INHIBITION OF THE MEK/ERK PATHWAY IN GLOBLASTOMA MULTIFORME CANCER STEM CELLS WITH U0126 INHIBITS PROLIFERATION AND MIGRATION

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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 GSCs. 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. 10μM of U0126, a highly selective, non-competitive MEK1/2 inhibitor was then applied to cells for a 96-h duration and the effects quantified.

Results: Under normal culture conditions, GSCs continue to proliferate and migrate out from their spheres. However, when 10μM 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 GSCs 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

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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: −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

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Introduction: Cerebral arteriovenous malformations (AVMs) are congenital vascular abnormalities associated with significant mortality and morbidity. Conventional treatment paradigms insufficiently address large deeply seeded 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-Gy 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 a peak time point (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.

THE LONG NONCODING RNA – PRINS AS A NOVEL TUMOUR SUPPRESSOR IN ADRENOCORTICAL CARCINOMA

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Introduction: Adrenocortical carcinoma (ACC) has high recurrence rates and poor outcomes. We have shown expression of PRINS, a long noncoding RNA (lncRNA) can predict ACC recurrence. In psoriasis, PRINS has a positive functional role with TP53. TP53 mutation is a major driver of ACC. We sought to establish a biological basis for PRINS as a predictor of ACC outcomes by investigating a tumour suppressor RNA action.

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

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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

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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 in adhesion formation in animal models by modulating the peritoneal fibrinolytic pathway. This randomised clinical trial investigated the effect of oral simvastatin in prevention of adhesions after colorectal surgery.

Methods: 144 patients undergoing elective colorectal resection for any indication, or reversal of Hartmann’s procedure, or reversal of Hartmann’s procedure, were randomised to receive either 40 mg 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 and analysed for active tissue plasminogen activator (tPA), and PAI-1 levels were higher in the placebo group (P > 0.05). Total tPA levels were lower in the statin group compared to the placebo group (P > 0.05). Total PAI-1 levels were higher in the placebo group. Total PAI-1 levels were higher in the statin group (P > 0.05). Total tPA/PAI-1 complex levels were higher in the placebo group.

Conclusion: Oral simvastatin has minimal effect on the intraperitoneal fibrinolytic pathway in the first 24 hours following major colorectal surgery. Further studies are needed to evaluate whether fibrinolytic pathways beyond 24 hours are altered following systemic administration of statins, and to evaluate long-term clinical sequelae such as infertility and adhesive small bowel obstruction.

DEEP BRAIN STIMULATION TARGETING THE ZONA INCERTA MODULATES EYE MOVEMENTS IN HUMANS

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Introduction: The posterior subthalamic area (PSA) is considered to be a critical target region for deep brain stimulation (DBS) in the treatment of Parkinson’s disease (PD) and essential tremor (ET). The objective of the current study was to test the hypothesis that PSA DBS affects saccadic eye movements in humans.

Methods: Sixteen patients 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 recorded using a direct-current electro-oculography (EOG) in the medicated state pre and post-operatively on a horizontal predictive task sub-tending 30°. Post-operative assessments consisted of stimulation-off constituting a microlesion (ML) condition and high frequency stimulation (HFS: frequency = 130 Hz) up to 3 volts. REX/MARK software allowed for analysis of saccade amplitude, peak velocity, 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% (95% CI 8.6–12.2) and 12.6% (95% CI 10.0–15.9) in the PD and ET groups respectively. With HFS peak velocity was reduced by 14.7% (95% CI 11.7–17.6) in the PD and 27.7% (95% CI 23.7–31.7) in the ET group. HFS leads to PD patients performing 21% (95% CI 16–26) and ET patients 31% (95% CI 19–38) more saccadic steps to reach the target.

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 in the GABAergic inhibitory pathway, it is likely that PSA DBS 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 INTRA-MUSCULAR BRANCING PATTERNS

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Introduction: The medial sural artery perforator (MSAP) flap is a versatile fasciocutaneous flap. The main difficulty encountered when raising the MSAP flap in obtaining adequate pedicle length during intra-muscular dissection. The objective of this study was to determine the pattern of intra-muscular 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 13 cm.
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(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 cI/R 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.

