENTS WITH FAECAL INCONTINENCE: A FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI) STUDY

Mirbagheri N (A), Hatton S (B), Lagopoulos J (B) & Gladman MA (A)

(A) Academic Colorectal Unit, Sydney Medical School - Concord, University of Sydney, NSW, Australia. Email: m.a.gladman@sydney.edu.au
(B) Brain and Mind Research Institute, University of Sydney, Australia

Introduction: Sacral Neuromodulation (SNM) is widely used in Faecal Incontinence (FI), although its mechanism of action remains poorly understood. Emerging evidence suggests that one of the possible mechanisms that SNM exerts its effect is via central neuromodulation. Therefore, the aim of this study was to investigate central brain responses to rectal stimulation following SNM in patients with FI using fMRI.

Methods: Patients with FI and no contraindication to MRI were recruited. A baseline fMRI scan was performed prior to a trial of SNM followed by a second scan 6 weeks after permanent SNM implantation. Scanning involved acquisition of resting state and rectal distension paradigm-driven images. Rectal stimulation was performed using a barostat and involved distension at fixed (15 and 45mmHg) and variable (set at 10% above sensory threshold) pressures. Data were analysed using FEAT(FMRI Expert Analysis Tool)

Results: 20 patients who were offered SNM for FI were invited to participate, 14 of whom participated. No adverse events were observed. At baseline (n=14) no mean group activation was seen at fixed, low pressure rectal distension. By contrast, significant increases in blood oxygen level-dependent (BOLD) signal was observed in the cingulate gyrus, bilateral thalamus and insular cortex, right inferior cortex, caudate nucleus and the cerebellum in response to fixed, high rectal pressure distension. After SNM, an increase in BOLD signal was observed in the left insular cortex / putamen and bilateral frontal cortices in response to fixed low and high pressure rectal distensions, respectively.

Conclusion: This first fMRI study of patients with SNM has shown both safety and feasibility. Importantly, altered cerebral BOLD signals were observed after SNM in patients with faecal incontinence in response to rectal distension. This suggests that the processing of rectal afferent signals is affected by SNM, which may contribute to its clinical efficacy.

ABROGATING THE CONTRIBUTION OF HISTONES TO CARDIAC ISCHEMIA REPERFUSION INJURY
**Introduction:** Cardiac ischemia reperfusion injury (cIRI), a complication of intervention for myocardial infarction, involves the release of histone-studded chromatin webs by activated neutrophils. Histones (H) are cytotoxic for endothelial cells and prothrombotic thus exacerbating reperfusion injury. In this study novel polyanionic compounds (PACs) were tested in 3 experimental models of cIRI.

**Methods:** (1) Human Microvascular Endothelial Cells (HMECs), were exposed to H in simulated ischemia/reperfusion injury (SI/R) conditions with/without PACs and LDH release measured. (2) PACs were tested in a rat model of cIRI with microvascular obstruction and myocardial necrosis (ischemic zone - IZ) assessed. (3) Plasma from reperfused coronary vessels of myocardial infarction (MI) patients was incubated with HMECs to determine the ability of PACs to preserve cell viability.

**Results:** (1) HMEC SI/R injury was significantly exacerbated by the addition of H (SI/R: 13 ± 1%, SI/R + H: 67 ± 3% dead cells, p<0.0001), while PACs significantly attenuated this injury (SI/R + H + PACs: 10 ± 4% dead cells, p<0.0001). (2) In a rat model of cIRI PACs significantly reduced microvascular obstruction (saline treated: 15 ± 3 vs PACs: 8 ± 2% IZ, p<0.05) and myocardial necrosis (saline: 41 ± 6% vs PACs: 25 ± 3% IZ, p<0.05). (3) PACs also attenuated the cytotoxic effects of plasma from MI patients for HMECs (saline: 24 ± 2% vs PACs: 50 ± 4% viable cells, p<0.0001).

**Conclusion:** Histones, released by activated neutrophils, apoptotic- and necrotic cells, can act as procoagulants and are toxic for endothelial cells. Treatment with novel PACs reduced ischemia reperfusion pathology both in-vitro and in-vivo, thus these compounds offer great therapeutic potential.
Dusseldorf JR and Pennington DG
Department of Plastic & Reconstructive Surgery, Australian School of Advanced Medicine, Macquarie University

Introduction: The absolute weight of tissue that a single perforating blood vessel can reliably perfuse remains an unanswered question in reconstructive microsurgery. We have developed an equation, known as the Flap Viability Index (FVI), to help guide decision-making. The aim of this study was to determine the clinical efficacy of the FVI and to investigate its biological plausibility with ultrasonography.

Methods: Clinical Study: We prospectively analysed 118 consecutive free DIEP flaps collecting pre-operative measurements of perforator diameter, FVI, flap weight, as well as data on total and partial flap necrosis. Ultrasonographic Study: We used Color Doppler Flow quantification in 10 consecutive cases to measure absolute arterial flow through the DIEP flap pedicle post-operatively and determine its correlation with pre-operatively measured perforator diameter and flap viability index.

Results: There were no flap failures and the partial flap necrosis rate was 6% (7/118). All cases of partial necrosis occurred in flaps with FVI less than 10 (our recommended minimum) confirming the predictive ability of the equation. Routine use of the index also lead to harvest of larger flaps based on smaller perforators and increased FVI measurements (28.38 vs 15.67; p=0.003). A highly significant linear correlation was found between absolute flow rate in DIEP flap pedicles and the FVI (r=0.82, p=0.01).

Conclusion: The results of this study confirm the biological plausibility of the FVI equation and validate its utility in improving safety in DIEP flap breast reconstruction. Utilization of the FVI equation holds the potential advantages of improving aesthetic outcomes whilst reducing donor-site morbidity, operative time and complications.

FRAILTY MODELS PREDICT MORBIDITY AND MORTALITY AFTER MAJOR GENERAL AND VASCULAR SURGERY
Aitken SJ; Blyth FM; Naganathan V.
Department of Vascular Surgery, Concord Hospital; Centre for Research in Ageing; University of Sydney.

Introduction: Frailty is defined as a cumulative decline across multiple physiological systems leading to decreased resistance to physiological stress. Formal measures of frailty exist for predicting...
preoperative risk but surgeons often intuit frailty—the intangible sense of the ‘old’ older patient. The prognostic ability of frailty indices to predict perioperative adverse outcomes of surgery is reviewed.

**Methods:** A systematic review of all studies assessing frailty in vascular and general surgery was performed, searching MEDLINE, EMBASE, Cochrane and reference lists. Studies were required to assess frailty with a predictive model for mortality or morbidity. The development phase, discrimination and calibration for each model was assessed. Peer-reviewed guidelines for study quality and risk of bias derived from emerging methodological frameworks for systematic reviews of prognostic studies were used.

**Results:** 20 studies (10 models) were included from a search result of 807 titles. Six studies were in vascular surgery, with the remaining 14 studies in general surgery. Models predicted mortality in 9 studies and were predictive of morbidity in 12 studies. Eight studies reported frailty model development, six studies internally validated their model and 12 were external validation studies. 55% of studies assessed model discrimination and calibration. Predictive ability of models ranged between 0.62-0.82 (AUC analysis). Study quality and risk of bias varied, according to PROBAST and CHARMS criteria. The most externally validated model was the modified Frailty Index applied to NSQIP data (n=7).

**Conclusion:** Frailty predicted adverse outcomes after major vascular and general surgery but model predictive accuracy varied. Methodological quality of prognostic models for frailty is poor, hindering model applicability. Emerging evidence-based checklists and methodological frameworks can improve development and reporting of prediction model studies.

**CONGENITAL DIAPHRAGMATIC HERNIA: OBSERVED/EXPECTED LUNG-TO-HEAD RATIO AS A PREDICTOR OF LONG-TERM MORBIDITY**

King SK (1), Gaitheiro R (2), O'Brien K (3), Moraes T (4), Humpl T (5), Marcon M (6), Chiang M (1), Reyes J (5), Beth Halliburton (1), Greg Ryan (7), Peter Cox (2) And Priscilla P. L. Chiu (1)

(1) Division of General and Thoracic Surgery, The Hospital for Sick Children, Toronto, Ontario, Canada
(2) Division of Critical Care Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada
(3) Division of Neonatology, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada
(4) Division of Respiratory Medicine, The Hospital for Sick Children, Toronto, Ontario, Canada
(5) Division of Cardiology, The Hospital for Sick Children, Toronto, Ontario, Canada
(6) Division of Gastroenterology, The Hospital for Sick Children, Toronto, Ontario, Canada
(7) Fetal Medicine Unit, Mount Sinai Hospital, University of Toronto, Toronto, Ontario, Canada

**Introduction:** Congenital diaphragmatic hernia (CDH) is a condition associated with a high risk of mortality and morbidity. We aimed to investigate the association of observed/expected (O/E) lung-to-head ratio (LHR) by prenatal ultrasound with long-term morbidity for isolated fetal CDH patients.

