Surgical Research Society

51st Annual Scientific Meeting

14 November 2014
Adelaide, South Australia

Basil Hetzel Research Institute
Queen Elizabeth Hospital
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Welcome

Welcome to the 51st Annual Scientific Meeting.

Today we have 23 ten minute oral presentations, and 6 posters scheduled.

It will be appreciated if you are ready for your presentation on time and are prepared to keep within the time limit. Please make sure your poster has been displayed, and don’t forget to pick it up again after the meeting. Posters will be displayed in the annexe.

Before we start, please make sure you have registered at the registration desk just outside in the atrium. Whilst you are in the atrium, please do not make any loud noise as there are people working in open offices upstairs and around you.

If you need to use a phone, there is a room provided off of the lunch room, aptly signed “Phone Call Room”. Otherwise you can make your calls outside but you will need to be let back in.

Tea, percolated coffee and water will be available all day in the atrium, which is where morning tea, lunch and afternoon tea will be held.

Smoking is not permitted within the property, including outdoor areas such as the car park.

There is no onsite all day visitor parking at the BHI. Attendees will have to park at the Queen Elizabeth Hospital car park across the road. The cost for the day is approximately $13.00.

If you have any questions, please approach the registration desk.

We hope you have an enjoyable and productive day.

Organised by: Surgical Research Society
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Program 2014
Surgical Research Society 51st Annual Meeting
Friday 14 November 2014
Basil Hetzel Institute, The Queen Elizabeth Hospital
Chair, SRS: Leigh Delbridge
Convenor: Guy Maddern

08:30  Registration, Opening and Welcome
Professor Leigh Delbridge

Session 1
Chair, Mr Richard Hanney

09:00  Guest Speaker – SUS Visitor, Dr Taylor Riall, MD, PhD, FACS
Professor in the Department of Surgery/the John Sealy Distinguished Chair in Clinical
Research at the University of Texas Medical Branch (UTMB) in Galveston.
Pancreatic Cancer: Translation of Outcomes Research into Practice.

09:30  Oral Presentations (Clinical - Colorectal)
1. Naseem Mirbagheri 4. Rebekah Jaung
2. Primal Singh 5. Cameron Wells

10:30  Morning Tea

Session 2
Chair, Professor John Windsor

11:00  Guest Speaker – AAS Visitor, Dr George Chang, MD, MS, FACS, FASCRS
Associate Professor of Surgery, Chief of Colorectal Surgical Oncology/Associate Medical
Director of the Colorectal Center/Director of Clinical Operations for the Minimally Invasive and
New Technologies in Oncology Surgery Program at the University of Texas, MD Anderson
Cancer Center.
RAMPing up the Quality of Rectal Cancer Surgery

11:30  Oral Presentations (Cancer Genetics)
7. Steven Due 10. Siddhartha Deb
8. David Gyorki 11. Deborah Wright
12:30  
*Lunch in the foyer*

*Poster Display with Poster Discussion at 1.00pm*  
*(ANNEXE – please take your lunch through)*

P1. Li Lian Kuan  
P2. Wayne Ng  
P3. Pramudith Sirimanna  
P4. Anannya Chakrabarti  
P5. Reizal Rosli  
P6. Sarah Aitken  
P7. Anannya Chakrabarti

**Session 3**  
Chair, Professor Leigh Delbridge

1.30  
*Jepson Lecture - Professor Julian Smith MBBS, MS, Grad.Cert. Surg.Ed., FRACS, FACS, FCSANZ, FAICD*

Head of the Department of Surgery (Monash Medical Centre) at Monash University/Head of the Department of Cardiothoracic Surgery at Monash Health (Monash Medical Centre)  
*Research in Surgical Education – a Personal Perspective*

2:00  
*Oral Presentations (Clinical – Gastrointestinal and Endocrine)*

13. Joseph Do Woong Choi  
14. Pramudith Sirimanna  
15. Ryan Holmes  
16. Ahmer Hameed  
17. Jaewook Oh  
18. Bruce Su’a

3:00  
*Afternoon Tea*

**Session 4**  
Chair, Professor Marc Gladman

3:40  
*Oral Presentations (General – Oncology, Trauma, Vascular)*

19. Sarah Aitken – Recipient of the Inaugural Senior Lecturer College Fellowship  
20. Kheng-Seong Ng  
21. Anthony Glover  
22. Deepali Kamalapurkar  
23. Helen Pham

4:30  
*Short break*

4:45  
*Presentation of Young Investigator Award, DCAS Award, Travel Grants and Best Poster Award*

5:00  
*Summary and Close*
Biographies
Taylor S. Riall, M.D., Ph.D. is Professor in the Department of Surgery and the John Sealy Distinguished Chair in Clinical Research at the University of Texas Medical Branch (UTMB) in Galveston.

Dr. Riall completed her general and pancreaticobiliary surgery training at Johns Hopkins in 2005. In 2007, she received her Ph.D. in Clinical Science from UTMB with a focus in Biostatistics and health services/comparative effectiveness research. Her clinical practice includes complex pancreaticobiliary surgery and general surgery. In 2009 she established the Center for Comparative Effective and Cancer Outcomes at UTMB. The current research focus of the Center includes health services/comparative effectiveness research, surgical outcomes research, quality improvement initiatives, and patient-centered outcomes research.

Dr. Riall is currently funded by the NIH and the Cancer Prevention and Research Institute of Texas (CPRIT). She is co-director of a T32 training grant which provides protected time to train surgical residents interested in outcomes and health services research. Her research involves population-based outcomes in pancreatic cancer and comparative effectiveness studies of the management of gallstones disease. She is also interested in national trends in over- and under-utilization of testing/treatment, as well as quality of care. She has over 120 publications in high quality journals. She has been elected to membership in the Southern Surgical Association, the American Surgical Association, the Society for Surgery of the Alimentary Tract, the Society of University Surgeons, the Association for Academic Surgery and many more.
George J. Chang, M.D., M.S. is an Associate Professor of Surgery, Chief of Colorectal Surgical Oncology, Associate Medical Director of the Colorectal Center, and Director of Clinical Operations for the Minimally Invasive and New Technologies in Oncology Surgery Program at the University of Texas, MD Anderson Cancer Center.

He is a graduate of the University of California, Berkeley (Biochemistry) and the University of California, Los Angeles School of Medicine (Medical Doctorate). He completed his residency at the University of California, San Francisco and Fellowship in Colon and Rectal Surgery at the Mayo Clinic. He received his Master of Science in Clinical Research degree from The University of Texas Health Sciences Center.

He is a colon and rectal surgical oncologist and health services researcher, whose research program is focused on improving the outcomes and the delivery of cancer care through clinical comparative effectiveness, patient centered outcomes, quality measurement, and clinical trials based research. He is an internationally recognized expert in colorectal cancer treatment, outcomes, and post-treatment risk stratification.