PREOPERATIVE CARBOHYDRATES FOR ENHANCING RECOVERY AFTER ELECTIVE SURGERY: A MULTIPLE-TREATMENTS META-ANALYSIS

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Introduction: Preoperative carbohydrate administration, a component of many ERAS protocols, has been widely investigated, with trials reporting mixed findings. Intervention and control group heterogeneity between these trials add to the uncertainty in assessing the benefits of this intervention. Multiple-treatments (network) meta-analysis allows for robust synthesis of available evidence in these situations.

Methods: We systematically searched article databases for RCTs comparing preoperative carbohydrate treatment (administered within 4 hours before elective surgery) with water, a placebo drink or fasting. Primary outcomes were length of hospital stay and complication rate. Secondary outcomes included postoperative vomiting, fatigue and well-being. We performed a multiple-treatments meta-analysis to account for the different carbohydrate doses and control treatments used in the trials.

Results: We included 34 trials, involving 2541 participants. Most trials were of low to moderate methodological quality. Compared to fasting, preoperative low dose (10–44 g) and high dose (45 g or greater) carbohydrate administration decreased length of stay by 0.6 days (95% confidence interval (CI) 0.1–1) and 0.3 days (95% CI 0.1–0.5) respectively. Compared to water or a placebo drink, there was no significant decrease in length of stay for the carbohydrate groups. Preoperative carbohydrate administration did not affect the postoperative complication rate, or result in a significant difference in any of the secondary outcomes.

Conclusion: The administration of low or high dose carbohydrates before elective surgery confers a minor reduction in length of stay when compared to fasting, and no significant reduction when compared to water or a placebo drink. It does not otherwise significantly affect postoperative outcomes.

DIFFERENCES IN COLONIC TRANSIT FOLLOWING ANTERIOR RESECTION: A STUDY USING NOVEL 3D SINGLE-PHOTON EMISSION COMPUTED TOMOGRAPHY (3DSPECT) SCINTIGRAPHY

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Introduction: Bowel dysfunction following anterior resection (AR) is well-documented, but its pathophysiology remains poorly understood. To date, no studies have assessed whether post-operative variation in colonic transit contributes to symptoms. Therefore, this study aimed to (i) measure colonic transit using a novel technique 3D-SPECT and (ii) compare transit parameters with clinical symptoms in AR patients.
Methods: Biplanar and SPECT scintigraphy were performed on randomly-selected AR patients. Dysfunction was assessed using the "LARS score". After Ga-67 ingestion, scintigraphy was performed at pre-defined timepoints. SPECT images defined 9 ‘regions of interest’ to allow the following measurements: (i) geometric centre (GC); (ii) percent isotope retained (%-retained); (iii) GC ‘velocity’; (iv) colonic half-clearance time (T1/2). Transit parameters were correlated to patient symptoms using ROC curve analyses.

Results: 50 patients (37M, 72[SD9] yrs) were studied, 17 had ‘major LARS’, 9 had ‘minor LARS’, and 24 had ‘no LARS’. Compared to ‘no LARS’, ‘major LARS’ patients had significantly different transit profiles: (i) GCs at 32hrs were greater (median 5.94 [range 2.35–7.72] vs. 4.30 [2.12–6.47], P = 0.015); (ii) ‘%-retained’ at 32h was less (median 53.8% [SEM5.6] vs. 89.9 [3.4], P = 0.002); (iii) GC velocities were greater (1.70 [1.18–1.92] vs. 1.45 [0.98–1.80], P = 0.013); (iv) T1/2s were shorter (38.3h [17.0–65.0] vs. 57.0 [32.1–160], P = 0.003). ‘%-retained’ at 32h best discriminated ‘major-LARS’ from ‘no-LARS’ (AUC 0.828). No differences in transit were observed between patients with ‘minor-LARS’ and ‘no-LARS’.

Conclusion: Colonic transit varies amongst patients following AR, being significantly accelerated in patients with ‘major’ but not ‘minor LARS’. Accordingly, objective alteration in colonic transit may be important in the development of postoperative bowel dysfunction in those with the most severe symptoms and its pathophysiology requires further evaluation.

VALIDATION OF A NOVEL TECHNIQUE TO ENSURE COMPLETE FLAP SURVIVAL IN PERFORATOR FLAP-BASED BREAST RECONSTRUCTION

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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

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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

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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 pre-natal 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 22.6–78.3%). 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 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 SCIA TIC NERVE DURING THE POSTERIOR APPROACH TO THE HIP

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

AB Latlonof Hepatic N eoplasm s using Irreversible Electroporation: A Systematic Review of the Literature

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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 were 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 carcinomas (75%), followed by metastatic adenocarcinoma (16%), and mesenchymal tumours (4%). The majority were treated using a single 30-s electric pulse with 1440 J/mm², 71% of patients achieved complete response.