**Methods:** We performed a retrospective study of prenatally diagnosed CDH from 18-38 weeks of gestation (01/2002 – 04/2010). Survivors with at least 1-year follow-up of prospectively collected long-term morbidity assessments were included.

**Results:** O/E LHR was available in 43 survivors (median 40%, range 22.8 – 78.3%). Follow-up data were available in 41 survivors (M:F = 24:17, left CDH = 39/41). Median follow-up was 6.5 years (1 – 11 years). Two cohorts of O/E LHR were defined (22.6 – 45%, 45.1 – 78.3%) based upon previous studies. Height/weight trajectories were similar between the two cohorts, with the majority below the 50th centile. There were no differences between the two cohorts by age 3 years for Bayley scales (developmental domains) and/or REEL-3 (language development). In addition, V/Q scans in the two cohorts demonstrated similar degrees of mismatch (mean delta V/Q = 35.4 versus 31.3).

**Conclusion:** In fetuses with isolated CDH, a reduction in O/E LHR does not predict a worse outcome in long-term follow-up. There is no association between a lower O/E LHR and a reduction in REEL-3 or Bayley score, nor V/Q mismatch.

**THE CHANGE IN POSITION OF THE SCIATIC NERVE DURING THE POSTERIOR APPROACH TO THE HIP**

Kanawati A, Stewart F
School of Rural Medicine UNE
Armidale, NSW, 2350, AUSTRALIA

**Introduction:** The position of the sciatic nerve in the gluteal region has not been described while the hip is dislocated and positioned
during THA using the posterior approach. The aim of this cadaver study is to determine the change in position of the sciatic nerve during positioning for the posterior surgical approach to the hip.

**Methods:** Method – We investigated the position of the sciatic nerve during the posterior approach to the hip by dissecting 22 formalin-treated cadaver hips. The distance between the sciatic nerve and the femoral neck was measured before and after hip dislocation, and in positions used during femoral preparation for arthroplasty.

**Results:** Results – The sciatic nerve moves closer to the femoral neck when the hip is internally rotated to 90 degrees (90 IR) and flexed to 30 degrees or more. The mean distance between the sciatic nerve and femoral neck was 43.1 ± 8.7 mm with zero degrees of flexion and 90 IR which significantly decreased to a mean of 36.1 ± 9.5 mm, 28.8 ± 9.8 mm and 19.1 ± 9.7 mm with 30, 60 and 90 degrees of hip flexion respectively, p = 0.000. In two hips (9%) the nerve was in contact with the femoral neck when the hip was flexed to 90 degrees.

**Conclusion:** Conclusions – This study demonstrates that the sciatic nerve comes into greater proximity to the operative field with progressive flexion of the hip.

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**ABLATION OF HEPATIC NEOPLASMS USING IRREVERSIBLE ELECTROPORATION: A SYSTEMATIC REVIEW OF THE LITERATURE**

**Spike E1, Pasch J1, Richardson A1,2, Yuen L1,2, Pleass H1,2, Lam V1,2**
1. Department of Surgery, Westmead Hospital
2. Discipline of Surgery, Sydney Medical School

**Introduction:** Irreversible electroporation (IRE) is an emerging method for the ablation of hepatic neoplasms. It utilises the application of an electric field to induce nanopores in tumour cell membranes and cause cell death. We perform a systematic review to evaluate the safety and efficacy of IRE in the ablation of hepatic neoplasms.

**Methods:** A literature search was performed using Medline and EMBase to identify published human clinical studies relating to the application of IRE in treating hepatic neoplasms. Data was collected regarding immediate success, local recurrence and complications.

**Results:** Eleven studies were included with 230 patients and 375 hepatic neoplasms ablated in total. All were case series, 5 being prospective and 6 retrospective. One study reported on open approach exclusively, 7 on percutaneous IRE and a further 3 on mixed approaches including laparoscopy. Mean tumour size was 21.4 mm (10-30). The majority were hepatocellular carcinoma and colorectal cancer metastases. Immediate success rate of ablation was 82%. Local recurrence rate was 22% at short term follow up. The overall complication rate was 30% and there was no perioperative mortality. Complications included cardiac arrhythmia, abscess formation and intra-abdominal haemorrhage.

**Conclusion:** IRE appears to be a safe and effective method of hepatic tumour ablation that may be utilised when resection and radiofrequency ablation are unsuccessful or inappropriate. Further studies should be performed to compare IRE to other treatment modalities and to assist in patient selection.

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**TISSUE ENGINEERING VASCULARISED HUMAN LIVER**

**Yap KK (1,2), Poon CJ (1), Taylor CJ (1), Yeoh GC (4), Morrison WA (1,2,3), Mitchell GM (1,2,3)**
1. O’Brien Institute Department of St Vincent’s Institute, Fitzroy, Victoria
2. University of Melbourne Department of Surgery, St Vincent’s Hospital, Fitzroy, Victoria
3. Australian Catholic University, Fitzroy, Victoria
4. Harry Perkins Institute of Medical Research & University of Western Australia, Perth, Western Australia

**Introduction:** Liver tissue engineering potentially offers new tissue for organ transplantation, disease modelling, and drug testing. We have created a transplantable liver organoid by combining liver progenitor cells, liver sinusoidal endothelial cells, and mesenchymal stem cells, supported by a liver-derived extracellular matrix gel to aid tissue assembly and a polyurethane scaffold for mechanical support.

**Methods:** Human liver progenitor cells, liver sinusoidal endothelial cells, and adipose-derived mesenchymal stem cells were combined (10:10:1 ratio, 1 million cells total), mixed in liver gel (human liver-derived), and seeded into polyurethane scaffolds (3 mm diameter, 0.8 mm thickness). In vitro organoids were analysed at day 1 and 3 in culture. Liver progenitor cells from 3 different patients were compared for consistency.

**Results:** Hepatic genes (HNF4a, albumin, CYP3A4, HGF) and coagulation factor 8 (from liver sinusoidal endothelium) were all upregulated over time. Functional analyses of albumin secretion (indicating synthetic
capacity of differentiating hepatocytes) and urea production (indicating ammonia metabolism) also increased over time. Interestingly, these parameters were all increased using liver gel in comparison to Matrigel, the industry's most widely used extracellular matrix gel. 

**Conclusion:** A functional human liver organoid can be engineered using a unique cell combination incorporating liver-specific vasculature, facilitated by liver-derived extracellular matrix. Further analysis is underway with additional functional parameters/histomorphology. Animal studies are planned to investigate the in vivo development of this organoid.

## Building a Bio-Artificial Neuromuscular-Electrode Interface for Tissue Reconstruction.

**Zhang B, Quigley A, Bourke J, Myers D, Knowell C, Kapsa R, Choong P**

Department of Surgery, St Vincent Hospital Melbourne, University of Melbourne Department of Orthopaedics, St Vincent Hospital Melbourne, University of Melbourne Department of Neuroscience, St Vincent Hospital Melbourne, University of Melbourne ARC Centre of Excellence for Electromaterials Science, Intelligent Polymer Research Institute, University of Wollongong

**Introduction:** Designing a bioartificial actuator system for severe neuromuscular injuries requires consideration of 3 key issues 1)reinnervating the muscle 2)transducing the muscle activity into electrical signals 3)designing the actuator system. Agrin and laminin were used to improve muscle innervation. Polypyrrole based electrode and actuators were tested for muscle activity detection and biocompatibility.

**Methods:** For the study of NMJ, muscle cells were treated with agrin and laminin and further innervated by PC12 neural cells. NMJ formation and function was assessed by immunocytochemistry and live cell imaging. Polypyrrole coated microelectrode arrays (MEA) were used to evaluate feasibility of detecting muscle electrical activity through conductive polymer electrodes. The biocompatibility of polypyrrole based actuators was assessed by implantation into rabbit muscle.

**Results:** Agrin and laminin enhanced the number and function of NMJ between muscle and neural cells. There was also superior muscle maturation in the cultures treated with agrin and laminin. Polypyrrole coated MEA were capable of detecting electrical activity from muscle cells over the 8 days that the cells were in culture. Polypyrrole based actuators were biocompatible when implanted into rabbit muscle with minimal tissue inflammation.

**Conclusion:** Agrin and laminin promotes synapse between nerve and muscle. Polypyrrole based electrodes and actuators are capable of detecting muscle activity and are safe for in vivo implantation. These results pave the way for further combination the three elements of neuromusculature, electrode and actuator into a singular bioartificial actuator system.

## Designer Doctors? How ‘Design Thinking’ Assists in Developing Targeted Prevocational Surgical Education Programs.

**Altken SJ; Huq F; Blyth F; So N.**

University of Sydney- Concord Clinical School; Concord Repatriation General Hospital Medical Education Support Unit

**Introduction:** ‘Design thinking’ is an innovative method of meeting a surgical learner’s needs in a technologically feasible and strategically viable way. Key collaborators meet to solve complex problems through a process of research, concept development, prototyping and testing. We utilised design thinking methods to develop three need-targeted prevocational junior doctor educational programs.

