The department provides opportunities for scientific research in a wide variety of fields in a warm, friendly and collegial atmosphere. Three separate research groups with international repute provide excellent opportunities for advancement in both basic science and clinical research. Researchers and students have easy access to supervisors and support and close supervision at all times. Modern facilities and easy access to transport ensure a pleasant working environment.

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At Johnson & Johnson medical, surgical training and medical education has always been an integral part of our commitment to transforming patient care and the advancement of minimally invasive surgery. We have facilitated the training of surgeons, operating room nurses and other health care professionals on the latest surgical procedures and instrumentation for decades. We believe in grass roots activity and will continue to support training programs long into the future.
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Research is to see what everybody else has seen, and to think what nobody else has thought.

- Albert Szent-Gyorgyi
The Austin Research Prize in Surgery & Anaesthesia

The Austin Research Prize in Surgery and Anaesthesia was inaugurated in 2003 and supported by Johnson and Johnson Pty Ltd. The main aim of the prize was to foster interest in clinical and basic science research amongst trainees at all levels within the Division of Surgery and reward excellence in achievement. It is gratifying to note that interest amongst trainees has remained high as seen by the number of high quality presentations submitted this year. Presenters in 2011 range from final year medical students and interns to unaccredited and accredited trainees doing full time clinical work as well as full time research. We hope to continue this trend by providing continuing opportunity for our trainees to partake in research programs.

We are grateful to Johnson and Johnson Pty Ltd who have remained strongly committed to supporting research at the Austin. In addition we are also indebted to the senior medical staff of the Austin who have encouraged research amongst the trainees. Without this support much of the work presented here would not be possible.

Any surgical trainee or surgeon aspiring to have significant input into surgical education and training, or achieve positions of surgical leadership will require additional skills in the future. A co-badged degree between the RACS and the University of Melbourne will commence in February to fulfil this need. This “Masters of Surgical Education” is currently open for enrollment. Any further details may be obtained from the Department of Surgery at the Austin Hospital or the University of Melbourne web site.

Prof C Christophi
Head, Department of Surgery
Austin Health
PROGRAM

1700 Refreshments courtesy of Johnson & Johnson Pty Ltd

1800 Introduction

1815 David A Westwood – “Gastrin-mediated adaptive responses to hypoxia in colorectal cancer.”

1830 Gaurang Shah – “Quality of Healthcare Data in a Tertiary Referral Hospital: Comparison of Clinical and Hospital Administrative databases.”

1845 Dragos Iorgulescu – “Experience with portal vein resection at the time of pancreatectomy in an Australian tertiary care centre.”

1900 Kiran Manya – “Outcomes of patients with histologically proven acute acalculous cholecystitis”


1930 Kapil Sethi – “Comparison of Renal Preconditioning techniques in a rat model”

1945 David Liu – “Prophylactic mesh reinforcement reduces stomal site incisional hernia after ileostomy closure”

2000 Renu Eapen – “Patterns of use of perioperative chemotherapy in patients treated with radical cystectomy for urothelial carcinoma of the bladder”

2015 Nicholas Low – “Fast track recovery program significantly reduces hospital length of following uncomplicated pancreaticoduodenectomy”

2030 Lawrence Lau – “18F-FDG PET for Colorectal Liver Metastases: Metabolic Response to Preoperative Chemotherapy Predicts Prognosis”

2045 Adjudication & Light Dinner courtesy of Johnson & Johnson Pty Ltd

2130 Announcement of successful trainees & presentation of Prize
Gastrin-mediated adaptive responses to hypoxia in colorectal cancer.

David A Westwood, O. Patel, A. Shulkes, G.S. Baldwin
The University of Melbourne, Department of Surgery, Austin Health, Melbourne

BACKGROUND: Understanding the molecular processes mediating colorectal cancer (CRC) tumorigenesis will enable the development of targeted therapies that selectively disrupt the pathways responsible for tumour growth. The gastrin family of growth factors promote CRC growth, invasion and angiogenesis. Hypoxic microenvironments, caused by tumours outgrowing their local blood supply, stimulate aggressive tumour behaviour. However, the effect of hypoxia on gastrin expression in CRC is unknown.

METHODS: Expression of the gastrin gene in human CRC cells was examined under conditions of normoxia and hypoxia. The effect of inhibiting expression of HIF-1alpha (the transcriptional master regulator of cellular responses to hypoxia) and of deleting HIF-binding sites in the gastrin promoter was investigated. The effect of inhibiting gastrin expression on CRC cell behaviour in vitro and on tumorigenesis in mouse xenografts was analysed.

RESULTS: Gastrin gene expression in CRC cells is stimulated by hypoxia by binding of HIF-1alpha to the gastrin promoter. The viability of gastrin knockdown CRC cells in vitro is diminished under hypoxic (1% O2) conditions due to loss of resistance against hypoxia-inducible apoptosis. The growth of tumour xenografts in mice exposed to hypoxia (10% O2) for 21 days is significantly reduced by knocking down gastrin expression.

CONCLUSIONS: This work provides evidence that gastrin expression is involved in the adaptation of CRCs to hypoxic microenvironments through resistance to apoptosis. Shrinkage of CRC liver metastases by the angiogenesis inhibitor bevacizumab is dependent on hypoxia-induced apoptosis. Therapies that target gastrin may enhance the therapeutic efficacy of bevacizumab and increase secondary resectability rates in patients with CRC liver metastases.

PERSONAL CONTRIBUTION
Planning/conceptualization: 80%
Laboratory work/data collection: 100%
Data analysis/discussion: 95%

David Westwood
Current Position: Full Time PhD Student
David Westwood is a SET 3 General Surgery trainee currently undertaking a PhD in the Department of Surgery at Austin Health. He is investigating the role of gastrin in colorectal cancer development under the supervision of Prof Graham Baldwin. His research interests are the early detection of colorectal cancer and targeted therapies for metastatic colorectal cancer.
Quality of Healthcare Data in a Tertiary Referral Hospital: Comparison of Clinical and Hospital Administrative databases.

Shah G, Mori K, Fink M, Nikfrajam M, Starkey G, Jones RM, Christophi C and Muralidharan V.
HPB/Liver Transplantation Unit, Department of Surgery, Austin Hospital, Melbourne

BACKGROUND: This study compares the quality and reliability of the data available from the administrative hospital database (HD) in comparison to the prospectively maintained and clinician validated unit database (UD).

METHODS: The comparison of the two data sources was performed for the HPB & Transplant Surgery Unit over a five year period. A ‘Data Request Form’ was developed which requested specific data including admissions, diagnoses, procedures, complications and key performance indicators (KPIs). The request was submitted to both the Hospital Information Service and the dedicated unit data manager and data collected for analysis. The study was aimed at demonstrating not only the differences in accuracy but also the ease of obtaining clinically relevant information from each of the two databases.

A further study was done on a random sample of 100 patients who underwent cholecystectomy over a period of twelve months. The patient records were considered gold standard and analysed by the investigators and the data collected compared to both the UD and HD to establish which more accurately reflected the information in the patient records.

RESULTS: The HD recorded 13.3% fewer total admissions, 77%, 9% and 28% fewer admissions with chronic cholecystitis, pancreatic cancer and hepatocellular cancer respectively and 71%, 8% and 18% more admissions with chronic pancreatitis, cholangitis and cholangio-carcinoma compare to UD respectively. With procedures, it (HD) recorded 5%, 5% and 25% fewer liver resections, groin hernia and incisional hernia repairs while it incorrectly recorded 25%, 9.5%, 15%, and 9% more open cholecystectomies, emergency cholecystectomies, bile duct explorations and laparoscopic appendicectomies respectively. No data was available from HD in relation to in-hospital referrals, specific procedure related complications and KPIs.

CONCLUSIONS: There is appreciable difference between the two sources. The quality, clinical relevance and reliability of the UD with clinician validated data is superior to that obtained from the HD.

PERSONAL CONTRIBUTION

| Planning/conceptualization: | 60% |
| Laboratory work/data collection | 60% |
| Data analysis/discussion: | 40% |

Gaurang Shah

Current Position: Unaccredited General Surgery Registrar

I am an unaccredited registrar at Austin health and will commence SET training in General surgery in 2013. I am an international medical graduate having obtained my MBBS and MS – Masters in General surgery in India. I have worked in Austin for two years in past and have also worked in Ballarat for two years in same role. My areas of interest are Emergency General Surgery, Colorectal surgery and Surgical education for medical students. Currently rostered in Upper GI and Endocrine surgery unit at Austin.
Experience with portal vein resection at the time of pancreatectomy in an Australian tertiary care centre.

Iorgulescu D, Ling S, Nikfarjam M, Fink M, Jones R, Muralidharan V, Starkey G and Christophi C.
HPB/Liver Transplantation Unit, Department of Surgery, Austin Hospital, Melbourne

BACKGROUND: Portal and superior mesenteric vein resection with pancreatectomy is now accepted practice in cases with suspected or confirmed vein involvement by tumour. We present our experience of this procedure over an eight year period with particular emphasis on morbidity, survival and the diagnostic accuracy of imaging in regards to major vein involvement by tumour.