He has extensive experience working with large cancer registry data including for the performance of large observational studies to inform treatment decisions and outcomes and for the development of clinical calculators. His research program is or has been funded by the Patient Centered Outcomes Research Institute, the National Cancer Institute and the ASCO Conquer Cancer Foundation.
Julian Smith, a Cardiothoracic Surgeon, has been Professor and Head of the Department of Surgery (Monash Medical Centre) at Monash University and Head of the Department of Cardiothoracic Surgery at Monash Health (Monash Medical Centre) since 2001.

He is currently a Councillor of the Royal Australasian College of Surgeons and the Chairman of Professional Development and the Academy of Surgical Educators. His previous College Council role was as Chairman of the Division of Research, Audit and Academic Surgery. He is the immediate past-President of the Australian and New Zealand Society of Cardiac and Thoracic Surgeons.

His main clinical and research interests are in less invasive cardiac surgery, robotically assisted surgery, mechanical support of the circulation, cardiothoracic surgery audit/databases, the use of evidence based medicine by surgeons and surgical education.
Sonographic Assessment of Gastric Function in Patients Following Major Colorectal Surgery

Naseem Mirbagheri¹, Graham Dunn², Michael Suen¹ & Marc A Gladman¹

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². Department of Radiology, Concord Repatriation General Hospital, Concord, NSW, Australia.

Introduction
Gastrointestinal dysfunction, manifesting as paralytic ileus, is a common morbidity after abdominal surgery. Currently, there is no objective, bedside tool to assess gastrointestinal function. This study aimed to evaluate bedside sonographic measurement of liquid gastric emptying, as a surrogate marker of gastrointestinal function, in patients following major colorectal surgery.

Methods
Following administration of 250mls of water, gastric antral cross-sectional area was measured 10 minutely using a portable machine (The Edge®, SonoSite). Time to complete emptying (T100% water) was used as an objective marker of liquid gastric emptying. 30 Healthy volunteers (HV) were studied to establish a normal range. Gastric function was assessed before and after major colorectal surgery in 30 patients.

Results
Median T100 % water for 30HV was 20min, giving a normal range of 10-40mins. 30/39 patients completed the study protocol. Median (range) T100% water for the patient group before surgery was 20 (10-40) mins with all patients falling within the normal range. On postoperative Day1, T100 % water was significantly prolonged with a median of 45 (10 to >60min, P<0.0001); notably T100 % water was outside of the normal range in 15 patients (50%). On Day2, gastric function was normal in 20 patients (67%). This group had less nausea (P=0.0003), days to flatus (P=0.011), earlier diet (P= 0.001), fewer cases of ileus (P=0.002) and shorter hospital stay (P=0.040).

Conclusion
Sonographic assessment of gastric emptying is feasible and its use in postoperative patients identified differences compared to normal/pre-op values. Patients with normal emptying on Day2 had earlier return of gut function and hospital discharge.
Randomised Controlled Trial of Perioperative Simvastatin Therapy in Major Colorectal Surgery

Singh P*, Lemanu D*, Soop M^, Bissett I¶, Harrison JΔ, Hill AG*

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Correspondence to: Dr P Singh (e-mail: dr.parrysingh@gmail.com)

Introduction
Statins have numerous benefits relevant to abdominal surgery and in retrospective clinical studies, their use has been associated with a reduction in the systemic inflammatory response syndrome (SIRS), wound infection and anastomotic leak following colorectal surgery.1,2 This study aimed to prospectively investigate whether perioperative statin therapy can attenuate the surgical pro-inflammatory response and reduce complications following major colorectal surgery.

Methods
A multi-centre, double-blind, randomised controlled trial was conducted at three tertiary hospitals in the Auckland Region between October 2011 and August 2013. Patients undergoing elective colorectal resection for any indication or reversal of Hartmann’s procedure were randomised to receive either 40mg oral simvastatin or placebo once daily for 3-7 days before surgery till 14 days after surgery. The primary outcome was the total incidence of complications for 30-days postoperatively. Secondary outcomes included the systemic and peritoneal cytokine response (IL-1α, IL-1β, IL-6, IL-8, IL-10, TNFα), measured on postoperative day 1.

Results
There were 132 patients included in the study (65 simvastatin, 67 placebo). There were no significant differences between the two groups at baseline. There were no significant differences between the two groups in the incidence, grade and type of postoperative complications. Systemic levels of IL-6, IL-8 and TNFα, and peritoneal concentrations of IL-6 and IL-8, were significantly lower in the simvastatin group postoperatively. CRP levels were significantly lower in the simvastatin group on postoperative days 1 to 3.

Conclusion
Perioperative simvastatin therapy in major colorectal surgery attenuates the early pro-inflammatory response to surgery but does not reduce postoperative complications.
Young-Onset Colorectal Cancer In Australia: A Population-Based Study

Michael Suen¹, S Alzahrani¹, Yuen Yi Lee¹, Natasha Nassar², Marc A Gladman¹

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². Clinical and Population Perinatal Health Research, Kolling Institute of Medical Research, University of Sydney, NSW, Australia

Introduction
Young-onset colorectal cancer (yCRC) is often presumed to be increasing in incidence and to carry a worse prognosis than in older patients. If yCRC occurs in context of HNPCC, tumour location may favour the right colon. The aim of this study was to determine the incidence, trends, tumor location and stage and survival of patients with yCRC in Australia.

Methods
A population-based study using linked statutory Cancer Registry Data and Registered Deaths of 34,119 patients diagnosed with CRC in NSW, 2000-2008. yCRC was defined as CRC in patients <50yrs and their characteristics and tumor-related factors compared with patients diagnosed with CRC in 50+yrs. Age-sex standardized incidence rates and trends were examined using Poisson regression analysis. 5-year cancer-specific survival rate for yCRC patients was compared with 50+yrs.

Results
yCRC accounted for 6.2% of cases (n=2,128; 1,101 males [51.7%]). The incidence of yCRC decreased slightly from 2001:13.7/100,000 to 2008:11.8/100,000; P=0.57. Tumours were located in the right colon in 19.2% (n=408) of yCRC (versus 28.2% [n=9,029] in 50+yrs), instead favoring the rectum (34.6% [n=736] versus 26.1% [n=8,342] in 50+yrs, P<0.001). 5-year cancer-specific survival was superior in yCRC (68.9%; 95% CI 66.3%-71.2%) compared with 50+yrs (65.8%; 95% CI 65.1%-66.5%; P<0.001), despite more metastatic disease (21.9% [n=466] versus 15.2% [n=4,873] in 50+yrs, P<0.001).

Conclusion
This population-based study has revealed that yCRC is not increasing in Australia. yCRC tended to occur more commonly in the rectum than in the proximal colon and was more advanced at presentation. Cancer-specific survival was superior compared to older patients.
Demographics and Trends in the Acute Presentation of Diverticular Disease – A National Study

Vather R, Broad J, Jaung R, Robertson J, Bissett I

Introduction
Diverticular disease (DD) is a major health problem in the Western world. This study aimed to describe demographics and trends in acute DD admissions in New Zealand.