**Methods:** Design thinking was used to create three educational programs: ‘Virtual Anatomy’, 'Doctors as Teachers' and 'Integrated Ultrasound'. These programs were developed in collaboration with the university clinical school, hospital supervisors and junior doctors. All programs had pre-course needs analysis and ongoing assessment including qualitative feedback. Selected participant interviews and thematic analysis was performed. Course evaluation was assessed in formal reflection meetings.

**Results:** For the Virtual Anatomy and Doctors as Teachers programs, the pre-course needs analyses defined the educational goals, the course structure and content. After prototyping with a pilot program, both educational programs were redesigned based upon participant feedback. The 'Integrated Ultrasound Program' is currently in the prototyping phase. The final programs undergo an ongoing iterative process of testing and reevaluation. Design thinking is assisting in targeting the needs of these programs to junior doctors. Interviews with developers revealed
the design process was useful in reimagining course development based on user needs and targeted outcomes. **Conclusion:** Design thinking methodology helped translate needs analysis into educational programs relevant to prevocational junior doctors. Iterative feedback showed participant requirements were consistently met. Design thinking is a useful learner-centered tool for surgical educators creating future educational programs.

**BLOOD PRODUCT TRANSFUSION INCREASES RISK OF POSTOPERATIVE ATRIAL FIBRILLATION**

Bookun HR, Cheng A, Lee CS, Zhang XB
Department of Cardiothoracic Surgery and Cardiology Research Unit
University Hospital Geelong –Barwon Health, Victoria

**Introduction:** Red Blood Cell (RBC) transfusion instigates an inflammatory reaction by direct infusion of inflammatory mediators, which further augments the inflammatory response from cardiopulmonary bypass and cardiac surgery. Although the exact mechanism is still unknown, evidence strongly supports the role of inflammation as a significant contributor of Postoperative Atrial Fibrillation (POAF). Our objective is to test the hypothesis that RBC transfusion increases the risk of POAF in patients after cardiac surgery. **Methods:** Between January 2008 to September 2014, 2657 patients underwent cardiac surgery at the University Hospital Geelong. 240 patients were excluded from analysis as they had a preoperative history of AF. Demographic and perioperative data were collected prospectively for 2417 patients. Descriptive statistics were used to characterize the sample with regards to demographic and perioperative variables. A logistic regression model was used to investigate the impact of RBC transfusion on the incidence POAF. **Results:** Overall incidence of POAF was 32.9% (n=795). Patients who developed POAF were generally older, had worse renal function, and received more RBC and non-RBC transfusions. The overall transfusion rate was 55.1% for RBC or non-RBC blood products, 18.5% for RBC only, 8.3% for non-RBC, and 28.3% for both RBC and non-RBC. RBC transfusion was positively correlated with increase in POAF rates. Our regression model suggested that for every additional unit of RBC transfused, there was a corresponding increase in the odds of developing POAF by a factor of 1.07 (95% CI: 1.04-1.10, p<0.001).

**Conclusion:** RBC transfusion is associated with an increased rate of Postoperative Atrial Fibrillation after cardiac surgery and this is supported with our multivariate logistic regression model. These results are in agreement with the current literature in the sense that POAF is increased with blood product transfusion and its associated inflammatory response. Patients receiving transfusions should have a reduced threshold for consideration of prophylactic treatment for POAF.

**CURRENT MANAGEMENT OF ACUTE DIVERTICULITIS: A SURVEY OF AUSTRALASIAN SURGEONS (POSTER PRESENTATION)**

Jaung R1, Robertson J1, Rowbotham D2, and Bissett I,3
1Department of Surgery, The University of Auckland, New Zealand (R Jaung MBChB, J Robertson MBChB, IP Bissett MD FRACS), 2Department of Gastroenterology & Hepatology, Auckland City Hospital, New Zealand (DS Rowbotham MD FRCP), 3Department of Surgery, Auckland City Hospital, New Zealand (IP Bissett MD FRACS)

**Introduction:** AD is a frequent indication for hospital admission under the General Surgery service. However, there is a striking lack of consensus regarding the management of AD, particularly the more common uncomplicated episodes. This survey aims to describe current practice and the decision-making processes of clinicians who are currently managing patients with AD in Australasia. **Methods:** An online survey was distributed to all Australasian colorectal surgeons and all general surgeons in the Auckland region. Responses were collected over a two-month period and analysed to identify points of consensus and areas of significant difference in opinion between the two groups. **Results:** Responses were received from a total of 99 of 200 (49.5%) Colorectal Surgeons and 19 of 36 (52.7%) General Surgeons. Hinchey Classification was the most commonly used measure of disease severity, used by 67 (95.7%) colorectal surgeons and 12 (92.3%) general surgeons. There was a lack of consensus around important aspects of AD management including antibiotic therapy, and use and modality of follow-up imaging. Selective antibiotic therapy and use of anti-inflammatory medication as adjuncts to treatment were practised by a minority of those surveyed. **Conclusion:** Newer approaches to management were being utilised by some of
the respondents. The lack of consensus regarding management of AD may be a consequence of a paucity of high-level evidence to support specific management approaches, particularly in patients with uncomplicated AD.

SINGLE VERSUS MULTIPLE PORT LAPAROSCOPIC CHOLECYSTECTOMY: A META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS
Cao AM, Eslick GD, Cox MR
The Whiteley-Martin Research Centre, Discipline of Surgery, The University of Sydney, Nepean Hospital, Penrith, New South Wales, Australia.

Introduction: Single incision laparoscopic cholecystectomy (SILC) aims to improve cosmesis, reduce recovery time whilst maintaining the same safe surgical outcomes seen in conventional laparoscopic cholecystectomy (LC). SILC has been gaining popularity and there have been multiple studies published comparing SILC and LC.

Methods: An electronic search of major databases was performed between 1997 and 2015 for randomized controlled trials comparing outcomes between single port LC and two or more port LC. The primary outcome measures were mortality rates, complication rates, conversion rate to an open procedure, operating time, blood loss, postoperative pain and cosmesis.

Results: 46 RCT were included with a combined total of 3635 patients. There was no statistically significant difference between SILC and two or more port LC in mortality, complications, bile duct injuries, bile duct leaks, blood loss and duration of hospital stay. SILC were less likely to convert to an open procedure (RR 0.69, p = 0.51) however were more likely to require additional trocars to complete the operation than LC (RR 3.24, p = 0.34) and had a significantly longer operating time. SILC had slightly superior cosmetic outcomes but longer operation times.

Conclusion: Currently there is inadequate evidence to conclude on definite benefits in surgical outcomes of SILC compared to LC. The most attractive advantage of SILC appears to be the potential of improved cosmesis or wound satisfaction. However better quality RCTs that are higher powered are required for more definitive conclusions.

DETERMINANTS OF EARLY AND LATE MORTALITY IN CHILDREN BORN WITH OESOPHAGEAL ATRESIA
Fearon E (1), Teague W (1, 2), Hutson J (1, 3, 4), King SK (1, 2, 3)
(1) Surgical Research, Murdoch Childrens Research Institute, Melbourne, Australia
(2) Department of Paediatric Surgery, The Royal Children’s Hospital, Melbourne, Australia
(3) Department of Paediatrics, The University of Melbourne, Melbourne, Australia
(4) Department of Urology, The Royal Children’s Hospital, Melbourne, Australia

Introduction: Oesophageal atresia (OA) is a congenital interruption of the oesophagus. Despite advances in care, a significant proportion of patients still die. Incidents of late mortality (deaths following initial discharge) have not been analysed comprehensively. We aimed to examine the rates and associations of early and late mortality amongst patients with OA.

Methods: All patients with OA managed at The Royal Children’s Hospital, Melbourne between 1980-2015 were identified using the Nate Myers OA database. Patients were categorised into cases of early mortality (death before discharge), late mortality, and survivors. Records were reviewed for demographics, known risk factors for death, and pre-operative, operative and post-operative findings.

Results: Rate: A total of 589 patients were identified. There were 83 deceased patients (overall mortality rate - 14%). Approximately a quarter of total deaths were cases of late mortality (19/83, 23%). Early mortality cases were most often the result of palliation for trisomy 18. Late mortality cases were most frequently the result of respiratory compromise, sudden unexplained deaths at home, and Fanconi’s anaemia. Associations: Anorectal and skeletal anomalies were significantly more common in the early mortality group compared to survivors. The VACTERL association was significantly more common in both the early and late mortality group compared to survivors.

Conclusion: These results suggest that there are clear predictors of early and late mortality in OA. These predictors should alert clinicians to potential mortality risks so they may pursue management options more aggressively and better inform parents about the survival prospects of their affected child.