METHODS: A retrospective analysis of a prospectively kept database was used. Information obtained included patients demographics, radiological and histological evidence of major vein involvement, postoperative morbidity and hospital length of stay. Disease and recurrence free survival were also calculated using Kaplan-Meyer curves and compared to a similar cohort where no vein resection was performed.

RESULTS: Portal vein/SMV resection was performed on 17 patients with pancreatic malignancy and presumed venous involvement. Procedures included pancreatico-duodenectomy (11), total pancreatectomy (6) and reoperations (3). Pathological staging showed 2x T2N0, 5x T3N0, 1x T1N1, 2x T2N1 and 7x T3N1 tumours. 6 cases (35%) had positive microscopic margin. Preoperative imaging predicted venous involvement in 8 (47%), while the other 10 were assessed clinically. Portal vein was confirmed to be involved histologically in only 58% of total patients (10/17). Preoperative imaging had a false positive rate of 25% (2/8) and a false negative rate of 44% (4/9).

13 patients (70%) had significant postoperative morbidity – grades 2 to 4 Clavien. 6 patients developed PV thrombosis (35%), all with significant clinical consequences. Median hospital stay was 16 days. Overall and recurrence free survival was compared with other pancreatectomies without PV resection and with the published literature.

CONCLUSIONS: PV/SMV resection seems justified and produces some survival benefit. Overall diagnostic accuracy of PV involvement is just over half based on clinical and radiological criteria compared to histology. The morbidity is high and a significant proportion developed portal vein thrombosis with clinical sequelae. Routine postoperative anticoagulation may be indicated in this group.

PERSONAL CONTRIBUTION

| Planning/conceptualization: | 100% |
| Laboratory work/data collection | 70% |
| Data analysis/discussion: | 90% |

Dragos B Iorgulescu
Current Position: HPB Fellow (ANZHPBA Fellowship)
Trained at St. Vincent’s Hospital Melbourne, worked 4 years in Adelaide as a Trauma/General surgeon, done 2 years of HPB Fellowship at Queen Elizabeth and Royal Adelaide Hospital, currently HPB/Liver transplant Fellow at Austin Hospital. Has a Masters Degree in Molecular Biology at the University of Melbourne
Outcomes of patients with histologically proven acute acalculous cholecystitis

Kiran Manya, Michael Fink, Andrew Hadj, Vijayaragavan Muralidharan, Graham Starkey, Robert Jones, Christopher Christophi, Mehrdad Nikfarjam

BACKGROUND: Acute acalculous cholecystitis (AAC) is traditionally described in the setting of critical illness, where the diagnosis is based on clinical assessment and imaging criteria. Very few studies have assessed the features and outcomes of AAC in patients treated by cholecystectomy.

METHODS: Patients with histologically confirmed acute cholecystitis treated in a specialized unit in a tertiary hospital between 2005 and 2011 were identified from prospectively maintained database. Retrospective review of data was undertaken and patients with AAC were compared with those patients with acute cholecystitis and confirmed gallstones.

RESULTS: AAC was identified in 35 of 412 (8.5%) patients with acute cholecystitis. These patients were older (69 years versus 61 years; P = 0.004) and were more likely to be febrile (46% versus 21%; P = 0.001) and hypotensive (23% versus 5%; P < 0.001) at initial presentation. There was a higher incidence of chronic obstructive airways disease (COAD) in the AAC group (26% versus 6%; P < 0.001). Other co-morbidities were similar among the groups. Operative outcomes were similar between the groups. There were no overall differences in postoperative complications between AAC and calculus acute cholecystitis patients (17% versus 16%; P = 0.063). However, the postoperative length of stay was higher in the AAC group (5 days versus 3 days; P = 0.026).

CONCLUSIONS: AAC more commonly occurs in older patients and those with COAD. The operative outcomes and complications of AAC treated by cholecystectomy are similar to cases of acute calculous cholecystitis.
Health information quality on the internet in benign prostatic hyperplasia and its treatment: A multilingual evaluation.

Chen C. E1, Manecksha R.P1, Abouassaly R2 and Lawrentschuk N1,3.

1Department of Urology, Austin Hospital, Heidelberg, Victoria 3084, Australia

2Urological Institute, University Hospitals Case Medical Center, Case Western Reserve University, Cleveland, OH

3Department of Surgery, University of Melbourne, Australia

BACKGROUND: Internet information quality for benign prostatic hyperplasia (BPH) is considered variable but no comprehensive analysis exists. Our objective was to compare the quality of BPH-related websites and to assess for language and other differences across Western languages.

METHODS: Health on the Net (HON) principles may be applied to websites using an automated toolbar function. Using the Google search engine (www.Google.com), in 2011, 9000 websites were assessed for Benign Prostatic Hyperplasia and associated common surgical and medical treatments. For disease, keywords searched were BPH, benign prostatic hyperplasia, benign prostatic hypertrophy, benign prostatic enlargement, prostomegaly; for surgical treatment, TURP, transurethral resection of prostate, greenlight laser prostate, laser prostate surgery, holmium laser prostate, diode laser prostate, prostatectomy; and for medical treatment, medical therapy prostate, alpha blocker prostate and alpha reductase prostate. All searches were performed in English, French, German and Spanish. The first 150 websites in each language had HON principles measured. A further analysis of site sponsorship was performed.

RESULTS: 9000 websites were assessed; disease search (3000) surgical treatment (4200) and medical treatment (1800). Regardless of language or search keyword, the majority of sites are not HON accredited. English (32%) has consistently more HON accredited sites than French (30%), German (20%) and Spanish (18%). Significant differences were found comparing language, disease, surgical and medical treatments. Keywords such as Benign Prostatic Hyperplasia and Medical Therapy Prostate had the most accredited websites with 16% overall. The quality of the websites was also assessed based on the types of web sponsors. Accredited sites were mainly sponsored by commercial (45%), government/educational (38%) and non-profit organizations (32%).

CONCLUSIONS: A lack of validation of most BPH sites related to the disease and treatment should be appreciated by urologists. Further, there is a discrepancy in quality and number of websites across major Western European languages. We need to encourage informative, ethical and reliable complimentary health websites on the Internet and direct patients to them.

PERSONAL CONTRIBUTION

| Planning/conceptualization: | 30% |
| Laboratory work/data collection: | 90% |
| Data analysis/discussion: | 70% |

Emily C Chen

Current Position: Unaccredited General Surgery Registrar

Emily currently works as the Non-accredited General Surgical Registrar at Austin Health. Her current research interest includes Bladder Cancer management and Benign Prostatic Disease. She graduated from the University of Notre Dame Australia, W.A in 2008 and has previously undertaken scientific research at the Alfred Hospital where she obtained a Class IA Honours degree in Haematology.
Comparison of Renal Preconditioning techniques in a rat model.

K Sethi, O Patel, J Ischia, L Xiao, G Baldwin, A Shulkes, DM Bolton

BACKGROUND: Renal preconditioning (RPC) is a technique that exposes tissue susceptible to ischaemia into triggering a family of intracellular transcription factors, the Hypoxia Inducible Factors (HIFs), to protect against kidney injury. Preconditioning may offer protection to cells against irreversible nephron loss and tolerate ischaemia beyond the accepted critical ischaemia time. Whilst these techniques have been explored in other organs, no study has compared the effects of these techniques in the kidney. There is also emerging evidence that a combination of these preconditioning techniques may confer greater protection in tissue.

METHODS: 24 solitary kidney-model Sprague Dawley rats were divided into groups of 6 undergoing either a) control, b) 30mg/kg subcutaneous cobalt chloride (CoCl₂) treatment over 24 hours, c) intermittent clamping (IC) consisting of 5 minutes renal artery clamping followed by 10 minutes reperfusion over 4 cycles, or d) a combination of both CoCl₂ and IC. Following preconditioning, all rats underwent 40 minutes of renal artery clamping (critical ischaemia) and were followed up with serum renal function tests and animal health scores for 7 days.

RESULTS: All rats demonstrated the greatest rise in serum creatinine at 24 hours, and urea at 72 hours with a return to basal levels by day 7. All preconditioning methods improved renal function following critical ischaemia up to 72 hours (mean +/- SEM creatinine in µmol/l: control group, 273.3 +/- 40.3; CoCl₂, 76.3 +/- 10.7 p<0.0005; IC, 76.3 +/- 36.2 p<0.05; combination, 271.1 +/- 76). Rats treated with CoCl₂ had the lowest rise in serum creatinine at 24 hours (Control 390.5 +/- 18.4; CoCl₂, 144.7 +/- 31.5 p<0.0001). Whilst the control group had a 50% mortality rate, no rats in the preconditioning groups died (p<0.005).

CONCLUSIONS: Individual cobalt treatment offers greater protection against renal damage than intermittent clamping or a combination of these techniques in the kidney. Development of similar agents that specifically target the same mechanistic pathway of HIF activation would offer the greatest benefit in renal preconditioning for clinical application. An approach that stimulates kidney cells into protecting themselves by preconditioning prior to ischaemic damage has great promise for use in a wide variety of medical and surgical conditions in the future.