Methods
Information pertaining to acute hospital admissions between January 2000 and June 2012 for a primary diagnosis of large bowel DD was retrieved from an ICD-10 coded national database. This contained electronic records of clinical discharge summaries from all New Zealand public hospitals and included patients with acute diverticulitis, diverticular bleeds and obstruction due to DD.

Results
There were 25,167 acute admissions for DD. Mean age was lower in men than women (61.4 vs 67.4 years, p<0.001). Although men comprised 45.2% of the cohort they were over-represented in the 18-44 year group (68.6% vs. 31.4%; p<0.001). The number of admissions per year increased by 1,300 (7.5% /year) between 2001 and 2011. This exceeded New Zealand’s rate of population growth (0.8% /year). Admissions were higher in more deprived populations (p<0.001). During the study period LOS reduced from 5.8 days to 4.1 days (p<0.001), CT scanning doubled (29.7% to 59.2%; p<0.001), the use of inpatient colonoscopy (26.1% to 13.2%; p<0.001) and emergent surgery (14.8% to 7.2%; p<0.001) were halved and percutaneous drain use increased from 0.6% to 1.1% (p=0.003).

Conclusion
Acute DD is a source of considerable morbidity in New Zealand and the number of hospital admissions have increased dramatically over the last decade. There is also an unexpectedly high rate of admissions for young males. These findings have important implications for service provision.
Temporary Diversion Ileostomy Is An Independent Long-Term Predictor For The Development Of Anterior Resection Syndrome

Cameron I. Wells, Ryash Vather, Michael J.J. Chu, Jason P. Robertson, Ian P. Bissett. Department of Surgery, The University of Auckland, New Zealand

Introduction
Evacuatory dysfunction after distal colorectal resection varies from incontinence to obstructed defaecation and is termed anterior resection syndrome. This study aimed to identify risk factors for the development of anterior resection syndrome.

Methods
All anterior resections undertaken at Auckland Hospital from 2002-2012 were retrospectively evaluated. An assortment of patient and peri-operative variables were recorded. Cases were stratified by occurrence of anterior resection syndrome symptoms from 1-5 years post-operatively.

Results
277 patients were identified. Prevalence of anterior resection syndrome decreased progressively from 61% at 1 year to 43% at 5 years. Univariate analysis identified anastomotic height, surgeon, pT stage, procedure year and temporary diversion ileostomy as recurring significant correlates ($p<0.05$). Logistic regression identified lower anastomotic height (OR 2.12, 95%CI 1.05-4.27; $p=0.04$) and obstructive presenting symptoms (OR 6.71, 95%CI 1.00-44.80; $p=0.05$) as independent predictors at 1 and 2 years respectively. Post-operative chemotherapy was a predictor at 1 year (OR 1.93, 95% CI 1.04-3.57; $p=0.03$). Temporary diverting ileostomy was an independent predictor at 2 (OR 2.49, 95% CI 1.04-5.95; $p=0.04$), 3 (OR 4.17, 95% CI 1.04-16.78; $p=0.04$), 4 (OR 8.05, 95%CI 1.21-53.6 $p=0.03$), and 5 years (OR 49.60, 95% CI 2.17-1134.71; $p=0.015$) after correcting for anastomotic height.

Conclusion
Anastomotic height, post-operative chemotherapy and obstructive presenting symptoms were independent predictors at 1 and 2 years. Temporary diversion ileostomy was an independent predictor for the occurrence of anterior resection syndrome at 2, 3, 4, and 5 years even after correcting for anastomotic height. Prospective assessment is required to facilitate more accurate risk factor analysis.
Comparing Oncological Outcomes of Laparoscopic Versus Open Surgery for Colon Cancer: Analysis of a Large Prospective Database


Introduction
Laparoscopic surgery is increasingly utilised in the treatment of colon cancer, with level one evidence of improved short term outcomes compared to open surgery. Oncological outcomes have also been shown to be equivalent, but only in the setting of randomised controlled trials on highly selected patients. The aim of this study is to investigate whether this finding holds true in a more general clinical practice.

Methods
Analysis of prospectively collected data on colon cancer surgery between 2003 and 2009 was undertaken, utilizing the linkage and analysis resources of the BioGrid Australia oncological database. Five year overall survival, and cancer specific survival rates for open and laparoscopic surgery were compared, and cox regression analysis performed to control for the confounders of age, sex, body mass index (BMI), ASA score, hospital site, year surgery performed, procedure, tumour stage, and adjuvant chemotherapy.

Results
During the study period 1387 patients underwent resection for colon cancer. There were significant differences between the laparoscopic and open cohorts in BMI, procedure performed, post-operative complication rate, and tumour stage. Five year overall survival was higher in the laparoscopic group (75.9% vs 69.2%, P = 0.015), with no difference in cancer specific survival (82.7% vs 78.3%, P = 0.074). Cox regression analysis showed no difference in 5 year overall survival (P = 0.254), or cancer specific survival (P = 0.866) when confounders were accounted for.

Conclusion
This large prospective clinical study validates previous trial results, and confirms that there is no difference in oncological outcome between laparoscopic and open surgery for colon cancer.
The Oestrogen Receptor: A Novel Therapeutic Target in Oesophageal Adenocarcinoma

Due SI, Watson Di, Bastian I, Sukocheva O, Hussey Dj.

**Introduction**
Oesophageal adenocarcinoma (OAC) is a highly lethal malignancy and is increasing in incidence faster than any other cancer. Preliminary data from our laboratory indicate that OAC tissues and cell lines express oestrogen receptors (ERs), and therefore may respond to therapy with selective oestrogen receptor modulators (SERM).

**Methods**
Immunohistochemistry was used to identify ERα and ERβ in human OAC resection specimens. ER expression in OAC cell lines was characterised by Western analysis. OAC cell lines were subcultured and treated with SERM and conventional chemotherapy agents. Treatment effects were assessed with an MTS cell proliferation assay and dose-response curves generated. Cell killing via apoptosis was confirmed using annexin V/PI flow cytometry.

**Results**
Human OAC specimens were found to express ERα and ERβ. ERs were also identified in ten OAC cell lines. Treatment experiments were conducted in two cell lines (OE-19 and OE-33), which expressed both ERα and ERβ. IC50 values for OE-19 and OE-33 were 11.2 and 7.1 μM for tamoxifen, 19.6 and 4.7 μM for cisplatin, and 1.7 and ~5.0 μM for 5-fluorouracil (5-FU), respectively. Apoptosis was detected in 28.4% and 60% of cells treated with tamoxifen, 26.1% and 28.6% cells treated with cisplatin, and 22.2% and 27.3% cells treated with 5-FU at their IC50 concentrations. Combined SERM and chemotherapy treatment demonstrated an additive effect on cell death.