OPTIMAL DOSING OF BOTULINUM TOXIN FOR TREATMENT OF CHRONIC ANAL FISSURE: A SYSTEMATIC REVIEW AND META-ANALYSIS
Lin JX, Krishna S, Su’a B, Hill AG.
**Introduction:** Chronic anal fissures (CAF) are associated with significant morbidity. Studies have investigated the efficacy and safety of botulinum toxin (BT) with variable results. Thus there is currently no consensus on BT dose and injection sites. This review aims to systematically analyse trials studying the efficacy of BT for treatment of CAF in order to identify an optimum dosage and injection regimen.

**Methods:** A comprehensive review of the literature was conducted according to the PRISMA guidelines. The electronic databases Pubmed/Medline, Embase, Scopus and the Cochrane Library were searched for studies up to and including June 2015. Clinical trials (randomised and non-randomised) were selected according to specific criteria. Clinical outcomes, dosage and injection site were extracted and meta-analysis was performed.

**Results:** There were 1158 patients, with 661 in BT treatment arms, from 18 clinical trials included in this review. The outcomes of interest were 3-month healing rate, incontinence and recurrence rates. Meta-regression demonstrated a small decrease in healing rate (0.34%, 95% CI 0-0.68, P = 0.048) with each increase in dosage, a small increase in incontinence rate (1.02 times, 95% CI 1.0002-1.049, P = 0.048) with each increase in dosage and a small increase in recurrence rate (1.037 times, 95% CI 1.018-1.057, P = 0.00002) with each increase in dosage. The optimum injection site could not be determined.

**Conclusion:** Lower doses of BT are at least as effective as higher doses in terms of healing, incontinence and recurrence rates. Further studies with long-term follow-up are needed to confirm these observations. Randomised controlled trials are also needed if the optimum injection site is to be determined.

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**GENERATING LEVEL I EVIDENCE FOR SURGICAL TREATMENT OF UNDESCENDED TESTES**

Michail P (1), Smith GHH(2), Deshpande AV(3)

1. Westmead Hospital, Sydney
2. Department of Pediatric Urology, Westmead Children’s Hospital, Sydney
3. Department of Pediatric Urology, John Hunter Children’s Hospital, Newcastle

**Introduction:** Undescended testes is one of the commonest indications for surgery in childhood. Under the aegis of the Cochrane collaboration, we have developed a protocol for a Systematic review on interventions for undescended testes, of which the following meta-analysis is a part.

**Methods:** Published studies were searched on CENTRAL, MEDLINE (OvidSP), EMBASE (OvidSP), BIOSIS Previews, International Clinical Trials Register (ICTRP) Search Portal and ClinicalTrials.gov with predetermined search terms. Two reviewers independently assessed studies against predetermined criteria. Two reviewers independently extracted data and assigned overall quality and strength of evidence ratings using the GRADE criteria. Statistical data analysis was completed using revman program 5.3.

**Results:** We identified 6 randomized control trials (median sample size = 130) of moderate to high quality. Surgical treatment is associated with overall success rates ranging from 88% to 100%. Inguinal approach was more effective in achieving testicular descent in comparison to the single scrotal incision approach (two trials, 569 participants), both after surgery (OR 4.43; 1.57 to 12.50 p= 0.005) as well as at follow-up (OR 3.77; 1.51 to 9.43 p = 0.004). Laparoscopic single stage orchiopexy was associated with decreased surgical time (mean difference -19.51; -19.71 to -19.31 p < 0.001) and hospital stay (mean difference -0.8; -1.13 to -0.47, p <0.001) compared to open primary orchiopexy.

**Conclusion:** There is a paucity of randomised trials comparing surgical techniques for undescended testes. Single incision scrotal orchiopexy appears to have suboptimal outcomes compared to inguinal orchiopexy. Laparoscopic and open techniques reported largely equivalent outcomes. This study highlights the need for more trials comparing long term outcomes.

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**A SYSTEMATIC REVIEW OF THE EMBRYOLOGY AND ANATOMY OF THE URACHUS: WHERE ARE THE CLINICALLY RELEVANT GAPS IN OUR KNOWLEDGE?**

Fidock EJ, Deshpande AV, Stringer MD

1. School of Medicine and Public Health, University of Newcastle
2. Paediatric Urology and Surgery, John Hunter Children’s Hospital
3. Paediatric Surgery, Christchurch Hospital

**Introduction:** Despite various manifestations, urachal anomalies tend to be regarded as a single entity in paediatric surgical literature. This may hinder accurate descriptions of urachal anomalies which could compromise optimum clinical management. We undertook a systematic review of the embryology and
anatomy of the urachus in order to highlight current gaps in our knowledge of potential clinical relevance.

**Methods:** An Ovid MEDLINE and PubMed search (1996 to September 2015) was conducted to identify original studies that focused on the embryology and anatomy of the urachus. This was supplemented by a hand search of reference lists and scientific texts. Data on the development and obliteration of the normal urachus and the mechanism of bladder descent were collated.

**Results:** Eight studies satisfied the criteria for inclusion in the systematic review (Fig 1). The urachus is derived from the ventral cloaca and is continual with the allantois; they act as a urinary conduit until urethral patency is established. The urachal lumen obliterates craniocaudally beginning from the 9th week of gestation and becomes completely obliterated by the 18th week. Subsequent descent of the bladder results in elongation of the urachus. No studies investigating the molecular triggers for descent of the bladder or closure of the urachus were identified. Urachal remnants are usually detectable at birth using ultrasound but in most infants are no longer visible after 3 months of age.

**Conclusion:** There are considerable gaps in our current knowledge about the triggers, processes and timing of urachal closure. Improved knowledge of these may facilitate the classification and the development of a more tailored approach to managing urachal anomalies.

**LOSS OF NORMAL ADIPOSE-DERIVED STEM CELL HETEROGENEITY IN DISEASE AND AGING- IMPLICATIONS FOR STEM CELL THERAPIES, AGING AND DISEASE.**

Findlay MW, Than PA, Davis C, Rennert RC, Sorkin MS, Januszky M, Lorenz HP, Rivas H, Morton JM, Gurtner GC

Division of Plastic and Reconstructive Surgery, Stanford University Department of Surgery, Stanford CA, USA and The University of Melbourne Department of Surgery Royal Melbourne Hospital, Parkville VIC 3052, Australia.

**Introduction:** Despite the immense potential of adipose-derived stem cells (ASCs), clinical application has been hampered by significant variability in the results. We sought to determine whether loss of normal stem cell heterogeneity occurs in conditions known to have abnormal stem cell responses (eg diabetes mellitus) and whether such changes could account for the variable results in ASC therapies to date.

**Methods:** Bariatric, post-bariatric and control adipose tissue samples were obtained from elective patients under appropriate institutional ethics approval across a broad range of age and comorbidities. Heterogeneity loss within the CD45-/CD31-/CD34+ cell population was assessed by studying 96 genes per cell, spanning a variety of stemness, differentiation, pro-angiogenic and surface marker profiles.

**Results:** 90 patients were enrolled in the study alongside a minimum of 5 animals per group, performed in duplicate. Heterogeneity loss was identified by the consistent depletion of a specific subpopulation of ASCs in diabetic individuals (both humans-70-fold reduction and animal models, p=0.0002). Similar depletions were seen with obesity (9-fold, p=0.0065), advanced age appeared to reduce resilience to subpopulation depletion and depletion trended towards worse long-term health outcomes.

**Conclusion:** A novel technique to test for ASC heterogeneity loss has been developed with significance for screening of patients prior to autologous stem cell therapies. Characterization of ASC subpopulations prior to therapy may be transformative to understanding variability and ensuring consistent success in ASC-based therapies.

**PERCUTANEOUS VS ENDOSCOPIC PRE-OPERATIVE BILIARY DRAINAGE IN HILAR CHOLANGIOCARCINOMA**

Hameed A, Pang T, Pleass H, Lam V, Hollands M, Johnston E, Richardson A, Yuen L

Department of Surgery, Westmead Hospital, Sydney

**Introduction:** Hilar cholangiocarcinoma (HCCA) is an uncommon malignancy of the proximal bile duct. The strategy for preoperative management of biliary obstruction in these patients is not clearly defined. The objective of this study was to compare the utility, complications and therapeutic efficacy of endoscopic (EBD) compared to percutaneous (PTBD) biliary drainage prior to surgical resection.

**Methods:** Study inclusion criteria consisted of articles with HCCA patients undergoing biliary drainage prior to curative resection. Articles were identified by a literature search of the EMBASE and Medline databases. Data was extracted/analysed by two independent reviewers, and included the type of biliary drainage, its complications and therapeutic efficacy, and post-operative morbidity and mortality by type of drainage.
Results: Fifteen studies were included, with a total of 1036 patients undergoing preoperative biliary drainage. EBD was undertaken in 52% of patients, and PTBD in 48% of patients. In both groups, unilateral drainage of the liver remnant was undertaken in 90% of cases. Twenty-four percent of EBD patients required conversion to another form of drainage, compared to 1% of PTBD patients. Of the EBD patients, 27% had procedure-related cholangitis, in contrast to 13% of PTBD patients. Close to 4% of PTBD patients however had cancer seeding of the drainage tract. Perioperative hepatic failure was 11% and 13% in the EBD and PTBD groups, respectively, with septic complications occurring in 14% and 17%.