PERSONAL CONTRIBUTION

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<tr>
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Kapil Sethi

Current Position: Accredited SET1 Urology Trainee

Kapil Sethi is a Urology trainee currently completing his MD undertaken at the Department of Surgery, Austin Hospital under Prof Arthur Shulkes and Prof Damien Bolton since 2008. He completed his basic surgical training through Austin and Northern Health, and is currently a SET 1 trainee at Eastern Health.
Prophylactic mesh reinforcement reduces stomal site incisional hernia after ileostomy closure.

David Liu1, Elisabeth Banham2, Srini Yellapu2.

1Austin Health, Heidelberg, Victoria, Australia
2The Royal Hobart Hospital, Hobart, Australia

BACKGROUND: Stomal site incisional hernia is a common complication following ileostomy closure. The effectiveness of prophylactic mesh placement at the time of stomal closure is unknown due to fear of mesh infection and subsequent wound complications. This study investigated whether prophylactic mesh placement reduces the rate of incisional hernia after ileostomy closure without increasing wound complications.

METHODS: Retrospective review of consecutive ileostomy closures undertaken at a tertiary referral centre between January 2007 and December 2011. Hernias were identified through clinical examination and computer tomography.

RESULTS: Eighty-three cases of ileostomy closure were reviewed, 47 patients received mesh reinforcement, and 36 underwent non-mesh closure (controls). In total, 16 (19.3%) patients developed incisional hernia. Thirteen (36.1%) occurred in the control group and 3 (6.4%) in the mesh group (OR: 8.29, 95% CI: 2.14 – 32.08, p=0.001). Incisional hernia repair was performed for 3 (23%) patients in the control group, no hernias in the mesh group required surgery. There was no significant difference in wound infection rates between mesh (2 patients, 4.3%) and control (1 patient, 2.8%) groups. No mesh infection was found. Multivariate analysis demonstrated that malignancy (OR: 21.93, 95% CI: 1.58 – 303.95, p=0.021) and diabetes (OR: 20.98, 95% CI: 3.23 – 136.31, p=0.001) independently predicted incisional herniation, whilst mesh reinforcement prevented hernia development (OR: 0.06, 95% CI: 0.01 – 0.36, p=0.002).

CONCLUSIONS: Mesh placement significantly reduced the incidence of incisional hernia following ileostomy closure without increasing complication rates. This technique should be strongly considered in patients at high risk of hernia development.

David Liu
Current Position: General Surgery Registrar (SET2) undertaking full time clinical work.

PERSONAL CONTRIBUTION
Planning/conceptualization: 90%
Laboratory work/data collection: 70%
Data analysis/discussion: 100%
Patterns of use of perioperative chemotherapy in patients treated with radical cystectomy for urothelial carcinoma of the bladder.

Mun Sem Liew¹,², Ali Tafreshi¹, Renu Eapen³, Ian D Davis¹,²,⁴,⁵ & Shomik Sengupta ²,³

¹Joint Austin-Ludwig Oncology Unit, Austin Health, ²Ludwig Institute for Cancer Research, Austin Health, ³Department of Urology, Austin Health, ⁴University of Melbourne, ⁵Monash University

BACKGROUND: Radical cystectomy (RC) for curative treatment of invasive urothelial cancer (UC) of the bladder is associated with high relapse rates, especially in patients with extravesical (pT3) and node positive (N+) disease. The aim of this study was to review the peri-operative use of chemotherapy, shown to improve survival after RC, and its impact on oncological outcomes.

METHODS: Using health information system coding, 88 patients undergoing RC between 2004 and 2011 were identified. Clinical & pathological data, recurrence and death were assessed by retrospective chart review. Survival analysis was carried out using Cox proportional hazard models.

RESULTS: The median (range) age of the patients was 65y (37-84), and 66 (75%) were males. Pathologic features included 84 (95%) UC (pure or mixed), 81 (92%) high grade tumours, pT-stage ≥T3 in 34 (38.6%) and pN+ in 10 (11.4%) of patients. Twenty-five (28.4%) patients underwent peri-operative chemotherapy, including 8 (9%) neoadjuvant and 21 (24%) adjuvant. There was a significant trend over the study period in the use of neoadjuvant but not adjuvant chemotherapy. Patients undergoing chemotherapy were more likely to be node positive (p<0.05) and had a trend toward higher T-stage (p=0.06). Twenty-four (27%) patients relapsed at a median interval (range) of 11 (1-83) months and 29 (33%) patients died, at a median interval (range) of 17 (0-84) months. Relapse free survival (RFS) and overall survival (OS) were comparable between chemotherapy and non-chemotherapy patients, but on multivariate analysis after adjusting for age, pT-stage and pN-stage, chemotherapy significantly impacted RFS (RR 0.34, p<0.05) but just failed to reach statistical significance for OS (RR 0.39, p=0.057).

CONCLUSIONS: There was a trend over the study period in increased use of neoadjuvant chemotherapy, but overall, peri-operative chemotherapy remains under-utilized. Patients who received chemotherapy had poorer prognostic features, but had better RFS after adjusting for other factors.

PERSONAL CONTRIBUTION

| Planning/conceptualization: | 40% |
| Laboratory work/data collection | 40% |
| Data analysis/discussion: | 40% |

Renu Eapen

Current Position: Accredited (SET 5) Urology Trainee

I am a SET 5 urology trainee. I have recently completed the fellowship examination in urology. I am currently the urology registrar at the Austin Hospital. I have previously worked at Ballarat Base Hospital and the Monash Medical Centre. My interests lie in uro-oncology, especially the treatment of bladder cancer, and reconstructive urology and hope to pursue a fellowship in these areas.
Fast track recovery program significantly reduces hospital length of following uncomplicated pancreaticoduodenectomy

Mehrdad Nikfarjam1, Laurence Weinberg2, Nick Low1, Vijayaragavan Muralidharan1, Michael A Fink1, Graham Starkey1, Robert Jones1, Christopher Christophi1.

University of Melbourne Department of Surgery1 and Anaesthesia2, Austin Health, Heidelberg, Victoria, Australia.

BACKGROUND: Factors affecting length of hospital stay after uncomplicated pancreaticoduodenectomy (PD) have not been reported. While fast track recovery program(s) (FTRP) are increasingly utilised in colorectal surgery to expedite patient recovery, their utility following uncomplicated PD is uncertain. We hypothesized that patients undergoing uncomplicated PD treated by FTRP would have a shorter length of hospital stay compared to those managed by a standard program.

METHODS: The records of patients without surgical or medical complications following PD managed by fast track or standard protocols, between August 2005 and December 2011 were identified. Patient demographics, peri-operative details and clinicopathological features were compared to determine prognostic predictors for length of hospital stay.

RESULTS: Forty-one patients treated by PD had no medical or surgical complications during this period. Of these patients, 20 underwent FTRP compared to 21 who underwent standard care. Patients in the standard group were more likely to have a feeding jejunostomy tube, pylorus preserving procedure and a nasogastric tube in place longer than 24 hours post-operatively (p<0.05). The mean post-operative length of stay was shorter in the FTRP group (8 (range: 7-16) days versus 14 (range: 8-29) days; p<0.001). There were three readmissions in the FTRP program related to abdominal pain and none in the standard group. The overall length of stay, accounting for readmissions, still remained significantly shorter in the FTRP group (9 days versus 14 days; p<0.001). There were no significant differences in discharge destination between groups. On univariate analysis, the factors associated with discharge by day 8 post surgery were FTRP (Odds ratio (OR) 37 (4.1-338); p<0.001), a negative fluid balance on post-operative day 2 (OR 3.8 (1.0-14.9); p=0.049) and absence of a feeding jejunostomy (OR 1.6 (1.2-2.1); p=0.017). On multivariate analysis, the only factor independently associated with post-operative discharge by day 8 was FTRP (OR 37 (4.1-338); p=0.001).

CONCLUSIONS: FTRP achieved significantly shorter length of stay following uncomplicated PD.

PERSONAL CONTRIBUTION

Planning/conceptualization: 30%
Laboratory work/data collection: 70%
Data analysis/discussion: 30%

Nicholas (Nick) Low

Current Position: Unaccredited General Surgery Registrar

Dr. Nicholas (Nick) Low is one of Austin’s 2012 provisional general surgical registrars. He graduated from Monash University in 2008 and has worked for the Austin since 2011. During this period, Nick has also been involved in research evaluating outcomes associated with fast track pancreatic surgeries at the Austin. In addition, Nick is also the vice president elect for Austin 2013 HMO society.
**18F-FDG PET for Colorectal Liver Metastases: Metabolic Response to Preoperative Chemotherapy Predicts Prognosis.**

Lawrence Lau¹², Sze Ting Lee¹³, Andrew Scott¹³, Mehrdad Nikfarjam¹², Michael Fink¹², Robert Jones¹, Graham Starkey¹, Christopheri Christopheri¹², Vijayaragavan Muralidharan¹².

¹Austin Health, Melbourne, Australia, ²University of Melbourne, Melbourne, Australia
³Ludwig Institute for Cancer Research, Melbourne, Australia

**BACKGROUND:** Biological characteristics of colorectal liver metastases (CRCLM) are major determinants of patient outcome. This study evaluates the prognostic value of metabolic response to preoperative chemotherapy as quantified by 18F-FDG PET for patients undergoing liver resection of CRCLM.