**Conclusion**
ERs are present in OAC cells, and these cells respond to treatment with SERM *in vitro*. The addition of SERM to existing chemotherapy drugs in this setting appears to be feasible.
Developing a Protocol for the Identification, Phenotyping and Culture of Tumour Infiltrating Lymphocytes from Resected Melanoma Metastases

Gyorki DE\(^1,2\), Westwood JA\(^3\), Petrone P\(^3\), Neeson P\(^3\), Darcy PK\(^3\), Spillane J\(^1\), Henderson MA\(^1\) And Kershaw MH\(^3\)

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Introduction
Melanoma is a highly immunogenic malignancy. Tumour infiltrating lymphocytes (TIL) are located within melanomas and recognise a variety of epitopes on the tumour cell. TIL are unable to perform their normal immune function due to a variety of immunosuppressive mechanisms employed by the tumour. We sought to identify and phenotype TIL from resected melanoma specimens and grow them in culture to create a translational research tool.

Methods
Patients undergoing surgical resection for metastatic melanoma were prospectively recruited to the study. A portion of the resected specimen was delivered fresh and sterile from the operating theatre to the laboratory. A single cell suspension was created to allow phenotyping of TIL using flow cytometry with a dedicated panel of immune markers. Fragments of tumour were placed in cell culture from which TIL irrupted and proliferated, using interleukin-2 as a growth factor.

Results
Of 13 patients recruited, 11 have had evaluable tissue. The specimens were subcutaneous (45%), nodal (36%), intramuscular (9%) and lung (9%). TIL were successfully grown in culture in 100% of evaluable cases. A flow cytometry panel was able to classify TIL into effector and regulatory T cell subsets and further characterise these using markers of activation and differentiation. We identified a wide variation in TIL phenotype between melanoma specimens.

Conclusion
A protocol for the fresh and sterile transfer of tissue from the operating theatre to the laboratory allows molecular characterisation of TIL from resected melanoma specimens. This is an invaluable tool to study tumour-host interactions in patients with advanced melanoma.
New Predictive and Prognostic Markers for ACC Identified Utilising Immunohistochemistry and Tissue Microarray Technology

Dr. Julian C. Y. Ip, MBBS, B Med Sc (Hons)¹,², Dr. Tony C. Y. Pang, Mbiostat MS, FRACS²,⁴, Dr. Anthony R. Glover, MBBS FRACS¹,²,³, Dr. James C. Lee, MBBS, FRACS¹, Dr. Justin S. Gundara, MBBS¹,², Dr. Jing Ting Zhao, Phd¹,², Dr. Patsy Soon, Phd, FRACS⁵, Prof. Bruce G. Robinson, FRACP, MD¹,², A/Prof. Anthony J. Gill MBBS, FRCPA¹,⁶, Prof. Stan B. Sidhu, Phd, FRACS¹,²,³

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Introduction

Adrenocortical carcinoma (ACC) is a rare but highly lethal malignancy with limited treatment options. The aim of this study was to identify novel protein signatures that would predict clinical outcomes in a large cohort of patients with ACC.

Methods

A tissue microarray was generated from the paraffin tissue blocks of 61 patients with complete clinical data. Based on the results of previous gene expression microarray profiling studies, candidate protein biomarkers were identified using immunohistochemistry. Patterns of staining were compared with clinical outcomes and a multivariate analysis undertaken to identify potential predictive and prognostic biomarkers.
Results
Median overall survival was 45 months, with the 5-year overall survival being 44%. Median disease-free survival was 58 months, with a 44% 5-year disease-free survival. The proliferation marker Ki-67 and DNA topoisomerase TOP2A were associated with significantly poorer overall and disease-free survival. There was also a strong correlation between the transcriptional repressor EZH2 and TOP2A expression, suggesting a novel role for EZH2 as an additional marker of prognosis. In contrast, increased expression of the BARD1 protein, with its ubiquitin ligase function, was associated with significantly improved overall and disease-free survival, which has yet to be documented for ACC.

Conclusion
We report on a novel panel of protein markers that have been validated in a cohort of patients with ACC that are able to predict both poor and improved survival outcomes. It is hoped that these new markers will aid in tailoring additional therapy as well as being potential targets of molecular therapy themselves.
RAD21 Cohesion Overexpression is a Prognostic and Predictive Marker Exacerbating Poor Prognosis in KRAS Mutant Colorectal Carcinomas.

Siddhartha Deb1, Huiling Xu2, Jurriaan B Tuynman3, Joshy George4, Yuqian Yan5, Jason Li6, Robyn Ward7, Neil Mortensen3, Nicholas Hawkins7, Michael Mckay8, Robert G Ramsay2, Stephen B Fox4.

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7. School of Medical Sciences, University of New South Wales, Sydney, NSW, 2052, Australia.
8. University of Sydney and North Coast Cancer Institute, Lismore, NSW 2480, Australia

Introduction
RAD21 is a component of the cohesion complex and is integral to chromosome segregation and error-free DNA repair. RAD21 is functionally important in tumour progression but its role in colorectal carcinoma (CRC) is unclear. We therefore assessed its clinicopathological and prognostic significance in CRC, as well as its effect on chemosensitivity.

Methods
A retrospective observation study examined RAD21 expression in 652 CRCs using a tissue microarray approach. Correlation with clinicopathological factors including gender, tumour grade, mucinous subtype, TNM stage, disease-specific survival (DSS), BRAF and KRAS mutation status, tumour p53 immunostaining, tumour microsatellite instability and tumour CpG island methylator phenotype was performed. Colorectal cancer cell clones with stable RAD21 knockdown were generated and tested for cellular sensitivity to conventional chemotherapeutic drugs.

Results
RAD21 expression was significantly correlated with male gender (56.7% vs 43.3%, P=0.02), well-differentiated histology (14.4% vs 4.0%, P=0.0001), higher T-stage (36.1% vs 27.0%, P=0.01), presence of metastasis (18.8% vs 12.6%, P=0.03), and shorter DSS (hazard ratio (HR) 1.4, 95% CI 1.1 to 1.9, P=0.01) in both univariate and multivariate analysis. RAD21 expression was associated with shorter DSS in patients with KRAS mutant tumours (HR:2.6, 95% CI:1.4-4.3, P=0.001) and in patients receiving adjuvant chemoradiotherapy (HR:1.9, 95% CI:1.2-3.0, P=0.008). Colorectal cancer cells with RAD21 knockdown exhibited enhanced sensitivity to 5-fluorouracil, either alone or in combination with oxaliplatin.

Conclusion
RAD21 expression in CRC is associated with aggressive disease especially in KRAS mutant tumours and resistance to chemoradiotherapy. RAD21 may be an important novel therapeutic target.
Impact of Inconsistencies in Clinicopathological Data on Survival and Molecular Analyses

Wright DM¹, Mehta SY², Munro F¹, Merrie AEH³, Print CG² and McCall J¹

Introduction
Translational research efforts are being made to combine biological and clinical data to improve outcomes for cancer patients, however cancer databases report error rates of up to 27% in clinical datasets. Despite this, inadequate attention is paid to the impact of these errors on translational research findings.

Methods
Review of the clinicopathological annotations of 206 prospectively collected colorectal cancer samples from a New Zealand cohort elucidated the presence of data inconsistencies. The aim of this study was to carefully revise these data, to evaluate the impact of data revision on survival analyses and gene expression associations, and to implement processes to avoid error and omission during future data collection.