Conclusion: Preoperative drainage of the liver remnant in jaundiced HCCA patients is the common practice. EBD appears to have higher rates of conversion to alternative drainage procedure(s) and cholangitis, which must be balanced with the avoidance of tumour seeding in EBD. Further prospective studies are required to clearly elucidate the best method.

UNCOMPROMICATED ACUTE DIVERTICULITIS: IDENTIFYING CANDIDATES FOR CONSERVATIVE MANAGEMENT (ORAL PRESENTATION)

Jaung R1, Robertson J1, Vather R1, Rowbotham D2, and Bissett I1,3
1Department of Surgery, The University of Auckland, New Zealand (R Jaung MBChB, J Robertson MBChB, R Vather MBChB, IP Bissett MD FRACS), 2Department of Gastroenterology & Hepatology, Auckland City Hospital, New Zealand (DS Rowbotham MD FRCP), 3Department of Surgery, The University of Auckland and Auckland City Hospital, New Zealand (IP Bissett MD FRACS)

Introduction: The management of uncomplicated acute diverticulitis (AD) has become increasingly conservative, with a focus on supportive management. Clear criteria for patient selection are imperative in order for these new approaches to be implemented safely. This retrospective study aimed to identify risk factors for severe clinical course in patients with CT-proven uncomplicated AD.

Methods: Patients admitted to General Surgery at Auckland District Health Board from January 2012 to June 2013 were included. Demographic, physical examination and laboratory data were recorded. Univariate and multivariate analyses were carried out in order to identify significant risk factors for having a more severe clinical course. Severe clinical course was measured by two end points, the need for procedural intervention, and admission ≥7 days.

Results: Mortality occurred in 2 of 240 patients. 204 patients (85%) had uncomplicated AD. Independent predictors for admission ≥7 days were patient-reported pain score >6 out of 10 (OR 16.11), and meeting the criteria for systemic inflammatory response syndrome (SIRS) at the time of admission (OR 12.54). SIRS was also an independent risk factor for requiring procedural intervention (OR 11.9).

Conclusion: Current management practices and demographic data for AD in a single Auckland centre were examined. Admission pain score >6 and SIRS were identified as predictors of worse outcome in uncomplicated AD. These findings have the potential to inform prospective treatment decisions in patients with AD.
compared to 23.8%) & (20.8% compared to 8.3%) respectively. While post-operative pain for bilateral and recurrent hernias was comparable across the two groups, male patients under the age of 55 with BMI <35 were more likely to be selected for TEP herniorrhaphy. There was no difference in recurrence rates between the two groups. Conclusion: Open herniorrhaphy is associated with less post-operative pain when compared to TEP hernia repair and are equivalent in post-operative pain for bilateral and recurrent hernias. Future research is necessary to determine the indication for TEP approach.

THE YIELD OF ADENOMAS AND COLORECTAL CANCERS FROM A SECOND COLONOSCOPY WITHIN 5 YEARS OF A NEGATIVE COLONOSCOPY: ARE THE GUIDELINES GUIDING?

Tee CL, Stephensen B, Foxcroft M, Sloss A, Grieve DA
Department of General Surgery, Nambour Hospital, Queensland

Introduction: Screening for colorectal cancers outside of the recommended guidelines presents a considerable burden to resource management in many public hospitals. The aim of this study is to evaluate the frequency, indications and outcomes for repeat colonoscopy that were performed within 5 years of a normal colonoscopy.

Methods: A retrospective review of all colonoscopies at Nambour Hospital in 2008 was performed to identify those with a negative colonoscopy. The charts of patients undergoing repeat colonoscopies at the same institution within 5 years of a negative colonoscopy were examined further, and data obtained regarding indications and outcomes of subsequent colonoscopies.

Results: A total of 616 colonoscopies were performed at Nambour Hospital in 2008. Of the 616 initial scopes, 427 (69.3%) were negative for adenoma and carcinoma. Of these, 74 (17.3%) underwent repeat colonoscopy at Nambour Hospital within five years. 1 (1.4%) cancer was detected, and 11 patients (14.9%) also had polyps detected at the repeat colonoscopy.

Conclusion: The yield of a second colonoscopy within five years of a good quality negative colonoscopy is low but not zero. In absence of new concerning symptoms or other risk factors, patients can be reassured and guidelines adhered to.

PREVALENCE, MANAGEMENT AND OUTCOMES OF ENTERAL TUBE FEEDING INTOLERANCE: A RETROSPECTIVE COHORT STUDY IN A TERTIARY CENTER.

Wang K, Windsor JA, Mciroy K, Plank L, Petrov MS.
1. HBP/Upper GI Unit, Auckland City Hospital
2. Nutrition Services, Auckland City Hospital
3. Department of Surgery, School of Medicine, University of Auckland

Introduction: Enteral tube feeding (ETF) is the most common form of artificial feeding in hospitalised patients. Failure to ETF is most commonly due to the development of intolerance (EFTI). In this study we aim to determine the prevalence of EFTI, the clinical consequences and the current management approach to EFTI in hospitalised adult patients.

Methods: Patients having ETF were identified from a prospective database in the Nutrition Services at Auckland City Hospital. Further information was obtained by the review of clinical records of adult patients for a 12 month period, up to December 2014. Data extracted included the medical specialties, ICU admission, the form of ETF, achievement of nutritional goal, the occurrence of FI, complications and subsequent management.

Results: The prevalence of ETFI was 33%. Patients with ETFI were less likely and took longer to achieve feeding goal rate (p<0.01). Univariate analysis showed significant difference in the ETFI occurrence with age, specialties, ICU admission, nutritional formula and acute mesenteric ischaemia (p<0.05). Multivariate analysis identified younger age, specific specialties, ICU admission and acute mesenteric ischaemia as independent predictors of ETFI (p<0.05). The management of ETFI was highly variable. Drug treatment was most common, while feeding protocol changes such as reducing infusion rate, stopping, changing the route of ETF and adding parenteral nutrition were also common.

Conclusion: ETFI is a frequent problem in adult patients having ETF and is associated with worse clinical outcomes. While the pathophysiology is poorly understood, there also appears to be no standard, evidence based treatment. Studies investigating the mechanisms and optimised management of ETFI are indicated.

CONTINUOUS LOCAL ANAESTHETIC WOUND INFUSION FOR MIDLINE LAPAROTOMY: A SYSTEMATIC REVIEW AND META-ANALYSIS

Ying A, Kakala B, Liang S, Affan E, Yeh ZYT
**Introduction:** Midline laparotomy carries more risk of post-operative pain than minimally invasive surgery. Unalleviated pain can increase respiratory complications and prolong length of stay. Opioid analgesics can control pain but carry unfavourable side effects. Continuous local anaesthetic wound infusions (CLAWI) are a promising addition to multimodal postoperative analgesic regimens.

**Methods:** Medline, Embase, CENTRAL and relevant reference lists were searched to March 2015. Abstracts were screened for placebo-controlled randomised trials of CLAWI after midline laparotomy in general surgery. Meta-analyses were performed using a random-effects model (RevMan 5, Cochrane).

**Results:** We screened 1876 results and identified five trials totalling 507 participants, all in the elective colorectal surgery setting. Compared with placebo, CLAWI did not significantly reduce 10-point visual analogue pain scores at rest on any of the first three postoperative days (all p>0.05). Opioid consumption was significantly reduced on day 1 (-11.24mg morphine equivalent, 95% CI -19.88 to -2.59) and day 2 (-11.97mg, 95% CI -21.39 to -2.55) and non-significantly reduced on day 3 (-5.73mg, 95% CI -12.72 to 1.26). This was reflected in reduction of some opioid related side effects, such as reduced time to stool (-0.69 days, 95% CI -1.19 to -0.20) and subsequent reduced length of stay (-1.14 day). Compared with placebo, continuous local anaesthetic wound infusion after midline laparotomy for colorectal surgery reduces post-operative opioid consumption and some related side effects.

**Conclusion:** Compared with placebo, continuous local anaesthetic wound infusion after midline laparotomy for colorectal surgery reduces post-operative opioid consumption and some related side effects.

**Prognostic Factors in the Management of the Open Abdomen:**

**A Systematic Review and Meta-analysis**

Cristaudo A1, Hitos K2, Jennings S3, Gunnarsson R4

1 PhD Student, Surgery, University of Sydney, Sydney Medical School, Camperdown, NSW, Australia
2 Senior Research Fellow, Surgery, Westmead Clinical School, Westmead, NSW, Australia

**Conclusion:** Prognostic factors in the categories for complications, resuscitative measures and clinical scoring systems all have a significantly greater effect on delaying definitive fascial closure than those in the interventions category. Future research should focus on the development of a prognostic model in regards to these outcomes.