**METHODS:** All patients (n=82) who had staging 18F-FDG PET prior to liver resection for CRCLM at Austin Health in Melbourne between 2004-2011 were included. Thirty-eight patients had PET and CT imaging before and after preoperative chemotherapy. Semi-quantitative PET parameters: maximum standardized uptake variable (SUVmax), metabolic tumour volume (MTV) and total glycolytic volume (TGV) were derived. Metabolic response was determined by the proportional change in PET parameters (dSUVmax, dMTV, dTGV). CT size response was evaluated by RECIST criteria. Correlation to recurrence-free (RFS) and overall survival (OS) was assessed using receiver operating characteristic/area under the curve (AUC) and Kaplan Meier survival analysis.

**RESULTS:** Median follow-up time was 39 months with 40% RFS and 66% OS. Parameters on staging PET prior to chemotherapy were not predictive of prognosis while all parameters after chemotherapy were prognostic for RFS and OS. OS was best predicted by dSUVmax (AUC = 0.83). Patients with metabolic responsive tumours had an OS of 85% at 39 months vs. 38% with non-responsive or progressive tumours (p=0.003). Tumour size change based on RECIST criteria did not predict survival.

**CONCLUSIONS:** Tumour metabolic response to preoperative chemotherapy as quantified by 18F-FDG PET is predictive of prognosis in patients undergoing resection of CRCLM. In comparison, changes on CT according to RECIST criteria were not predictive of outcomes. Metabolic response uniquely characterizes tumour biology allowing future optimization of patient and treatment selection.

**PERSONAL CONTRIBUTION**

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**Lawrence Lau**

**Current Position:** Full-time PhD Student

Lawrence Lau is a SET 3 general surgical registrar at the Austin Hospital. Currently undertaking full time research towards PhD. After graduating from University of Sydney in 2005, he went on to finish his internship at the Royal Prince Alfred Hospital before moving to St. Vincent’s Hospital in Melbourne. His current research interests are in predicting patient prognosis based on cancer biology, in particular, with non-invasive modalities such as PET imaging.
Surgery and Scientific Research: Why do it?
Research Opportunities & The Academic Research Program

The Austin Hospital is a major hub for surgical training with 45 General Surgery training positions and many others within the surgical subspecialties. The commitment of the Department of Surgery towards surgical education and research provides excellent opportunities for the trainees at every level. We also endeavour to establish strong links with other departments to develop collaborative research including the Peter McCallum Hospital, Ludwig Institute for Cancer Research, and clinical departments such as Anaesthesia, Radiology, Oncology and Intensive Care.

Research Opportunities for Surgical Trainees: The department strongly encourages surgical trainees to undertake formal research in the form of full time research higher degrees. Alternatively they may undertake research concurrent with their clinical activities. Research activity has progressively increased in importance to the surgical trainee over the past years as more emphasis has been placed on a scientific approach to surgical problems. Increasing demands are made on trainees to conduct, present and publish on surgical research not only as a component of their accredited training but also to increase their career opportunities and successful applications for future fellowships. The Department of Surgery continues to strongly support research undertaken by trainees either as full time research higher degrees or on a smaller scale during their clinical tenure.

Trainees at all levels from junior hospital medical officers to advanced SET trainees are encouraged to seek opportunities early in the year to begin work on at least one research project. If trainees have a particular interest in a subspecialty, they are encouraged to approach members of that unit for a potential research project. If not, the Department of Surgery will be able to provide a number of options for small, relevant clinical studies based on our ongoing prospective data collection service. The aim would be to present the results at the Austin Research Prize presentation and subsequently to have it published in a relevant peer reviewed journal. The presence of ongoing active laboratory based research projects, a comprehensive general surgical database and the access to surgical tissue samples from the Victorian BioBank provide a wide variety of opportunities in clinical and basic science research. This allows research projects to be tailored to the trainee's expectations and level of experience. Trainees who undertake research have the opportunity to present their results at Austin Research Week as well as the annual Austin Research Prize in Surgery and Anaesthesia.

Scholarship support for surgical trainees undertaking full time research is readily available from the generous support of the Royal Australasian College of Surgeons as well as The University of Melbourne Melville Hughes Scholarship.

Research Higher Degree (RHD) Program
The Department of Surgery strongly encourages higher degrees by research (PhD, MPhil, DMedSc and MSurg). The main focus of such research is related to cancers and diseases of the liver, pancreas and biliary tree, organ transplantation, renal and prostate cancer, and spinal cancer and biology. Students from both medical or biomedical fields are welcome. Basic laboratory science projects include techniques such as in vivo animal models, molecular biology, histopathology and microscopy, and in vitro cell culture. Clinical research includes PET imaging, retrospective studies and laboratory work with human samples from the Victorian Cancer Biobank.

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The University of Melbourne is recognised internationally as a leader in graduate research. As one of our students, you will enjoy opportunities to work with leading researchers in first rate facilities, developing skills essential to your future career. The departmental philosophy supports the timely completion of all research undertaken by providing the necessary facilities, mentorship, technical expertise and funding support. Researchers are expected to present their results at local, national or international meetings and are strongly encouraged to publish their work in peer reviewed journals.
Pathways to Discovery:
This is the flagship publication for the research arm of the department. Printed as an A4 full colour booklet it contains details of all undergraduate and post graduate research degrees offered by the department along with information on research groups and research projects available to science students and surgical trainees to undertake. It is also available in electronic format and downloadable from the departmental web site.

It’s better to light a candle than curse the darkness.

- Carl Sagan
AUSTIN RESEARCH PRIZE
PAST WINNERS

2003: Mehrdad Nikfarjam - The Influence of Vascular Inflow Occlusion on Progressive Liver Necrosis and Microvasculature Following Interstitial Laser Thermotherapy


Stephen Warrilow (Joint Winner) - A randomised, double-blind, placebo-controlled cross-over pilot study of glibenclamide in patients with septic shock

2005: Nathan Lawrentschuk - In-vivo tumour hypoxia, angiogenesis and characterisation of carbonic anhydrase IX expression with xenografted human Renal Cell Carcinoma in animal models using 124I-cG250 Positron Emission Tomography, Biodistribution, and Oxygen studies.

2006: Cris Cuthbertson - Capillary morphology is changed by severe acute pancreatitis and is improved by hyperbaric oxygen.

2007: Peter Wong (Basic Science Prize) - 18f-Fluorothymidine Positron Emission Tomography (Flt-Pet) As A Marker Of Cellular Proliferation In Renal Cell Carcinoma

Laurence Weinberg (Clinical Prize) - Pharmacoeconomics Of Inhalational Anaesthetics Agents: An 11-Year Cost Identification Analyses

2008: Russell Hodgson (Basic Science Prize) - Blockade with soluble ICOS-Ig prolongs survival of cellular xenografts

Julian Liew (Clinical Prize) - An anatomic feasibility study: Nerve transfer to the triceps muscle using the posterior division of the axillary nerve.

2009: Russell Hodgson (Basic Science Prize) - Local Expression of ICOS-Ig Promotes Xenograft Survival Through The Induction of Regulatory T Cells

Simon Chong (Clinical Prize) - Minimally invasive measurement of cardiac output during surgery and critical care: A meta-analysis of accuracy and precision.

2010: Russell Hodgson (Basic Science Prize) - ICOS-Ig Secreting Xenografts Have Prolonged Survival And Are Associated with Increased T Regulatory Cells And IL-10 Expression.

Vacchara Niumsawatt (Clinical Prize) - Risk factors of development of Acute Gangrenous Cholecystitis and its treatment outcomes

2011: Stanley Tay - SAVE Study: Reduced volatile agent usage following introduction of Et-control system
Impact of blood flow occlusion on direct and indirect laser induced thermal liver injury

M Nikfarjam, C Malcontenti-Wilson, C Christofi.

BACKGROUND:
Laser, radiofrequency and microwave are common techniques for local destruction of liver tumours by focal hyperthermia. The main limitation of focal hyperthermia treatment is the volume of necrosis that can be achieved. Blood flow occlusion is commonly advocated as an adjunct to focal hyperthermia to increase the volume of tissue necrosis based on macroscopic and histological assessment of immediate or direct thermal injury. This study examines the impact of blood flow occlusion on direct and indirect laser induced thermal liver injury in a murine model using histochemical methods to assess tissue vitality.

METHODS:
Focal hyperthermia produced by laser (Nd-YAG - wavelength 1064 nm) was applied to the liver of inbred male CBA strain mice at 2W for 50 seconds (100J). Treatment was performed with and without temporary portal vein and hepatic artery blood flow occlusion. Animals were killed upon completion of the procedure to assess direct thermal injury and at 24, 48 and 72 hours to assess the progression of tissue damage. The maximum diameter of necrosis was assessed by vital staining for nicotinamide adenine dinucleotide (NADH) diaphorase. Microvascular changes were assessed by laser Doppler flowmetry, Confocal in-vivo microscopy and scanning electron microscopy.