Results
Staging data was found to be missing from 50% of samples, and disease recurrence data from 25%. Survival analyses showed significant differences between the original and revised datasets. Disease free survival (DFS) at five years was 62% in the original dataset and 83% in the revised data set (P=0.005). For 106 of these tumours, revision of clinicopathological tumour annotation alone was found to result in a statistically significant association between DFS and APC expression (P<0.05) that was not apparent in the original data (P=0.09).

Conclusion
This study demonstrates that accurate clinicopathological data play a critical role in translational research. Moreover, these results support the need for optimal methods to prevent, detect and correct inaccuracies in the clinicopathological annotations used for translational research to be established, as are being implemented to our dataset.
**APR-246/PRIMA-1**

**Delays Growth and Induces Apoptosis in Oesophageal Adenocarcinoma Expressing Mutant P53**

David SH. Liu, Nicholas Clemons, Matthew Read, Christina Fennell, Carleen Cullinane, Cuong P. Duong, Wayne A. Phillips.

**Introduction**

Oesophageal adenocarcinoma (OAC) has poor clinical outcomes with limited treatment options. p53, a master tumour suppressor protein is mutated in 70% of OAC, resulting in resistance to chemo-radiotherapies and poor patient survival. In this study, we evaluated the potential therapeutic effects of restoring wild-type activity to mutant p53 protein in OAC, using the small molecular compound APR-246.

**Methods**

Twelve cell lines (8 mutant, 3 null and 1 wild-type p53) were treated with APR-246, and their response measured using clonogenic survival, proliferation, cell cycle and apoptosis assays. Ectopic expression and gene knockdown studies of mutant p53 were performed to interrogate p53-dependent drug effects. Wild-type p53 target gene expression was examined using RT-qPCR and western blot. The growth inhibitory effects of combining APR-246 with conventional chemotherapies were also evaluated while *in-vivo* drug activity was assessed using cell line and patient derived xenograft models.

**Results**

APR-246 preferentially induced apoptosis in OAC cells harbouring p53 mutations and led to expression of wild-type p53 target genes. Sensitivity to APR-246 correlated with cellular levels of mutant p53 protein. Ectopic expression of mutant p53 genes sensitised p53-null cells to APR-246, whilst p53 gene knockdown diminished drug activity. Importantly, APR-246 synergistically enhanced the inhibitory effects of cisplatin, 5-flurouracil and epirubicin in a mutant p53 dependent manner. Finally, APR-246 demonstrated potent anti-tumour activity in cell line and patient derived xenograft models, and restored chemo-sensitivity to a cisplatin/5-flurouracil resistant xenograft model.

**Conclusion**

Restoring wild-type activity to mutant p53 protein using APR-246 is a promising therapeutic strategy for OAC.
Cinacalcet Associated Acute Potassium Rise Associated with Hypocalcaemia after Arathyroidectomy for Renal Hyperparathyroidism

Guan C. Chong, Fracs, Frcs Facs, Joseph Do Woong Choi, Mbbs, B Sc (Adv), Tack Tsiew Lee Fracs.

Introduction
An impression that patients with prior treatment with cinacalcet and undergoing parathyroidectomy for renal hyperparathyroidism had greater acute potassium rise and hypocalcaemia intraoperatively/postoperatively day 0 prompted this study.

Methods
A single institution study was performed between January 1993 and August 2014. Sixteen patients were on cinacalcet prior to parathyroidectomy, whilst 106 patients were controls. Perioperative biochemical and histological variables were compared, in particular, intraoperative and postoperative potassium and corrected calcium.

Results
81.25% of the cinacalcet group recorded an intraoperative or postoperative day 0 potassium value ≥6.00mmol/L compared to 2.99% in the controls (P<0.001). More importantly, 43.75% of the cinacalcet group registered an intraoperative or postoperative day 0 potassium value ≥7.00mmol/L compared to 1.49% in the controls (P<0.001). 75.00% of cinacalcet patients had a potassium rise of ≥1mmol/L from preoperative value compared to 11.94% (n=8/67) (P<0.001). This was correlated with greater degree of hypocalcaemia at postoperative day 0 (2.09 ± 0.22 vs. 2.31 ± 0.28 mmol/L, (P< 0.01)) and greater need for IV calcium (93.75% vs. 43.40%, (P < 0.001)) in the cinacalcet group compared to controls.

Conclusion
This is the first report of acute rise in potassium seen in the intraoperative/postoperative day 0 periods following parathyroidectomy in patients on cinacalcet for renal hyperparathyroidism. This was correlated with greater degree of hypocalcaemia and greater need for intravenous calcium. The authors propose that intracellular potassium mobilises out of cells due to hypocalcaemia to maintain extracellular electrical neutrality. Our findings have led us to alter our protocol of intraoperative monitoring to prevent serious complications.
Validation Of A Virtual Reality Simulation Model For Laparoscopic Appendicectomy And Incorporation Into A Proficiency-Based Curriculum

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Introduction
Proficiency-based training curricula using virtual reality (VR) simulation improves operating theatre performance. Surprisingly, training in laparoscopic appendicectomy (LA) has received little attention. This study aimed to validate a VR LA model as a training and assessment tool and identify benchmarks of proficiency prior to incorporation into a training curriculum.

Methods
10 experienced (>50 LAs), 8 intermediate (10-30 LAs) and 20 inexperienced (<10 LAs) operators were recruited. Construct validity of a high-fidelity VR LA simulator (consisting of guided/unguided modules) was determined by the ability to differentiate levels of experience, based on simulator-derived metrics (number of movements, path-length, idle and task time). Inexperienced operators performed 10 repetitions for learning curve analysis. Proficiency benchmarks were defined by experienced operator performance.

Results
All guided modules demonstrated construct validity for all metrics (P<0.05), with learning curves that plateaued between sessions 6 and 9 (P<0.01). The unguided LA module demonstrated construct validity for number of movements (1101 vs 690.5 vs 532, P<0.01), path-length (1797.1cm vs 1573.5cm vs 1315.1cm, P<0.01), idle time (325.4s vs 160.4s vs 118.5s, P<0.01) and task time (864.5s vs 477.2s vs 352.1s, P<0.01), with learning curves that failed to plateau. Proficiency benchmarks included task time (352s), path-length (1315cm), and number of movements (532) for the unguided module. Validated modules were used for curriculum construction with proficiency benchmarks used as performance goals.

Conclusion
A VR simulation model of LA was validated as a training and assessment tool. Consequently, the first evidence-based training curriculum for LA was constructed that facilitates skill acquisition to proficiency.
Introduction
The advent of ‘fast track’ surgery has led to a heightened interest in length of hospital stay as a marker of surgical quality. Comparisons of length of stay between institutions and clinical trials remain difficult due to a lack of defined discharge criteria. The DeMorton Mobility Index (DEMMI) is a means of measuring functional mobility, which has been shown to be a valid scoring mechanism for the purpose of rehabilitation medicine. The aim of this study was to determine whether the DEMMI scoring system is a valid measure of functional recovery and readiness for discharge following surgery.