**Head and Neck Cancer Patient Education and Support Needs - A Multi-Institutional Study**

Jabbour J1, Clark J2 Abdul-Razak M3, Ebrahim A4, Milross C5, Sundarsan P6, Dhillon H7, Roshan D8
1Head and Neck Surgery, Central Clinical School, Royal Prince Alfred, Camperdown, NSW, Australia.
2Head and Neck Surgery, Chris O’Brien Lifehouse, Camperdown, NSW, Australia.
3Head and Neck Surgery, The Crown Princess Mary Cancer Centre, Western Sydney Local Health District, Westmead, NSW, Australia.
4Head and Neck Surgery, Liverpool Hospital, Liverpool, NSW, Australia.
5Radiation Oncology, Chris O’Brien Lifehouse, Camperdown, NSW, Australia.
6Radiation Oncology, The Crown Princess Mary Cancer Centre, Western Sydney Local Health District, Westmead, NSW, Australia.
7Cancer Survivorship at the Centre for Medical Psychology and Evidence-based Decision-making (CeMPED), Central Clinical School, Camperdown, NSW, Australia.
8Head and Neck Surgery, Westmead Clinical School, Westmead, NSW, Australia.

Introduction: Head and neck cancer (HNC) encompasses a spectrum of malignant tumours and consequently providing appropriate and tailored education to patients prior to, during and following treatment is a major challenge.

Aims: 1) Characterize the experience of HNC patients regarding information and support provision; 2) identify key areas of unmet needs; 3) identify survivorship issues.

Methods: Methods: Patients who had received treatment for HNC at Royal Prince Alfred Hospital and Westmead Hospital were invited to complete a study designed questionnaire.

Results: Four hundred and sixty six patients completed the questionnaire. The average patient age was 60. The information received about the type of head and neck cancer and stage of cancer was quite substantial in 76% (352) and 67% (310) of patients respectively. Fifty two percent (244) received little or no information about coping with stress and anxiety. Over half (57%) reported being provided with minimal psychosexual health information after cancer diagnosis. Patients in 57% (165) of cases received little or no information about patient support groups for their partner and themselves. Most patients (77%, 358) reported preferring multiple formats of information delivery about their cancer.

Conclusion: HNC patients report preferences for multiple media formats as an adjunct to guide them through their diagnosis and management. Areas of survivorship that need supplementation are psychological well being, availability of patient support groups and psychosexual health. A website could cater this need for a readily accessible resource of HNC.

3D PRINTING- THE DEVELOPING FUTURE OF MEDICINE: A PUBLICATION TREND ANALYSIS
Chuen J, Kuchal T, Cole-Black J
Vascular Surgery, Austin Health

Introduction: 3D printing in medicine remains in its infancy but will likely grow into an enormously beneficial technology. With this comes an apparent exponential growth in research pertaining to its medical applications. The purpose of this study is to identify current publication output, research areas and characterize the field of 3D printing in medicine through a publication trend analysis.

Methods: A literature search of 3D printing citations indexed in Medline and Pubmed was performed and analyzed to establish publication trends, journal frequency and predominance of clinically related versus non-clinical research.

Results: The search returned 610 papers, of which 356 were deemed suitable for this analysis. In 2005 and 2014 there were 2 and 127 articles published respectively. This indicates a 625% growth in annual citations over 10 years. The greatest growth has been since 2012 (14 articles), roughly tripling both in 2013 (44) and 2014 (127). To date there have been 122 articles in 2015. 108 (30% of) publications were in Regenerative Medicine, followed by Maxillofacial Surgery (10%) and Orthopaedic Surgery (5%). 24 papers were related to non-clinical uses of 3D printing, 146 related to clinical uses (surgical planning, prosthesis development etc) while the majority (163) were in bioengineering.

Conclusion: 3D printing is a developing application in medicine. From its first publication in 1998 through to 2012 there has been a steady presence of 3D printing in medical literature. Since then there has been an exponential growth in the rate of research output, with publication numbers for 2015 already rivaling 2014, this is projected to continue.

RUNNING BARBED SUTURE QUILTING REDUCES ABDOMINAL DRAINAGE IN PERFORATOR – BASED BREAST RECONSTRUCTION
Liang DG¹, Dusseldorp JR¹, Van Schalkwyk C¹, Hariswamy S², Wood S³, Rose V³, Moradi P².
1. Department of Plastic and Reconstructive Surgery
Concord Hospital, Hospital Rd, Concord, Sydney Australia
2. Department of Plastic and Reconstructive Surgery
Westmead Hospital, Darcy Rd, Westmead, Sydney, Australia
3. Department of Plastic and Reconstructive Surgery
Charing Cross Imperial National Health Service (NHS), London, UK
4. Department of Plastic and Reconstructive Surgery
Prince of Wales Hospital, Barker St, Sydney, Australia

Introduction: Prolonged abdominal drainage after perforator-based breast reconstruction is a common problem that can result in seroma formation, patient morbidity and increased duration of hospital stay. Abdominal quilting with progressive tension sutures has been effective in reducing abdominal drainage in abdominoplasty patients, which we have adopted and studied in the abdominal closure of deep inferior epigastric artery perforator (DIEP) flap breast reconstruction.

Methods: We studied consecutive unilateral mastectomy patients undergoing breast reconstruction with a DIEP flap. The initial 27 cases underwent breast reconstruction without any form of abdominal plication. The subsequent 26 cases underwent an identical DIEP flap raise procedure after which the abdominal flap was progressively tensioned using a running barbed suture quilting technique. All patients had closed suction drains inserted bilaterally until daily drain outputs was less than 40mL in two consecutive days. Independent statistical analysis was performed using Welch’s t-test.

Results: A statistically significant decrease in the mean total abdominal drainage was found after quilting (238mL vs 526mL; p=0.0005). Patients in the quilting group also showed a reduction in mean duration of hospital stay.

Conclusion: Quilting of the abdominal flap not only helps to reduce abdominal drainage in abdominoplasty patients but also in patients undergoing breast reconstruction with DIEP flap.

HbA1c AS A PREDICTOR OF OUTCOME IN LOWER LIMB AMPUTATION
Penna A, Cranwell WC, Bruscino-Raiola F, Topliss D

Introduction: Dysvascularity secondary to Diabetes Mellitus is the most common indication for lower limb amputation. Glycated haemoglobin (HbA1c) is a routine clinical tool used to monitor glycaemic control in diabetic patients. Evolving evidence suggests a correlation between HbA1c and surgical outcomes. Despite its routine measurement in diabetic patients undergoing lower limb amputation, its role as a predictive tool has not previously been investigated. We are seeking to disprove the null hypothesis that HbA1c levels are not related to post-operative outcomes in diabetic patients undergoing amputation.

Methods: In this retrospective study we reviewed the records of 304 consecutive patients undergoing lower limb amputation at the Alfred hospital between January 2002 and March 2010. Of these 110 had a pre-existing diagnosis of Diabetes Mellitus (Type 1 or 2) and had a diabetes related amputation (dysvascularity/infection). HbA1c levels were recorded if taken two months prior to, or three months after surgery. Demographics, comorbidities, length of stay and complications were recorded from patient admission records. Mortality was also recorded at 60 days, 1 year and 5 years through Alfred hospital records. We stratified our cohort according to HbA1c < 7%, 7-8.5% and > 8.5%, recognising a HbA1C of 8.5% as the calculated equivalent level of cell of damage secondary to hyperglycaemia.

Results: Of our consecutive cohort of 110 patients, 93 had documented HbA1C levels within the specified range. Of these 93 patients we currently have 5 year mortality data for 60 patients, with 33 lost to follow-up prior to 5 year review. Patients with HbA1C <7(n=22) had 60 day, 1 year and five year mortality rates of 9%,36%,77%. This compares to rates of 17%,43% , 52% and 36%, 57%, 64% for the 7-8.5%(n=23) and >8.5%(n=14) groups respectively. We are in the process of contacting General Practitioners to achieve full 5 year mortality follow-up on our cohort. We anticipate full findings will be available by November.

Conclusion: Our preliminary findings suggest that the HbA1c measurement may have a predictive role in estimating early mortality for diabetic patients undergoing lower limb amputation.

UTILITY OF DELAYED FLEXION-EXTENSION X-RAYS FOR CLEARANCE OF THE CERVICAL SPINE FOLLOWING TRAUMA
Miranda RM, Rogers J, Devadas M, Hsu J

Introduction: Flexion- extension films have been included in the trauma protocol for clearance of the cervical spine to detect ligamentous injury. We sought to evaluate the
effectiveness of our current protocol, where delayed (two weeks), active flexion-extension x-rays are performed in those trauma patients who are neurologically intact, with a negative CT cervical spine (CS) scan, but persistent neck pain.