RESULTS:
The direct thermal injury (mean(S.E.) assessed by NADH diaphorase staining was significantly greater following focal hyperthermia treatment without blood flow occlusion than with blood flow occlusion (3.3(0.4)mm vs. 2.9(0.3)mm; P=0.005). Tissue disruption, cracking and vacuolization was more pronounced adjacent to the fibre insertion site in the group treated with focal hyperthermia combined with blood flow occlusion. There was an equivalent increase in the extent of injury following therapy in both groups that reached a peak at 48 hours. The maximum diameter of necrosis in the focal hyperthermia alone group at 48 hours was significantly greater than the focal hyperthermia combined with blood flow occlusion group (5.8(0.4)mm vs.5.3(0.3)mm; P=0.011). The patterns of microvascular injury were similar in both groups, varying in extent.

CONCLUSIONS:
Temporary blood flow inflow occlusion appears to decrease the extent of initial injury measured by vital staining techniques and does not alter the time sequence of progressive tissue injury following focal hyperthermia therapy.

N Lawrentschuk, C Murone, AMT Poon, J Sachinidis, G O'Keefe, LG Johns-Putra, Z. LIU, I Davis, AM Scott, DM Bolton

BACKGROUND:
The purpose of our research is to evaluate oxygen levels and angiogenesis within renal cell cancers (RCC), as evidence suggests they are hypoxic, given their resistance to radiotherapy and chemotherapy. Hypoxia has now been shown in other tumours to correlate with resistance to treatment and poor prognosis. Our study builds on the finding of hypoxia in RCC and explores its relationship with immunohistochemical markers of hypoxia and a new novel marker of hypoxia in tumours, serum osteopontin.

METHODS:
Patients who were undergoing radical nephrectomy for RCC had: 1) Evaluation of oxygen levels (pO2) within their renal cell cancers in vivo using a Polarographic Oxygen Sensor. 2) Immunohistochemistry including microvessel density to confirm at a sub-cellular level the relationship of hypoxia with the expression of proteins associated with hypoxia and angiogenesis in RCC and 3) Human osteopontin ELISA immunoassay techniques to analyse the serum levels of osteopontin.

RESULTS:
30 patients have been recruited thus far and we have demonstrated that RCC are relatively hypoxic (median pO2 7.2mmHg) compared to normal renal tissue (26.3mmHg). Microvessel density is increased in RCC compared to normal tissue indicating increased angiogenesis. Other markers of hypoxia were also increased. Serum osteopontin in patients with RCC was greater at 17.65 ± 5.3 ng/ml (mean ± 95% C.I.; range 5-41) compared to controls 8.75 ± 2.17 ng/ml (range 8-12).

CONCLUSIONS:
Renal cell cancers are relatively hypoxic and more angiogenic compared to normal tissue within the same kidney. This may explain resistance to radiotherapy and chemotherapy whilst helping to identify future therapeutic targets in the management of advanced renal cell cancer. Serum osteopontin has been demonstrated to be raised in RCC and is a novel tumour marker for renal cell carcinoma.
A randomised, double-blind, placebo-controlled cross-over pilot study of glibenclamide in patients with septic shock

Stephen Warrillow, Moritoki Egi, Rinaldo Bellomo

BACKGROUND:
Severe sepsis often causes a hypotensive shock state. Hyperpolarisation of the vascular smooth muscle cell membrane, due to the marked K+ efflux prevents Ca2+ entry into cells and may be responsible for ‘vasoplegia’. Glibenclamide (normally an oral hypoglycaemic agent) blocks the ATP-dependent K+ channel and may prevent hyperpolarization this restoring intra-cellular Ca2+ levels and re-sensitising vascular smooth muscle to noradrenaline. Animal studies have demonstrated that glibenclamide restores vascular sensitivity to noradrenaline. However, this effect has not been previously studied in humans.

Objective: To test whether glibenclamide restores noradrenaline responsiveness in septic shock patients.

METHODS:
Prospective, double-blind, placebo-controlled cross-over pilot study, in 10 patients with septic shock requiring an infusion of noradrenaline to receive either enteral glibenclamide 20mg or placebo. After twenty-four hours, each patient crossed over to receive the alternative therapy. The primary end-point was the change in noradrenaline infusion rate over time with maintenance of target mean arterial pressure. Secondary end-points included changes in heart rate and serum lactate levels.

RESULTS:
Glibenclamide was adequately absorbed enterally and, as expected, induced a significant decrease in serum glucose concentration (Mean glucose: 5.97 ± 2.17 vs 7.65 ±2.43 (P<0.0001) and increased the need for parenteral glucose administration. During glibenclamide treatment mean noradrenaline requirements fell from 13 to 4 µmol/min compared to a change from 19 to 7 µmol/L for placebo. The two changes represented a decrease of 78.9% and 71.1% in dose respectively (NS). There were also no significant changes in heart rate, mean arterial blood pressure and lactate concentration.

CONCLUSIONS:
Glibenclamide was well absorbed enterally and exerted its hypoglycaemic effect reliably. However, it failed to achieve a greater reduction in noradrenaline dose than placebo. Our observations suggest that, in septic humans, blockade of ATP-potassium dependent channels does not have a potent effect on vasomotor tone.
**In-vivo tumour hypoxia, angiogenesis and characterisation of carbonic anhydrase IX expression with xenografted human Renal Cell Carcinoma in animal models using 124I-cG250 Positron Emission Tomography, Biodistribution, and Oxygen studies.**

Nathan Lawrentschuk, C Murone, A Rigopolous, A Mountain, D Wang, G O’Keefe, G Jones, FT Lee, Ian Davis, Andrew M Scott, Damien M Bolton

**BACKGROUND:**
Hypoxia stimulates angiogenesis and has been demonstrated in tumours where it correlates with resistance to treatment and poor prognosis. We have demonstrated hypoxia in human Renal Cell Carcinoma (RCC). The purpose of animal models was to further evaluate oxygen levels within RCC whilst also focusing on expression of the protein carbonic anhydrase IX (CA IX). This protein is stimulated by hypoxia and involved in angiogenesis and may be a potential tumour target for imaging and future therapies. The human antibody cG250 binds to CAIX in vivo allowing biodistribution and PET studies when radiolabeled with iodine-124 (I124).

**METHODS:**
Balb/c nude mice had human RCC (SK-RC-52) xenografted subcutaneously. Tumours were grown to different volumes with oxygen levels measured. Further groups then had the radiolabelled monoclonal antibody 124I-cG250 (that binds to CA IX) injected intravenously and had Positron Emission Tomography (PET), gamma counting and oxygen studies performed on days 0, 1, 2, 3, 5, 7, 10 and 14 post injection. Immunohistochemistry and autoradiography was also performed.

**RESULTS:**
An inverse relationship between tumour volume and hypoxia within the model was established (P<0.001). Furthermore, CA IX was expressed by tumours with maximal uptake of 124I-cG250 on days 2/3 by distribution with gamma counting that could be correlated with uptake on PET imaging. Also, 124I-cG250 as read by gamma counter correlated with noninvasive PET scanning standardised uptake values of the radioisotope within tumours.

**CONCLUSIONS:**
The xenograft model confirms our previous findings that human RCC are relatively hypoxic compared to normal tissue. Also, that the level of hypoxia is inversely proportional to tumour size. CAIX was confirmed as an imaging and potential therapeutic target in RCC. Finally, a correlation was made between PET scanning with 124I-cG250 and biodistribution within tumours by gamma counting confirming the potential to serially PET scan animals rather than sacrifice in future biodistribution studies. This has major implications for animal ethics and the design of future biodistribution studies that are routinely used to characterised new radioisotopes and radiolabeled antibodies used to treat a variety of cancers.
Capillary morphology is changed by severe acute pancreatitis and is improved by hyperbaric oxygen.

C. Cuthbertson, K. Su, C. Malcontenti-Wilson, V. Muralidharan, C. Christophi

BACKGROUND:
Severe acute pancreatitis is characterized by alterations to the microcirculation, particularly affecting the capillary tree, which lead to pancreatic necrosis. The morphology of the pancreatic microvasculature is known to be affected in severe pancreatitis, but the effect of hyperbaric oxygen is unknown. The aims of this study are to determine the progression of pancreatic microvascular changes caused by acute pancreatitis and to determine the effect of the administration of hyperbaric oxygen (HBO).

METHODS:
Sixty seven male Wistar rats weighing 250-350g were induced with severe pancreatitis by bilio-pancreatic infusion of 4% sodium taurocholate. Animals were randomised to either HBO treatment or control. HBO treatment (100% oxygen for 90 minutes at 2.5 Atmospheres) was commenced 6 hours following induction of pancreatitis, and continued 12-hourly. Surviving animals underwent microvascular polymer casting of the pancreas at six, 24, 48 and 72 hours following commencement of treatment, and equivalent time points for control animals. Normal and Sham-operated animals also underwent casting. Microvascular casts were created by the injection of freshly prepared Mercox resin through a cannula in the thoracic aorta. The pancreas was removed after 24 hours of polymerisation and further prepared for scanning electron microscopy of the resin cast. Scanning electron micrographs of the casts were compared for capillary density, poor capillary filling, vessel diameter, and major morphological changes.