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.

Tissue Engineering Vascularised Human Liver

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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 (5 mm diameter, 0.8 mm thickness). In vitro organoids were analysed at days 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

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Introduction: Designing a bioartificial actuator system for severe neuromuscular injuries requires consideration of 3 key issues: (1) reinervating 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
DESIGNER DOCTORS? HOW ‘DESIGN THINKING’ ASSISTS IN DEVELOPING TARGETED PREVOCATIONAL SURGICAL EDUCATION PROGRAMS

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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 needs-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

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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 and 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. Descriptive statistics were used to characterize the sample with regard 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)

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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

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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, biliary 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 4.34, p = 0.36) 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

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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 and 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

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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 – 0.68, P = 0.048) with each increase in dosage, a small increase in incontinence rate (1.02 times, 95% CI 1.002 – 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 = 0.0002) 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.

GENERATING LEVEL I EVIDENCE FOR SURGICAL TREATMENT OF UNDESCENDED TESTES

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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 reym 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 85% to 100%. Inginal 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; −9.71 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.

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

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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 cranio-caudally 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.
OPEN HERNIORRHAPHY LEADS TO REDUCED POST OPERATIVE PAIN COMPARED TO TOTAL EXTRAPERITONEAL REPAIR: FACTORS INFLUENCING OPERATIVE DECISIONS

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Introduction: Totally extraperitoneal laparoscopic herniorrhaphy (TEP) has not shown to be superior to open repairs in areas such as recurrence, chronic pain and intra-operative complications. The purpose of this study was to determine the post-operative pain levels of patients who underwent TEP and open herniorrhaphy.

Methods: We conducted a retrospective analysis of all patients who underwent herniorrhaphy between November 2013 and November 2014 at Dandenong Hospital. Patients were identified through a prospectively maintained database. All patients were contacted to complete a questionnaire tool aimed at evaluating post-operative pain and overall satisfaction levels. This study was approved by the Monash Health Ethics Committee.

Results: A total of 132 patients were included, 84 open and 48 TEP hernia repairs. Open herniorrhaphy was associated with less post-operative pain (p = 0.0085) and less post-operative pain at 6–12 months (p = 0.004). TEP herniorrhaphy was more likely to be chosen for bilateral and recurrent hernias (43.6% compared to 23.8%) and (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?

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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 with five years of a good colonoscopy was low but not zero. In absence of new concerning symptoms or other risk factors, patients can be reassured and guidelines adhered to.

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

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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 (−11.24 mg morphine equivalent, 95% CI −19.88 to −2.59) and day 2 (−11.97 mg, 95% CI −21.39 to −2.55) and non-significantly reduced on day 3 (−5.73 mg, 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).

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

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Introduction: The open abdomen (OA) is an important approach for managing catastrophes and continues to be the standard of care. Despite this, challenges remain and the technique is still correlated with high complications and poor outcomes. Our aim was to identify prognostic factors related to complications and mortality and compare their categories against interventions associated with OA management.

Methods: A systematic review and meta-analysis was performed. All studies that described prognostic factors in regards to fascial closure, complications, and/or mortality in the management of the OA were eligible for inclusion. Data collected were synthesised per category of prognostic factor and then analysed using a meta-analysis to compare the categorised prognostic factors against interventions that occurred during OA management.

Results: The search identified 30 articles that were included in the final synthesis and 22 articles were subsequently included in the meta-analysis. Prognostic factors in categories for complications (mean difference (MD): 2.7, 95% CI: 2.3–3.0, P < 0.0001), resuscitative measures (MD: 1.8, 99% CI: 1.4–2.2, P = 0.0007), clinical scoring systems (MD: 0.25, 95% CI: 0.16–0.34, P = 0.009) had a significantly greater effect on delaying definitive fascial closure than those in the intervention category. There were no superiorly significant categories of prognostic factors influencing the development of intra-abdominal complications or mortality over interventions.

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

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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: 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

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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 rivalling 2014, this is projected to continue.