Methods: A retrospective study was carried out at a Level I Trauma Centre utilising the prospectively maintained trauma registry. All neurologically intact blunt trauma patients between 2013-2015, with a negative CT scan of the CS and persisting midline tenderness were included in this study. Demographic data was obtained. Primary outcomes were identified as the compliance rate with followup and identification of any CS injury on the flexion-extension x-ray.

Results: 72 patients were identified. The mean age was 52 years and over 55 % were male. No cervical injuries were identified on active flexion-extension films. No spinal cord injuries were identified. Compliance with the protocol was found to be poor with 52% of patients not attending followup. There was no corresponding readmission in these poor compliance patients for missed spinal injury

Conclusion: On initial examination, the protocol utilising delayed, active flexion-extension x-rays is extremely sensitive (100%), however it is likely that this component is unnecessary, given that there were no false negative CT scans. Clearance of the c-spine may be achieved with CT alone in this cohort of patients.

HYPERBILIRUBINAEMIA- ITS UTILITY IN NON-PERFORATED APPENDICITIS.

Sandstrom A, Grieve D
Department of General Surgery
Nambour Hospital

Introduction: Recent studies have suggested that serum bilirubin is a positive predictor in the diagnosis of appendiceal perforation and may be more specific than C- reactive protein (CRP) and white cell count (WCC). The aim of this study was to investigate the utility of the serum bilirubin level in patients with suspected acute but non- perforative appendicitis.

Methods: A retrospective chart review of 213 patients who presented with suspected appendicitis in a six month period to Nambour Hospital was performed. Serum bilirubin, WCC and CRP were recorded and analysed as to their utility in relation to the final diagnosis.

Results: 196 patients underwent an appendicectomy and 21% of these were negative. The specificity of hyperbilirubinaemia for appendicitis overall was 0.83 with a positive predictive value (PPV) of 0.86, compared with CRP (specificity 0.40, PPV 0.75) and WCC (specificity 0.67, PPV 0.85). The area under the ROC curve for bilirubin was 0.6289 compared to 0.6171 for CRP and 0.7219 for WCC. A subgroup analysis of those with complicated appendicitis demonstrated a PPV for bilirubin of 0.66 compared to 0.58 for WCC and 0.34 for CRP in agreement with the literature. Subgroup analysis of hyperbilirubinaemia in simple appendicitis demonstrated a PPV of 0.81 compared to CRP (0.71) and WCC (0.85).

Conclusion: Bilirubin had a higher specificity than CRP and WCC overall in patients with appendicitis. This study adds to the literature by demonstrating a high PPV for hyperbilirubinaemia in patients with simple appendicitis.

EVALUATION OF THE USE OF ELECTROCAUTERY VS HARMONIC FOCUS IN SEROMA FORMATION AFTER AXILLARY LYMPH NODE DISSECTION.

Selvendran S*, Segara D, Soon P
Breast and Endocrine Surgery, Bankstown hospital, NSW, Australia

Introduction: Seroma formation in patients who have undergone axillary lymph node dissection (ALND) may be a source of significant discomfort and morbidity in breast cancer patients. The aim of this study is to compare its incidence when Harmonic Focus (HF) or conventional diathermy (CD) is used for ALND.

Methods: This is a single institution retrospective study carried out in Bankstown Hospital over a 6 year period. The patients were categorised into HF and CD groups and were evaluated for volume of seroma formation, hospital stay and complications.

Results: Out of a total of 94 patients, 42 were in the HF and 52 in the CD groups, respectively. No statistical differences were identified in patient demographics. Two day median seroma volume for HF was 205 ml (IQR 95-265) and for CD was 227.5 ml (IQR 149-385). The total seroma output for HF was 270 ml (IQR 160-478) and CD was 385 ml (IQR 220-558). These results were not statistically significant. The operative time and complication rates between the groups were also not significant.

Conclusion: The use of Harmonic Focus in this study did not significantly reduce the seroma volume output in patients who were undergoing axillary dissection for breast cancer. There was also no difference in operative time or complication rate.
NON-INVASIVE STROKE VOLUME INDEX MONITORING IN SURGICAL PATIENTS ON THE WARD – A FEASIBILITY STUDY

Abdullah M, Gillespie C, Brockman S
General Surgery - QEII Jubilee Hospital, Brisbane, QLD

**Introduction:** Patients recovering from major abdominal surgery can have complex fluid shifts and require accurate assessment of fluid status and appropriate intravenous fluid prescription. It is well recognized that this is done poorly and most often by junior members of the surgical team. Variation in stroke volume with respiration has been shown to reflect fluid responsiveness and new technology allows this to be done on ward-based patients using non-invasive equipment. We hypothesized that this technology may assist with fluid management on surgical patients recovering from major abdominal surgery on the ward. This study aims to assess the feasibility of using noninvasive assessment of fluid responsiveness on the surgical ward by junior doctors.

**Methods:** Clearsight technology uses stroke volume variation to calculate a stroke volume index (SVI). A straight leg raise is used to simulate a fluid bolus and the response determines the patient’s fluid responsiveness. We used one investigator to record details and assess the hemodynamic status of 20 patients. The time taken for the assessment and correlation with clinical assessment of fluid responsiveness were recorded.

**Results:** The average time taken for noninvasive SVI assessment of fluid-responsiveness was 4.85 minutes (range 3-10mins). In fourteen of the twenty patients, the SVI conclusion in terms of fluid responsiveness was consistent with the clinical impression, in the remaining six patients it was not.

**Conclusion:** Non-invasive assessment of SVI and fluid-responsiveness can be performed on surgical patients in a ward-based setting by junior doctors. However the time taken to use this technology may limit its use in high-risk patients. A larger study is required to find the best role for this technology and for assessment of its reliability. It may have a promising role as an adjunct in fluid management for difficult patients.

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Cheng A, Bookun HR, Lee CS, Zhang XB
Department of Cardiothoracic Surgery and Cardiology Research Unit
University Hospital Geelong – Barwon Health, Victoria

**Introduction:** Postoperative Atrial Fibrillation (POAF) is the commonest complication of cardiac surgery with an incidence on up to 50%. POAF leads to an increase in adverse outcomes, resulting in higher resource utilisation. Although the exact mechanism is unknown, evidence supports the role of inflammation as a key contributor of POAF. White cell count (WCC) is often used as a surrogate marker of the cellular inflammatory response. The objective was to determine if an increased WCC is associated with POAF.

**Methods:** From January 2008 to September 2014, 2657 patients underwent cardiac surgery at University Hospital Geelong. Preoperative history of AF was noted in 240 patients, who were excluded from analysis. All patients had postoperative blood test results recorded for up to 7 days; means for each parameter were calculated and used for analysis. Descriptive statistics were used to characterize the sample with regards to demographic and perioperative variables. A logistic regression model was used to investigate the impact of postoperative WCC on the incidence POAF.

**Results:** Overall incidence of POAF was 32.9% (n=795). Patients who developed POAF were generally older (Age: 70 vs. 66, p<0.001) and had poorer preoperative renal function (eGFR: 83 vs. 75, p<0.001; Creatinine: 102 vs. 96, p<0.001). On postoperative blood tests, patients with POAF had lower: Haemoglobin (99.42 vs 101.68, p<0.001); Platelet count (187.09 vs 193.87, p=0.013); eGFR: 56.75 vs. 60.60, p<0.001; and Creatinine: 108.60 vs. 101.68, p=0.013); eGFR: 83 vs. 75, p<0.001); and Creatinine: 102 vs. 96, p<0.001). However, elevated WCC (10.43 vs. 10.10 p=0.009), Neutrophils (7.88 vs. 7.59 p=0.003), and Monocytes (0.86 vs. 0.81 p<0.001) were noted in patients with POAF. The logistic regression model showed an increase in odds of POAF by a factor of 1.038 for every 1x10^9 increase in WCC (β= 0.038, p=0.01).

**Conclusion:** Cardiac surgery is associated with a raised WCC postoperative; however, a more pronounced elevation in WCC is an independent predictor of POAF. This provides additional evidence to support the association between POAF and inflammation.

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ELEVATED POSTOPERATIVE WHITE BLOOD CELL COUNT IS AN INDEPENDENT PREDICTOR OF POSTOPERATIVE ATRIAL FIBRILLATION

**MOLECULAR BIOMARKERS FOR PREDICTING RESPONSE TO**
PREOPERATIVE CHEMO-Radiation in Patients with Locally Advanced Rectal Cancer.
De Lacavalerie PA(1,2,3), Lord SJ(4,5), Williams JF(6), Asghari R(7), Morgan MJ(2) And Kohonen-Corish M(1,8)
1 Cancer Research Division – Colon and Lung Cancer research group, The Kinghorn Cancer Centre / Garvan Institute of Medical Research, Darlinghurst, Australia. 2 Department of Surgery, Bankstown Hospital, Australia. 3 Southwest Sydney Clinical school, UNSW Medicine, UNSW Australia. 4 School of Medicine, University of Notre Dame, Darlinghurst, Australia. 5 NHMRC Clinical Trials Centre, The University of Sydney, Camperdown, Australia. 6 Library, UNSW Australia. 7 Department of Oncology, Bankstown Hospital, Australia. 8 St. Vincent's Clinical School, UNSW Medicine, UNSW Australia.