RESULTS:
Normal pancreatic microvascular casts showed a dense network of capillaries, with multiple anastomoses (Image 1). Significant morphological changes appeared at 24 hours post induction (Image 2). Microvascular casts demonstrated poor capillary filling, decreased capillary density and increased capillary cast diameter. Capillary diameter was increased (from 6.7µm to 10.3µm at 24hr, p<0.01, and 11.8µm at 48hr, p<0.001), capillary heterogeneity was increased (range increased from 13.8µm to 21.4 µm, p<0.001) and capillary density was reduced (from 1140µm-2 to 758µm-2, p<0.01). These changes occurred at 24hours post induction and were maintained at 48 and 72 hours. Treatment with HBO reduced the severity of microvascular morphological changes at each time point (Image 3). These changes became apparent at 48 hours post induction, and were maintained at 72 hours. At 48 hours, capillary diameter was decreased toward normal (from 11.8µm to 8.4µm, p<0.01), range was reduced, and capillary density was increased (from 722µm-2 to 901µm-2, p<0.01).

CONCLUSIONS:
Microvascular parameters are affected by acute pancreatitis, with changes detected at 24 hours and maintained until at least 72 hours. HBO improves the microvascular morphology parameters in acute pancreatitis towards normal values. HBO has potential as a unique alternative therapy in acute pancreatitis.
18f-Fluorothymidine Positron Emission Tomography (Flt-Pet) As A Marker Of Cellular Proliferation In Renal Cell Carcinoma

Wong P1,2; Lee ST2,3,4; Eng J3; Murone C2; Berlangieri SU2; Pathmaraj K3; O’Keefe GJ3; Byrne AJ3; Lawrentschuk N1,2; Davis ID2; Bolton DM1; Scott AM2,3,4.

1 Department of Surgery (Urology), University of Melbourne, Austin Health, Heidelberg, Australia. 2 Ludwig Institute for Cancer Research, Austin Health, Heidelberg, Australia. 3 Centre for PET, Austin Health, Heidelberg, Australia. 4 Department of Medicine, University of Melbourne, Austin Health, Heidelberg, Australia.

BACKGROUND:
18F-FLT-PET (Fluorothymidine Positron Emission Tomography) has been used to non invasively measure cellular proliferation in a number of tumour types. However, its role in renal cell carcinoma (RCC) has not been established. We aim to assess FLT-PET in RCC, and to compare it to immunohistological measurements of proliferation.

METHODS:
Patients with suspected RCC suitable for nephrectomy had preoperative FLT and FDG (fluorodeoxyglucose) PET/CT scans. Surgical samples were obtained for immunohistochemical analysis (Ki-67). Qualitative visual grading relative to normal kidney and analysis of maximum standardized uptake value (SUVmax) of each PET scan was assessed using co-registered low-dose 5mm CT and prior triple phase CT imaging. Uptake in RCC using FLT PET was compared to FDG PET. Statistical analysis comparing Ki-67 and SUVmax was performed.

RESULTS:
A total of 19 patients (13 clear cell, 5 papillary and 1 transitional cell carcinoma) underwent preoperative PET scans, with immunohistochemical data available for 13. Visual grading found most tumours had radiotracer uptake that was equal or less than the contralateral kidney. FLT uptake was generally less than FDG. Bivariate analysis showed a positive correlation between Ki-67 & FLT SUVmax (p-value 0.001, r = 0.8) and between Ki-67 & FDG SUVmax (p-value 0.005, r = 0.73).

CONCLUSIONS:
Uptake of FLT in RCC is less than FDG. There is positive correlation between FLT uptake and Ki-67 proliferative index in RCC suggesting that the degree of proliferation within RCC can be predicted by PET imaging. Further study is required to determine whether this correlates with patient outcome.
Pharmacoeconomics Of Inhalational Anaesthetics Agents: An 11-Year Cost Identification Analyses

Laurence Weinberg, David Story, Larry McNicol

BACKGROUND:
Anaesthetic departments account for 2-3% of the total hospital budget, with anaesthetic drugs accounting for 5-8% of total pharmacy expenditure. Inhalational agents account for 20% of anaesthetic drugs therefore are one of the areas that are most amenable to immediate cost reduction in the anaesthetic department budget. This study is a cost identification analyses assessing inhalational anaesthetic agent expenditure at Austin Health over an 11-year period. Pharmacoeconomic modeling is used to evaluate strategies to curtail costs.

METHODS:
The number of bottles utilised of three volatile agents (Isoflurane, Sevoflurane, Desflurane) was collected each month for the financial years ending 1997 to 2007. The acquisition costs and the cumulative drug expenditure in dollars for each agent were calculated. Inhalational agent utilisation patterns and unit price changes were evaluated. Pharmacoeconomic modeling using low fresh gas flow anaesthesia was performed to evaluate practical methods for reducing anaesthesia costs. The rational use of the cheaper generic volatile agent Isoflurane was used in pharmacoeconomic cost-containment strategy models.

RESULTS:
For the financial years ending 1997 to 2007, pharmacy acquisition costs for a bottle of Isoflurane (250mL), Sevoflurane (250mL) and Desflurane (240mL) were $157, $336, $170 respectively, and for the financial years ending 2005 to 2007, cost per bottle was $109, $265, $180 respectively. The number of bottles of Isoflurane decreased from 384 bottles/year in 1997 to 204 bottles/year in 2007. The number of bottles of Sevoflurane increased from 226 bottles/year in 1998 to 875 bottles/year in 2007. Desflurane use commenced at Austin Health in 2002 with 34 bottles being used. This increased to 163 bottles/year in 2007. Expenditure for Isoflurane decreased from $88,985/year in 1997 to $22,006/year in 2007. In contrast, Sevoflurane expenditure increased from $11,442/year in 1997 to $274,692/year in 2007. Desflurane expenditure increased from $5,855/year in 2002 to $29,340/year in 2007. Total cumulative expenditure for inhalational agents was $100,427/year in 1997, increasing to $326,038/year in 2007. Pharmacoeconomic modelling demonstrates that the cost of an inhalational agent for a 60-minute anaesthetic, at 1 Minimum Alveolar Concentration, at fresh gas flows of 1L/min (low flow), is $1.54 for isoflurane and $6.89 for Sevoflurane. At fresh gas flows of 6L/min (high flow), costs increase to $9.20 for Isoflurane and $47.47 for Sevoflurane. Cost modelling reveals if Sevoflurane usage between 1997 and 2007 would have been reduced by 40% per year and substituted for the cheaper inhalational agent Isoflurane, a total savings of $866,565 would have been achieved for this 11-year period. Similarly, conservative cost analyses predicts that if the current trends in volatile anaesthetic agents continue at Austin Health over the next 10 years, if a 40% reduction per year in Sevoflurane usage could be achieved by utilising Isoflurane in its place, a total net savings in excess of $1.8 million will result.

CONCLUSIONS:
Cost analyses of anaesthetic drugs is necessary is today’s economic climate. Low flow anaesthesia is a simple but highly effective method of cost minimization for inhalational anaesthetic agents. Cost containment is also influenced by the rational use of available inhalational agents.
An anatomic feasibibility study: Nerve transfer to the triceps muscle using the posterior division of the axillary nerve.

Liew J H, van Zyl N

BACKGROUND:
This study proposes the co-aptation of the posterior division of the axillary nerve to the lateral head of triceps nerve as a new, alternative option for triceps reconstruction in the tetraplegic patient. This study provides anatomical data in order to appraise the feasibility of nerve transfer to the triceps using the posterior division of the axillary nerve.

METHODS:
Morphologic features of the axillary nerve from the quadrangular space and the radial nerve from the triangular space were studied in 9 cadaveric arms under 2.0x loupe magnification. Nerve lengths, diameters, and branches were recorded.

RESULTS:
Average arm length was 312 mm. The average diameter of the posterior division of the axillary nerve was 2.5 mm whilst that of the lateral head of triceps nerve was 2.1 mm. Nerve transfer was possible in all upper limbs except one where no branch to the lateral head of triceps could be identified. In full adduction the average overlap of the nerve transfer was 16.75mm, whereas, when the arm was abducted to 90 degrees, the average amount of nerve overlap was 10.5mm.

CONCLUSIONS:
Nerve transfer from the posterior division of the axillary nerve to the lateral head of triceps is anatomically possible. It provides a possible alternative to reconstruct elbow extension with the advantages of preserving the anatomy and biomechanics of the native muscles, avoiding the need for synthetic prosthesis as well as avoiding donor defects from tendon graft harvest.
Blockade with soluble ICOS-Ig prolongs survival of cellular xenografts

Hodgson R, Christiansen D, Ierino FL, Sandrin MS

BACKGROUND:
Xenografts are one possible solution to the lack of donor organs for diseases such as Diabetes Mellitus. T cell costimulatory pathways are integral to acute cellular rejection against these grafts. Inducible Co-Stimulator (ICOS) pathway blockade has been shown to prolong allograft survival, but there is limited data for xenograft models. Our hypothesis is that local expression of the fusion molecule ICOS-Ig by cells in allograft or xenograft models will prolong survival of cellular grafts.

METHODS:
Porcine Iliac Endothelial cells (PIEC) were transfected with cDNA of the fusion molecule ICOS-Ig. Intracellular and secreted expression was confirmed and quantified using immunoperoxidase staining and Western Blot analysis. In vitro testing of supernatant in mixed lymphocyte reactions was performed. In vivo survival was examined using a subcutaneous graft model in mice.