Methods
The DEMMI score was calculated daily post-op, for 3 days, on 120 patients enrolled in a prospective randomized clinical trial assessing local anaesthetic abdominal blockade, in patients undergoing gastrointestinal surgery. Comparison was then made between DEMMI score and length of hospital stay.

Results
DEMMI scores rose consistently with time, and were easy to perform. 77% of patients who returned to a value of at least 90% of their preoperative DEMMI score were discharged within 72 hours of this reading. Spearman’s correlation revealed a weak association between DEMMI and length of stay (-0.12; two sided p value 0.181).

Conclusion
The DEMMI score provides a measure of mobility that may be useful for assessing post-operative recovery in surgical patients, and provide an objective comparison between unit outcomes and those reported in clinical trials. Correlation between DEMMI and length of stay, in the context of this trial was weak.
Significant Elevations of Serum Lipase Not Caused by Pancreatitis – A Systematic Review

Hameed, A.M., Lam, W.T., Pleass, H.C.

Introduction
Many authors advocate lipase as the preferred serological test for the diagnosis of pancreatitis, with an often quoted cut-off of ≥ 3 times the upper limit of normal (ULN). There exists no systematic review in the literature that explores alternative causes of lipase ≥ 3 times the ULN, which was therefore the objective of this study.

Methods
The Embase and Medline databases (1985 to August 2014, respectively) were searched for all eligible articles. Pre-determined data was extracted and independently analysed by two reviewers.

Results
In total, data from 58 studies was included in the final analysis. The following causes of lipase levels ≥ 3 times the ULN other than pancreatitis were found: reduced clearance of lipase due to renal impairment or macrolipase formation; other hepatobiliary, gastroduodenal, intestinal and neoplastic causes; critical illness, including neurosurgical pathology; alternative pancreatic diagnoses, such as non-pathological pancreatic hyperenzymaemia; and miscellaneous causes such as diabetes, drugs, and infections.

Conclusion
A series of differential diagnoses for significant serum lipase elevations (i.e. ≥ 3 times the ULN) has been provided by this study. Clinicians should utilise this knowledge in the interpretation and management of patients who have lipase levels ≥ 3 times the ULN, remaining vigilant for an alternative diagnosis to pancreatitis. The medical officer should be aware of the incorrect diagnosis in the asymptomatic patient.
Introduction
Laparoscopic cholecystectomy (LC) in the obese patients can be a challenging procedure for any surgeon. Although LC has been established as the gold standard treatment for symptomatic choledolithiasis, its safety and efficacy in the morbid/super obese patients is still unknown. The aim of this study is to investigate the safety and efficacy of elective LC in the morbid/super obese patients.

Methods
A retrospective review of the Lyell McEwin Hospital electronic database and medical records was conducted searching for all patients who underwent elective LC from 2010-2013. The data collected include patient demographics and BMI, length of hospital stay (LOS), duration of operation, peri-operative complications, bile duct injuries and open conversion rates.

Results
A total of 799 patients (76% female) with a mean age of 46 years and BMI of 31 were included in this study. The average duration of surgery was significantly longer in the morbid/super obese patients compared to those with normal BMI (85 vs 70 minutes, p<0.05). There were no significant differences in the LOS, peri-operative complication rates, open conversions or bile duct injuries among the BMI groups.

Conclusion
This study showed that LC can be performed safely for symptomatic choledolithiasis in the morbid/super obese patients.
Using Serum Biomarkers To Predict Anastomotic Leakage: A Systematic Literature Review

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Introduction
Anastomotic leakage (AL) following colorectal surgery is a dreaded complication associated with significant morbidity and mortality. The diagnosis of AL however, remains a clinical dilemma due to its non-specific presentation. An objective systemic biomarker emulating the intra-abdominal milieu surrounding the anastomosis would allow earlier AL diagnosis and expedite effective treatment. This systematic review aims to evaluate the effectiveness of serum biomarkers used in the diagnosis of AL following colorectal surgery.

Methods
A comprehensive review was conducted according to the guidelines in the PRISMA statement. All published studies evaluating serum biomarkers for the diagnoses of AL, were searched in three electronic databases (MEDLINE, PUBMED and EMBASE), from 1980 to July 2014. Clinical outcomes, serum biomarkers and their respective predictive analyses were extracted.

Results
Thirteen studies evaluating 10 different serum biomarkers met the inclusion criteria. Analysis of the biomarkers (immunological, inflammatory and ischaemic), showed that these can reliably predict AL, though with significant variability. The changes in serum concentrations of these biomarkers often precede AL; however, these were limited to small or retrospective studies.

Conclusion
The review demonstrates that measuring serum biomarkers has the potential to predict AL following colorectal surgery. Prospective studies with larger numbers of participants should be performed to determine the diagnostic utility of this approach.
Aortic Aneurysm Trials in Octogenarians: Are We Really Measuring the Outcomes that Matter?

Aitken S, Naganathan V, Blyth F

Introduction
This study aims to systematically review the types of outcomes reported in abdominal aortic aneurysm (AAA) trials of patients aged 80 and over. Specifically, it examines if patient-centred outcomes have been evaluated in studies of AAA surgery in people aged 80 and over.

Methods
A systematic review of open and endovascular AAA interventions with outcome data on patients aged 80 and over was conducted. Relevant articles were identified from searching the databases MEDLINE and EMBASE from 2000-2014. Articles were categorised according to structure, process or outcome indicators (using Donabedian’s framework for health quality indicators). Outcomes were further classified into procedural, complication, resource usage or patient-centred indicators.

Results
40 studies reported outcomes of elective AAA surgery in patients 80 years and over and were predominantly endovascular repairs (66%, n=24). The average study size was 167 participants, with a mean age of 84 years. Patient-centred outcome indicators were infrequently reported (13%, n=5), with limited outcomes of specific relevance to geriatric patients. No studies used validated assessment methods for physical function, activities of daily living or cognition. The majority of studies report short-term mortality results (95%, n=38), complications (85%, n=34) and resource usage indicators (60%, n=24).

Conclusion
The reporting of outcomes after aortic surgery in older patients requires a renewed focus upon outcome indicators of primary importance in clinical decision-making for geriatric patients. Quality and safety indicators already in use in other studies of older patients should be adapted to the specific needs, preferences and values of this cohort.
Quantitative Characterisation and Neurochemical Coding of the Normal Human Hindgut Myenteric Plexus

Ng KS\textsuperscript{ab}, Mahns DA\textsuperscript{c}, Gladman MA\textsuperscript{ab}

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Introduction
Current understanding of the human enteric nervous system (ENS) remains limited as most existing knowledge is derived from animal and/or human studies utilising inaccurate techniques (unpaired tissue-sections) rather than ‘gold-standard’ paired wholemount preparations. This study aimed to quantitatively investigate and neurochemically code the human hindgut myenteric plexus using paired wholemount techniques.