Introduction: Patients with locally advanced rectal cancer (LARC) are treated with total mesorectal excision, preceded by neoadjuvant chemoradiotherapy (nCRT). The molecular basis of patient variability in response is unknown and no routine medical test is currently available to determine who is likely to benefit from nCRT.

Methods: A Cochrane diagnostic test accuracy review to assess the literature on predictive biomarkers of response to nCRT in pre-operative biopsies before further treatment is advised. Eligible study designs include: randomised controlled trials, single arm trials, prospective cohort studies and consecutive case series that report prospective specimen collection for biomarker analysis from a clinically well-defined population and report tumour response based on pathological tumour regression grade (TRG). The molecular basis of patient variability in response is unknown and no routine medical test is currently available to determine who is likely to benefit from nCRT.

Results: This is the protocol for a review. The objectives are as follows:

1. To assess the accuracy of molecular biomarkers to predict complete pathological response versus no or partial response to preoperative nCRT in patients with LARC.
2. To compare the predictive performance of different biomarkers.
3. To assess the impact of different biomarker cut-off points, assay techniques, chemotherapy/ radiotherapy regimes and study quality on the predictive accuracy of the biomarker.

Conclusion: Early identification of the 25% of pts who do not respond to nCRT will be valuable to avoid delaying appropriate surgery in patients who will not benefit from nCRT. Moreover, the early identification of the 20% of pts who will show a complete pathological response may provide valuable information to help individualize decisions about nCRT agents.

UTILITY OF SMARTPHONE APP IN THE MANAGEMENT OF ACUTE RIGHT ILIAC FOSSA PAIN
Jenkins L 1, Amaratunga R 1, Fok KY 1, Chan S 1, Pang T 1,2, Lam V 1,2
1. Department of Surgery, Westmead Hospital
2. Discipline of Surgery, Sydney Medical School

Introduction: There is historically significant variability of the management of patients presenting to Emergency with right iliac fossa pain. We developed a protocol based smartphone application (ASU App) for acute general surgical conditions which aimed to standardise the care of these patients. This study aimed to assess its impact on the initial assessment, investigations and management of these patients.

Methods: Data was collected retrospectively over two 6-week periods, the first prior to the introduction of the ASU App and the second after the introduction of the App. Compliance to the management algorithms outlined in the App was evaluated for each patient. Outcomes for the two groups were compared with the primary outcomes assessed being the rate of acute appendicitis on histopathology and length of hospital stay.

Results: Data was collected for a total of 90 patients over two six-week periods. Compliance with the ASU App protocol was 61% in the post-App group. The rate of patients being discharged home from Emergency was similar between the Pre- and Post-App groups (22% vs 15%). The length of hospital stay was significantly lower in the post-APP group when compared to the pre-App group (1.9 days vs 2.5 days). The negative appendicectomy rate was also significantly lower in the post-App group compared to the pre-App group (17% vs 29%). There was no significant difference in the complication rate between the two groups.

Conclusion: The use of smartphone based App may improve the standardisation of management of patients presenting to Emergency with right iliac fossa pain. This reduced variation resulted in improvement in the overall negative appendicectomy rate and also reduced hospital length of stay.
LAPAROSCOPIC CHOLECYSTOSTOMY AS AN ALTERNATIVE TO OPEN CHOLECYSTECTOMY AND PERCUTANEOUS CHOLECYSTOSTOMY IN A RURAL SETTING

Han SP, Nq KS, Grassby J
DEPARTMENT OF SURGERY, DUBBO BASE HOSPITAL

Introduction: Emergency cholecystectomy in critically ill patients carries a high risk of morbidity and mortality. Laparoscopic cholecystostomy (LC) can be used as a temporising measure in those patients where cholecystectomy is deemed technically difficult for safe removal, or in those patients who present to a hospital without interventional radiology services, such as in many rural settings.

Methods: A retrospective review was undertaken of consecutive patients who underwent LC at Dubbo Base Hospital over a five-year period (2011-2015). In each case, LC was performed by placing a 5mm port in the right subcostal margin, which was later upgraded to a 10mm port. The gallbladder was then decompressed with a 10mm trocar and a 20Fr Foley catheter (held by its balloon and an anchoring suture) was placed in the gallbladder body and used as a cholecystostomy tube.

Results: Ten patients underwent LC. (Male=5, median age= 67 and range= 43-88) The main indication was severe acute cholecystitis, not amenable to laparoscopic cholecystectomy. One of the patients has significant morbidity (ASA 4) and had laparoscopic cholecystostomy as he was not responding to antibiotics and there was no interventional radiologist in the hospital. Seven patients had interval laparoscopic cholecystectomy in six months time and there was no complication during or after the procedure. Mean length of stay is five days. There are two patients readmitted to the hospital within thirty days with sub capsular collection around the right lobe of liver and postural hypotension.

Conclusion: It appears that the data suggest that laparoscopic cholecystostomy is a viable alternative to open cholecystectomy in technically difficult cases and alternative to percutaneous cholecystostomy in rural hospitals without interventional radiology services.

AN ENDOSCOPIC LOOK INTO PILONIDAL SINUS TREATMENT – EPSIT

Abdullah M, Grundy J, Naidu S
Department of General Surgery and Endoscopy, Queen Elizabeth II Jubilee Hospital, Brisbane, QLD 4108

Introduction: Pilonidal disease is a common condition that despite a multitude of operative interventions often still has a poor outcome. The new technique of Endoscopic Pilonidal Surgery (EpSIT) allows for faster recovery time and minimises pain whilst maximising patient satisfaction. The objective of our study was to evaluate the outcomes of EpSIT in our institution and compare them to the published literature.

Methods: Data was retrospectively collected from the medical records of those who underwent an EpSIT procedure at a single institution between January 2014 to March 2015. Data collected related to patient demographics, inpatient progress and post op follow up.

Results: A total of 21 patients were identified, 19 males and 2 females. The mean age was 26 (17-58). There were no operative complications. Immediate post op pain was minimal. and all patients were discharged the same day or day 1. There were 3 recurrences (14%). Follow up was over 12 months and mean time to resolution was 3 months (1-10months).

Conclusion: This study demonstrates EpSIT to be a simple and effective procedure for managing both simple and complex pilonidal disease. The key features of the E.P.Si.T technique being direct vision, allowing good definition of the involved area, removal of debris and hair and debridement of granulation tissue. EpSIT provides definitive management of the condition and by reducing the post-operative morbidity normally associated with conventional procedures, patients have reduced hospital stays, minimal pain and rapid return to normal activities.

THE RETROGRADE CONTINENCE ENEMA IN CHILDREN WITH SPINA BIFIDA: NOT AS EFFECTIVE AS FIRST THOUGHT

King SK (1, 2, 3), Stathopoulos L (2), Pinuck L (4), Wells J (5), Hutson J (2, 3, 6) and Heloury Y (6)

(1) Department of Paediatric and Neonatal Surgery, The Royal Children’s Hospital, Melbourne, Victoria, Australia
(2) Surgical Research Laboratory, Murdoch Childrens Research Institute, Melbourne, Victoria, Australia
(3) Department of Paediatrics, University of Melbourne, Victoria, Australia
Introduction: Faecal incontinence affects the majority of children with spina bifida. We aimed to investigate the effectiveness of Peristeen retrograde continence enema (RCE) in the management of faecal incontinence in children with spina bifida.

Methods: We identified an homogenous group of spina bifida patients in whom RCE was initiated (01/2006 – 07/2013). Confidential assessments included: (1) Fecal Incontinence Quality Of Life (FIQOL), (2) St Marks Faecal Incontinence score, (3) Cleveland Clinic Constipation score, and, (4) Neurogenic Bowel Dysfunction score.

Results: 11/20 patients (mean age 14.5 ± 5.3 years) were male. 9/20 patients were still using RCE (mean follow-up 4.1 years). Three patients ceased RCE within ten days, six after 4-12 months, and two after 36-48 months. Reasons for cessation: balloon difficulties (n = 4); procedure too difficult (n = 4); and; pain (n = 3).

There were no differences between the groups in length of training time for technique, instillate fluid/volume used, and time taken to perform RCE. There were no differences between the groups for quality of life, faecal incontinence or constipation scores.

Conclusion: We demonstrated a high rate of cessation with the RCE in patients with spina bifida. This could not be explained by associated conditions, or by enema-related parameters. One possible explanation is the lack of on-going outpatient support for the children and their families.