RESULTS:
ICOS-Ig containing supernatant gave a 99.5% reduction in proliferation of an allograft mixed lymphocyte reaction. Similarly, xenogeneic proliferation was inhibited by 84.3%. In addition an 84.5% reduction in proliferation was observed when PIEC expressing ICOS-Ig were used as stimulators. PIEC-ICOS-Ig xenografts showed prolonged survival compared to wild-type PIEC xenografts (mean survival 34 vs 12 days, p=0.0025) in a subcutaneous graft models in Balb/c mice.

CONCLUSIONS:
Blockade of T cell co-stimulation by the fusion molecule ICOS-Ig has been demonstrated to decrease proliferation in allograft and xenograft in vitro models. Further, there is significant prolongation of survival of PIEC transfected with ICOS-Ig in vivo. These data suggest that further investigations for the role of T cell co-stimulatory blockade in xenografts, through the local expression of ICOS-Ig, are warranted.
Minimally invasive measurement of cardiac output during surgery and critical care: A meta-analysis of accuracy and precision.

Philip J Peyton, Simon Chong.

BACKGROUND:
When assessing the accuracy and precision of a new technique for cardiac output measurement, the commonly accepted criterion for acceptability of agreement with a reference standard is that the percentage error (95% limits of agreement/mean cardiac output) should be 30% or less. We reviewed published data on four different minimally invasive methods adapted for use during surgery and critical care: pulse contour techniques, esophageal Doppler, partial carbon dioxide rebreathing, and transthoracic bio-impedance, to assess their bias and percentage error in agreement with thermodilution.

METHODS:
An English language literature search identified published papers since 2000 which examined the agreement in adult patients between bolus thermodilution and each method. For each method a parametric assessment was performed using studies in which the first measurement point for each patient could be identified, to obtain a pooled mean bias and percentage error weighted according to the number of measurements in each study.

RESULTS:
47 studies were identified as suitable for inclusion: N studies, n measurements: mean weighted bias [% error] were: pulse contour N = 25, n = 714: 0.1 L/min [40.7%]; esophageal Doppler N = 2, n = 57: -0.8 L/min [42.1%]; partial CO2 rebreathing n = 145: 0.0 L/min [43.6%]; transthoracic bio-impedance N = 13, n = 435: -0.1 L/min [42.9%].

CONCLUSIONS:
No method has achieved agreement with bolus thermodilution which meets the expected 30% limits. The relevance in clinical practice of these arbitrary limits should be reassessed.
Local Expression of ICOS-Ig Promotes Xenograft Survival Through The Induction of Regulatory T Cells

Hodgson R, Ziolkowski A, Christiansen D, Simeonovic C, Ierino F, Sandrin M

BACKGROUND:
Xenografts are one possible solution to the lack of donor organs for diseases such as Diabetes Mellitus. The acute cellular rejection of xenografts is one of the critical processes that must be overcome. We have previously shown that blockade of T cell co-stimulation with locally expressed ICOS-Ig can prolong the survival of cellular xenografts. The mechanisms for this prolongation of survival have hitherto remained unknown, with the induction of regulatory T cells (Tregs) being one possibility. Tregs, through their secretion of IL10, TGFβ and interferon-γ, suppress activated T cells to downregulate the immune response, and may also have a role in tolerance to transplanted grafts. We show here that locally expressed ICOS-Ig induces Tregs and prolongs cellular xenograft survival.

METHODS:
Porcine Iliac Endothelial cells (PIEC) were transfected with cDNA encoding the fusion molecule ICOS-Ig. Subcutaneous xenograft transplants with wild-type PIEC or PIEC-ICOS-Ig were performed in BALB/c mice; either single grafts, or a dual graft model with a wild-type PIEC graft on one flank and a PIEC-ICOS-Ig on the opposing flank. Grafts were sampled for immunohistochemistry and real-time PCR at days 7 and 14, with overall survival also being measured.

RESULTS:
Locally expressed ICOS-Ig prolongs xenograft survival when compared with wild-type grafts (median survival 34 vs 12 days, p=0.0025). When wild-type PIEC and PIEC-ICOS-Ig cells are grafted in the same mouse, wild-type PIEC graft survival is prolonged (median survival 28 vs 12 days, p<0.05), indicating a systemic effect of ICOS-Ig. Increased numbers of Tregs were found in the perigraft region of wild-type PIEC grafts in the dual graft model when compared with wild-type PIEC single grafts at days 7 and 14.

CONCLUSIONS:
Locally expressed ICOS-Ig prolongs survival of cellular xenografts, with the mechanism both local and systemic. The presence of ICOS-Ig induces perigraft Tregs which are associated with prolonged survival of xenografts. These data suggest that locally expressed ICOS-Ig may play an important role in prolonging xenograft survival and the induction of tolerance through the presence of Tregs.
AUSTIN RESEARCH PRIZE WINNER 2010 (Clinical)

Risk factors of development of Acute Gangrenous Cholecystitis and its treatment outcomes

V Niumsawatt.

BACKGROUND:
Gangrenous cholecystitis is considered a more severe form of acute cholecystitis. The risk factors associated with this condition and its impact on morbidity and mortality compared to non-gangrenous acute cholecystitis is poorly defined.

METHODS:
Patients with histologically confirmed acute cholecystitis treated between 2005-2010 were identified from a prospectively maintained database. Those with gangrenous cholecystitis were then compared to those with non-gangrenous acute cholecystitis.

RESULTS:
184 patients with non-gangrenous acute cholecystitis and 106 patients with gangrenous cholecystitis were identified. The risk factors associated with gangrenous cholecystitis included older age (P 0.001), diabetes (P 0.049), delay in operation (P <0.001), temperature of >38 oC (P <0.001), tachycardia (P 0.002), detection of muscle rigidity on examination (P 0.01), elevations in white cell count (WCC) (P <0.001), C-reactive protein (CRP) (P 0.001), bilirubin (P 0.029) a GGT (P <0.001), and elevated urea and creatinine. (P <0.05). There was no overall difference in complications between the two groups. There was a lower incidence of common bile duct stones in the gangrenous cholecystitis group (25% versus 13% P = 0.017). Gangrenous cholecystitis was however associated with an increase in post-operative ICU/HDU requirement (P 0.023) and was associated with increased mortality (P 0.017).

CONCLUSIONS:
Gangrenous cholecystitis has certain clinical features and associated laboratory findings that may help differentiating it from non-gangrenous cholecystitis. It is associated with a higher incidence of mortality. Minimizing a delay in operative management, which is noted in this condition may potentially improve treatment outcomes.
ICOS-Ig Secreting Xenografts Have Prolonged Survival And Are Associated with Increased T Regulatory Cells And IL-10 Expression

Hodgson R, Christiansen D, Ziolkowski A, Mouhtouris E, Simeonovic C, Ierino F, Sandrin M

BACKGROUND:
Many patients die waiting for organ transplantation due to a lack of donor organs. Xenografts are an unlimited resource, however solutions to barriers such as acute cellular rejection have yet to be elucidated. T regulatory cells (Tregs), through their secretion of IL10, TGFβ and interferon-γ, suppress activated T cells to downregulate the immune response seen in acute cellular rejection, and may also have a role in tolerance to transplanted grafts. We have previously shown that blockade of T cell co-stimulation with locally expressed ICOS-Ig can prolong the survival of cellular xenografts and now show that this response is xeno-specific and associated with increased IL-10 expression and induction of Tregs.

METHODS:
Porcine Iliac Endothelial cells (PIEC) were transfected with cDNA encoding the fusion molecule ICOS-Ig. Subcutaneous xenograft transplants with wild-type PIEC or PIEC-ICOS-Ig were performed in BALB/c mice; either single grafts, or a dual graft model with a wild-type PIEC graft on one flank and a PIEC-ICOS-Ig on the opposing flank. Grafts were sampled at days 7 and 14 and characterised with immunohistochemistry, flow cytometry and Q-PCR.

RESULTS:
Locally expressed ICOS-Ig prolonged xenograft survival when compared with wild-type grafts (median survival 34 vs 12 days, p=0.0025). When wild-type PIEC and PIEC-ICOS-Ig cells were grafted in the same mouse, wild-type PIEC graft survival is prolonged (median survival 28 vs 12 days, p<0.05), indicating a systemic effect of ICOS-Ig. This result was found to be xeno-specific, with no prolongation of similarly grafted EL4 allografts. Immunohistochemistry revealed increased numbers of FoxP3+ cells in the perigraft region of both PIEC-ICOSIg grafts and dual PIEC and PIEC-ICOS-Ig grafts at days 7 and 14. Flow cytometry of the graft infiltrating lymphocytes revealed the majority of these FoxP3+ cells to be of the CD4+CD25+FoxP3+ Treg phenotype. Furthermore, Q-PCR of these grafts revealed differences in expression of IL-10 but not TGFβ or IFN-γ.