RUNNING BARRED SUTURE QUILTING REDUCES ABDOMINAL DRAINAGE IN PERFORATOR-BASED BREAST RECONSTRUCTION

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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 burrred suture quilting technique. All patients had closed suction drains inserted bilaterally until daily drain outputs was less than 40 mL 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 (238 mL vs 526 mL; 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 MORTALITY IN LOWER LIMB AMPUTATION

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Introduction: Poor glycemic control has been associated with higher rates of adverse surgical outcomes. Glycosylated haemoglobin (HbA1c) is widely used in the pre-operative surgical assessment to evaluate glycaemic control. There is limited data analysing the efficacy of HbA1c in predicting surgical outcomes. At our institution, HbA1c is routinely measured in diabetics under peri-operative HbA1c levels and post-operative mortality outcomes.

Methods: In this retrospective study 269 consecutive patients underwent lower limb amputation at the Alfred Hospital, Melbourne, between 1 January 2002 and 1 March 2010. Of these, 110 had a pre-existing diagnosis of Diabetes Mellitus (DM) (Type 1 or 2) at time of admission and were considered to have undergone a lower limb amputation following a complication of their DM. HbA1c levels were reviewed in this group, with 91 patients having a HbA1c level performed 2 months prior to surgery, or 3 months following surgery. We reviewed the mortality of these patients at 60 days, 1 year and 5 years. We used the Fisher exact test to analyse our cohort in two groups of HbA1c ≥8.5% and <8.5%.

Results: Follow-up at 60 days, 1 and 5 years was 97.7%, 89% and 81% respectively. At 60 days mortality was less in the group with HbA1c <8.5% (11.1%) compared to the group with HbA1c ≥8.5% (29.41%), however this difference was not significant (P = 0.054). When a history of prior coronary artery disease or myocardial infarction was accounted for, the difference between the two groups became significant, with less mortality in the HbA1c <8.5% group (6.82%) compared to the HbA1c ≥8.5% group (36.56%; P = 0.024). There was no significant difference in mortality at 1 or 5 years.

Conclusion: This study shows that HbA1c may have a predictive role in estimating mortality in a diabetic ampute cohort at 60 days. No significant difference was shown at 1 or 5 years. This association requires further evaluation in larger prospective studies.

UTILITY OF DELAYED FLEXION-EXTENSION X-RAYS FOR CLEARANCE OF THE CERVICAL SPINE FOLLOWING TRAUMA

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Trauma

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 and 2015, with a negative CT scan of the CS and persisting midline tenderness were included in this study. Demographic data were 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.

HYPERBILIRUBINEMIA – ITS UTILITY IN NON-PERFORATED APPENDICITIS

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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 appendectomy and 21% of these were negative. The specificity of hyperbilirubinemia 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 hyperbilirubinemia in simple appendicitis demonstrated a PPV of 0.81 compared to CRP (0.71) and WCC (0.85).
ELEVATED POSTOPERATIVE WHITE BLOOD CELL COUNT IS AN INDEPENDENT PREDICTOR OF POSTOPERATIVE ATRIAL FIBRILLATION

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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. Whole 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 regard 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. 104.44, 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 1 x 10^7 increase in WCC (β = 0.038, p = 0.01).

Conclusion: Cardiac surgery is associated with a raised WCC postoperatively; 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.

MOLECULAR BIOMARKERS FOR PREDICTING RESPONSE TO PREOPERATIVE CHEMO-RADIATION IN PATIENTS WITH LOCALLY ADVANCED RECTAL CANCER

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Introduction: Patients with locally advanced rectal cancer (LARC) are treated with total mesorectal excision, preceded by neoadjuvant chemoradiation therapy (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)
Results: This is the protocol for a review. The objectives are as follows:
To assess the accuracy of molecular biomarkers to predict complete pathological response versus no or partial response to preoperative nCRT in patients with LARC.
1. To assess the accuracy of molecular biomarkers to predict any pathological response to nCRT versus no response 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 regimens 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
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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 these patients.
Methods: Data were 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 were 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 two groups (22% vs 15%). The length of hospital stay was significantly lower in the post-App group when compared with the Pre- and Post-App groups (19 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
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Introduction: Emergency cholecystectomy in critically ill patients carries a high risk of morbidity and mortality. Laparoscopic cholecystectomy (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 5 mm port in the right subcostal margin, which was later upgraded to a 10 mm port. The gallbladder was then decompressed with a 10mm trocar and a 20Fr Foley catheter (held by its balloon and a 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
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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 Sinus (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 were retrospectively collected from the medical records of those who underwent an EpsIT procedure at a single institution between January 2014 and 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 (1–10 months).
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.S.I.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
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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 homogeneous 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

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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.