Methods
Paired (same-patient) human colon/rectum were procured from anterior resection specimens. Wholemounts of myenteric plexi were prepared by dissecting mucosa/submucosa/circular muscle layers off the longitudinal muscle. Neuronal tripleimmunostaining was performed with fluorescent-labelled anti-Hu/NOS/ChAT antibodies. Wholemount images (~100mm\textsuperscript{2}) were acquired by motorised epifluorescence microscopy, allowing assessment of ganglionic density/size, ganglionic area density, and neuronal density. ‘Stretch-corrected’ values were calculated using stretched/relaxed tissue dimensions.

Results
12 paired colon/rectum samples were studied. Fluorescent dyes identified 3 subsets of neurons and ganglia, allowing their quantification. Colonic and rectal stretch-corrected ganglionic densities were similar (colon: median 564 ganglia/100mm\textsuperscript{2} [range 386–921], rectum: 581 [360–923]; P=0.70), as were average ganglionic sizes (colon: 57,047μm\textsuperscript{2} [42,350–90,363], rectum: 52,021 [38,701–90,210], P=0.43). Whilst ganglionic area density tended to be lower in the rectum (colon: 11.96mm\textsuperscript{2}/100mm\textsuperscript{2} [7.53–18.64], rectum: 9.76 [5.80–17.19], P=0.12), there was no difference in stretch-corrected neuronal densities (colon: 176.3 neurons/mm\textsuperscript{2} [107.4–357.3], rectum: 174.7/mm\textsuperscript{2} [94.7–313.3], P=0.58).

Conclusion
This is the first study to quantitatively assess the human hindgut myenteric plexus using paired wholemount immunostains accounting for tissue stretch. Despite differences in function, the ENS of the human colon and rectum is similar in terms of ganglionic density/size, ganglionic area density and neuronal density.
Restoring Expression of Microrna-7 Inhibits the MAPK and Mtor Pathways and Offers a Novel Therapy for Adrenocortical Cancer

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Introduction
Adrenocortical cancer (ACC) has a poor prognosis with limited treatment options. MicroRNA-7 (miR-7) is significantly under-expressed in ACC but it is not known if this is a part of ACC pathogenesis. We sought to establish the functional role of miR-7 as a tumour suppressor and assess miR-7 replacement as novel treatment.

Methods
miR-7 was transfected in ACC cell lines (H295R, SW-13) and compared to negative control (microRNA scramble sequences) transfected cells. A mouse xenograft model using H295R and primary ACC cells was treated by microRNA replacement by intravenously administered bacterially derived EGFR targeted EnGeneIC nanoparticle delivery vehicles (EDVs).

Results
miR-7s role as a tumour suppressor in vitro was confirmed after replacement lead to substantial reductions in cell proliferation and migration (P<0.05). Flow cytometry showed mean 8.1% and 15.7% increase in G1 arrest in H295R and SW13 cells following miR-7 replacement respectively (P<0.05). miR-7 predicted targets, EGFR and C-Raf, showed a reduction of 2-fold of both mRNA and protein expression (P<0.05). Co-transfection of the luciferase reporter vector containing 3’-UTR of EGFR or C-Raf, along with miR-7 mimics suppressed luciferase activity by 50% (P<0.05) confirming miR-7 targeting. Systemic miR-7 replacement delivered by EDVs in both mouse xenograft models caused a significant reduction in tumour growth with no evidence of toxicity and 2-fold target mRNA knock down of C-Raf, mTOR and CDK1 (P<0.05).

Conclusion
miR-7 acts as a tumour suppressor in ACC by inhibiting MAPK and mTOR pathways. MicroRNA replacement therapy delivered by EDVs offers a novel treatment of this deadly malignancy.
Therapeutic Reduction Mammoplasty – Oncological Efficacy and Description of Surgical Options


Introduction
Therapeutic reduction mammoplasty (TRM) offers an oncological and cosmetic advantage within the same operation. Our aim was to analyse this in our case series and describe the surgical options used.

Methods
Retrospective review of a single surgeons database on TRM was performed by viewing case-notes, operations and pathology report.

Results
In 37 female patients 38 TRM were carried out from November 2011 to August 2014, average age 56 years (IQR 45-65 years, range 37 to 81 years). The resection margins were positive in 7% (n=3). Mean tumour size was 23mm (IQR 12-30mm, range 6-55mm) and mean weight of total excised tissue was 209g (IQR 76-262g, range 20-710g). Distribution of T staging was Tis - 17% (n=7), T1 - 38% (n=15), T2 - 38% (n=15) and T3 – 7% (n=3). Return to theatre for 2 patients – one immediate postoperative haematoma and one debridement of non-viable skin at T-junction of inferior pedicle flap. Cellulitis seen in 2 patients responded to treatment with antibiotics. The surgical approach for reduction was via inferior pedicle in 71% (n=27), superior pedicle in 10% (n=4), inferolateral in 10% (n=4), superolateral in 5%(n=2) and one ‘round-block’ technique. In 68% (n=26) of patients, the axilla could be accessed via the same incision as for TRM.

Conclusion
In our series of patients, a low rate of 7% positive margin was seen1. Therapeutic mammoplasty was extended to patients with T3 staging2. The TRM incision approach was feasible for accessing the axilla and reasonably low complication rates were noted.
Traumatic Colonic Injuries in Westmead Hospital- A Paradigm Shift in Management Over 10 Years


Introduction
Management of penetrating colon injuries has evolved significantly over the past two centuries, with a trend towards less radical treatment, without fecal diversion and primary repair. There is strong evidence that most colon injuries from civilian trauma can be successfully managed with primary anastomosis. This is a cohort study of the management of penetrating colon injury at Westmead Hospital over the past 10 years.

Methods
Retrospective review of patients admitted with penetrating traumatic colon injuries from 1 January 2003 to 31 December 2013 at Westmead Hospital. Study parameters include demographics, site of colon injury, type of weapon used, injury to admission time, injury to surgery time, penetrating abdominal trauma index (PATI), duration of operation, injury severity score (ISS), surgical management, complications, and length of hospital stay (LOS). A 'P value' of less than 0.05 will be considered to be statistically significant.

Results
A total of 55 patients were included in the study with a median age of 38yrs (range 15-61 years). Majority of the patients were males (43/55, 78%). The transverse colon was the most common site of injury (53%) and the kitchen knife was the most common weapon used (58%). Primary repair was performed in 87% (48/55) and faecal diversion was performed in 13% (7/55). Colon related intra-abdominal complications occurred in 2 cases that underwent primary repair and 1 case that underwent faecal diversion. The average LOS was 12 days and the mortality rate was 5%.

Conclusion
From 2003 to 2013, there is a shift of management of penetrating colonic injuries from diversion to that of primary anastomosis and repair, with primary repair deemed as safe.
Disease Recurrence and Survival in Patients with Multifocal Breast Cancer – 7 Years Results

Article I. Li Lian Kuan, Leong Ung Tiong, Robert Parkyn, David Walters, Christine Lai, David C.A. Walsh

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Purpose
A few studies have shown that multifocal breast cancer (MBC) has poorer outcomes compared to unifocal breast cancer. There is currently no long term data on disease recurrence and survival in patients with MBC. The aim of this study is to evaluate whether patients with MBC have worse outcomes compared to unifocal breast cancer in respect to disease recurrence and survival.