CONCLUSIONS:
The presence of ICOS-Ig induces perigraft Tregs which are associated with prolonged survival of xenografts. The increased expression of IL-10 in these grafts indicates a critical role of T cell/macrophage binding and antigen recognition in the presence of ICOS-Ig. These data suggest that locally expressed ICOS-Ig may play an important role in prolonging xenograft survival and the induction of tolerance through the presence of Tregs.
SAVE Study: Reduced volatile agent usage following introduction of Et-control system

Stanly Tay¹, Laurence Weinberg², Phil Peyton²; Juris Briedis³

¹Anaesthetic Registrar, Austin/Northern Health ² Staff Anaesthetist, Department of Anaesthesia, Austin Health ³ Director of Anaesthesia & Perioperative Medicine, Northern Health

BACKGROUND: Total cumulative expenditure for inhalational agents at Austin Hospital was $270,000 for the 2010 financial year. Anaesthesia pharmacoeconomic modelling in our department shows that inhalational agent costs will continue to escalate whilst resources remain finite. In order to evaluate strategies to reduce costs within a finite hospital budget, we hypothesised that the use of Et control on the Aisys Carestation anaesthesia delivery system (GE Healthcare®) during volatile anaesthesia will significantly reduce usage compared to current practice. The Aisys Carestation is an anaesthesia delivery system designed to minimise fresh gas and volatile usage by achieving and maintaining set target values using an automated algorithm with low-flow anaesthesia.

METHODS: Following ethics approval, numbers and duration of volatile general anaesthesia cases, along with volatile costs and CO2 absorbent costs were reviewed from Health Information Service and Pharmacy in a 12-week period prior to and a 12-week period after the introduction of Et-control. Inclusion criteria were all general anaesthesia requiring a volatile agent. Primary end-point was average cost per day of volatiles. We also surveyed Et-control use, looking at rates of utilisation plus flow rates used, to determine the generalisability of our findings.

RESULTS: Over the two time periods, there were 1818 vs. 1810 cases analysed with no statistical difference between gender (p=0.32), age group (p=0.87), ASA scores (p=0.73) or mean workload (153 vs. 160 hr/wk, p=0.37). Use of Et control on the Aisys Carestation anaesthesia delivery system showed a substantial reduction in inhalational agent cost ($376/day vs. $316/day, p=0.01) representing a 19.7% daily cost reduction when corrected for number of anaesthesia hours. Sevoflurane use was 182 bottles (45.5L) vs 148 (37L), Desflurane the same at 20 (4.8L), and Isoflurane the same at 1 (0.25L). CO2 absorbent cost did not increase significantly ($0.07/day). Our survey had a 65% response rate (1169/1810), and showed Et-control was used in 89% of cases, with a mean flow rate of 0.63 vs 3.2L/min.

CONCLUSIONS: Low flow anaesthesia is a simple but highly effective method of cost minimisation for inhalational anaesthetic agents. Use of Et-control on the Aisys Carestation anaesthesia delivery system significantly reduces volatile cost compared to previous routine practice. Real cost savings were approximately 20% or $35,000 per 10,000 general anaesthetic hours.

PERSONAL CONTRIBUTION

| Planning/conceptualization: | 80% |
| Laboratory work/data collection | 90% |
| Data analysis/discussion: | 90% |

Stanley Tay

Current Position: Full Time Clinical Anaesthetic Registrar

Stanley Tay is a 4th Year Full Time Clinical Anaesthetic Registrar with interest in pharmacoeconomic research especially in the development and validation of cost-minimization techniques and emerging technologies.
If we knew what we were doing it wouldn’t be research.

- Albert Einstein
Masters in Surgical Education

The Graduate Programs in Surgical Education are a new suite of qualifications offered by the University of Melbourne through its Department of Surgery and Medical Education Unit in partnership with the Royal Australasian College of Surgeons (RACS). This suite of programs addresses the specialised needs of teaching and learning in a modern surgical environment. The programs’ content recognises the unique challenges that characterise the clinical settings and advanced technologies that are increasingly important in surgical training. Effective teaching skills are essential attributes for educators responsible for training the next generation of surgeons in the complex sets of skills required for safe surgical practice. The programs allow surgeons to gain formal skills in teaching and educational scholarship.

Program delivery includes core and elective subjects delivered through a combination of workshops, distance and online delivery modes. The program will expose students to a range of educational methods, which in turn increase program flexibility, allowing these studies to be balanced with clinical commitments. The content reflects critical issues in the broader education community together with specific challenges for surgical education – the role of regulatory bodies, balancing clinical service with training, ethical imperatives for simulation-based education, safer working conditions including safe hours and more. Students have the option of enrolling in the Graduate Certificate, Graduate Diploma or Master of Surgical Education based on their own educational needs.

Program Structure: Program delivery includes core and elective subjects delivered through a combination of workshops, distance and online delivery modes. The program will expose participants to a range of educational methods, which in turn increase program flexibility, allowing these studies to be balanced with clinical commitments. Students have the option of enrolling in the Graduate Certificate, Graduate Diploma or Master of Surgical Education based on their own educational needs.

<table>
<thead>
<tr>
<th>Graduate Certificate:</th>
<th>Successful completion of the four core subjects</th>
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<tr>
<td>Graduate Diploma:</td>
<td>Successful completion of the core subjects required for the Graduate Certificate PLUS 50 points of study selected from the electives.</td>
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<tr>
<td>Masters:</td>
<td>Successful completion of the subjects required for the Graduate Diploma, including the Compulsory Subject Research Methods in Surgical Education PLUS completion of the Minor Thesis. Students intending to enrol in the Masters program must include Research Methods in Surgical Education as one of their electives</td>
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<tr>
<th>Core Subjects</th>
<th>Elective Subjects</th>
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<tr>
<td>Context of Surgical Education 12.5 points</td>
<td>Recruitment and Selection in Surgery 12.5 points</td>
</tr>
<tr>
<td>Learning and Teaching in Surgical Practice 12.5 points</td>
<td>Teaching Professional Skills in Surgery 12.5 points</td>
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<tr>
<td>Educational Theory for Surgical Training 12.5 points</td>
<td>Managing Underperforming Trainees 12.5 points</td>
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<tr>
<td>Curriculum Design in Surgical Education 12.5 points</td>
<td>Simulation in Surgical Education 12.5 points</td>
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<tr>
<th>Compulsory Subject for Master’s</th>
<th>Research Methods in Surgical Education 12.5 points</th>
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| Research Project | Minor Thesis – Surgical Education 50 points |
Program Objectives: The program will provide students with a thorough grounding in theory and practice of medical and surgical education, allowing them to become leaders in developing the next generation of surgeons. During the course, students will:

• gain a theoretical background in the principles of education,
• explore the contexts in which medical education is delivered,
• develop teaching skills to support learning in clinical and other professional settings,
• develop skills allowing them to create robust educational programs,
• be introduced to a range of methodologies for educational research,
• develop an appreciation of educational scholarship and,
• learn how to apply all of the above to surgical education.

Course Delivery & Time Commitment: The course will be delivered part-time, with students expected to enrol in 2 subjects each semester. All subjects (with the exception of the Minor Thesis) will be taught using multiple delivery modes. This will include one full day (8 hours) workshop plus self-paced learning activities (eg. webinars, moderated interactive discussions, and tutorials) spread over 13-week semesters. The self-paced learning activities will be accessed through an online learning management system. Students should expect to commit approximately 8 - 10 hours per week to each subject. This includes formal learning activities, reading and private study.

Assessment: Each subject has specific assessment requirements, details of which can be found at www.mccp.unimelb.edu.au/surgical-ed. Typical assessment activities include completion of (or participation in) online activities, presentations and an assignment or essay.

Course Dates and Fees for 2012: In 2012, the following subjects will be offered:

**Semester 1**: 6 Feb – 11 May 2012
- Context of surgical education (workshop 13th February 2012)
- Learning and teaching in surgical practice (workshop 14th February, 2012)

**Semester 2**: 23 July – 26 October 2012
- Educational theory for surgical training (workshop 30th July, 2012)
- Curriculum design in surgical education (workshop 31st July, 2012)

Course Details: Current course fees can be found at www.mccp.unimelb.edu.au/surgical-ed. More information on the course and details of each subject can be found on the course website at www.mccp.unimelb.edu.au/surgical-ed

Venue: Workshops will be conducted at the Royal Australasian College of Surgeons, 250-290 Spring Street, East Melbourne VIC 3002 Australia.

Entry Requirements & Applications

All applications for entry will be assessed by the Selection Committee who will evaluate the applicant’s ability to successfully pursue the program. The following criteria specify entry requirements:

1. A Bachelor of Medicine/Bachelor of Surgery or equivalent qualification plus,
2. At least two years of relevant clinical work experience. It is important that students have an appreciation of clinical practice before they commence studies for this course.
3. Meet the English language requirements of the University of Melbourne. International Medical Graduates must also meet the English language standards required by the Medical Board of Australia (an IELTS score of 7.0 in each of the four components - listening, reading, writing and speaking).

The Selection Committee may conduct interviews and tests and may call for referee reports or employer references to assist in the selection process. Information on how to apply can be found at www.mccp.unimelb.edu.au/surgical-ed
I will not say I failed a thousand times. I will say that I discovered there are thousand ways that can cause failure

- Thomas Edison

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