Methods
This is a retrospective study of patients diagnosed with stage I–III MBC from 2000-2007 in comparison to unifocal disease with a median follow up of 7 years. Prognostic factors were prospectively collected and obtained from the breast cancer unit database. Cox Proportional Hazards Models were used to compare the rate of recurrence in the multifocal and unifocal breast cancer groups. Recurrence and overall survival rates were drawn from Kaplan–Meier curves.

Results
A total of 152 patients were included in this study; 75 with multifocal and 77 with unifocal breast cancer respectively. Breast cancer recurred in 9 (11.7%) patients in the unifocal group and 9 (12%) patients in the multifocal group respectively (HR: 1.13, 95% CI: 0.45-2.86, p=0.794). There were 10 (13%) mortalities in the unifocal group, as compared to 11 (14.7%) in the multifocal group (HR: 1.02, 95% CI: 0.42- 2.48, p=0.969). There were no statistically significant differences in the all-cause mortality and disease recurrence rates between the unifocal and the MBC groups.

Conclusion
This study shows that there were no statistically significant differences in disease recurrence or mortality rates between multifocal and unifocal breast cancer patients after a median follow-up of 7 years.
Lpa Signalling Contributes to Glioma Stem Cell Migration


Introduction
Molecular targeting in GBM treatment is of intense interest and lysophosphatidic acid (LPA) signalling has been putatively described as having a mechanistic role in cancer invasion.1 Initially described for its promitile effects in melanoma cells, it has since been described as a mediator of breast and ovarian cancer metastasis, with LPA inhibition able to retard metastases in murine breast cancer models.2,3,4 ATX/LPA receptor expression can be dysregulated in GBM and ATX expression has been shown to be differentially higher at the invasive edge, suggesting LPA signalling may modulate glioma cell invasion.5,6,7.

Methods
Patient-derived tumour explants were grown in neural stem cell neurosphere conditions. Relative mRNA expression of cell markers to assess stemness (NES, PROM1, SOX2 and POU5F1) and differentiation (GFAP and TUBB3) were measured using RT-qPCR. Relative mRNA expression of ATX/LPAR was also measured using RT-qPCR. Migration was assessed using 24 well transwell plates and either a luciferase reporter gene assay or LDH assay.

Results
In our panel of glioma stem-like cells (GSC), LPA receptors are differentially expressed. In particular, LPAR1 mRNA is commonly over-expressed compared to control neural stem cells (p<0.05). We show that GSC can migrate in a dose-dependent fashion in response to LPA stimulation. This response can be abolished with a selective LPA1/3 antagonist.

<table>
<thead>
<tr>
<th>GSC028</th>
<th>BSA*</th>
<th>LPA 0.1uM</th>
<th>LPA 1uM</th>
<th>LPA 10uM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2.75% +/- 0.75%; p=0.002</td>
<td>4% +/- 1%; p=0.06</td>
<td>5.5% +/- 1.2%; p=0.11</td>
<td>15% +/- 1.6%; p=0.002</td>
</tr>
<tr>
<td>GSC035</td>
<td>7.75% +/- 2.3%; p&lt;0.0001</td>
<td>10.75% +/- 2.6%; p=0.4</td>
<td>32.25% +/- 3.3%; p&lt;0.0001</td>
<td>53.88% +/- 3.9%; p&lt;0.0001</td>
</tr>
</tbody>
</table>

Migration rates relative to control (100% cells seeded to bottom chamber)
*BSA is the vehicle control
Conclusion

LPA stimulates migration in glioma stem-like cells and may represent a novel target for GBM therapy.

Face and Content Validation of a Virtual Reality Simulation Model for Laparoscopic Appendicectomy

Article III. Sirimanna P\textsuperscript{1}, Aggarwal R\textsuperscript{2}, Gladman Ma\textsuperscript{1}

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Introduction
Training using virtual reality (VR) simulators improves operative performance. However, to be useful these simulators must be realistic (face valid) and relevant (content valid). This study aimed to demonstrate the face and content validity of a VR model for laparoscopic appendicectomy (LA).

Methods
Eighteen surgeons (>10 LAs) performed eight tasks using a VR model of a LA on the LAPMentor\textsuperscript{TM} simulator. Participants completed a 23-item questionnaire to evaluate the face and content validity of the VR simulation model, using a 5-point Likert scale.

Results
Of the 18 participants, 16 (89\%) agreed or strongly agreed that the VR model was visually realistic and 17 participants (95\%) agreed or strongly agreed that it was representative of performing a LA. Specifically, 17 participants (95\%) regarded the VR anatomy as accurate and 16 (83\%) reported that it was visually comparable to an inflamed appendix. All participants deemed the VR instruments to be visually accurate and 16 (89\%) considered instrument movements and camera angles to be authentic. Despite only 4 participants (22\%) reporting tactile feedback to be realistic, tissue handling/behavior was regarded as accurate by 11 (61\%). Indeed, 17 participants (95\%) agreed that dissection and division of the mesoappendix and appendix was realistic. All participants supported the VR model as a training tool and 17 (95\%) supported its use as an assessment tool.

Conclusion
This study demonstrated the face and content validity of a VR model for LA. Therefore, its use as a training and assessment tool for junior surgical trainees deserves further evaluation.
Targeting Minimal Residual Disease in Breast Cancer

Article IV. Chakrabarti A.¹*, Leuchowius K.², Street ¹.², Anderson R.L³

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Breast cancer is an increasingly diagnosed disease in our society¹ resulting in the increased prevalence and longevity of cancer survivors. With increased survival, recurrence is a growing challenge and is attributed to the early dissemination of tumour cells. Currently, no targeted therapy exists for minimal residual disease, from which metastases accounts for 90% of cancer related deaths.

Aim
To find new therapeutic targets against dormant disseminated tumour cells.

Method
Using a novel in vitro model of dormancy, tumour cells are seeded on basement membrane and treated with the therapy of choice. A luminescent cell viability reporter is used for the analysis of tumour cell behaviour in response to the chosen therapeutic.

Results
The in vitro model is accurate at determining the in vivo behaviour of a tumour cell line, and is good platform to test potential therapies. Inhibitors of the MAPK pathway were effective at imposing dormancy.

Conclusion
Using the in vitro dormancy model, potential therapies can be screened and tested in a biologically relevant system. This may provide an avenue for the prevention and/or eradication of metastatic breast cancer.

¹ Australian Cancer Incidence and Mortality- Breast Cancer 2014
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Acknowledgements: Foundation of Surgery, Royal Australasian College of Surgeons, University of Melbourne, Cancer Australia, EMPathy Breast Cancer Network, National Breast Cancer Foundation.
Incidence of Pulmonary Embolus in High Risk Trauma Patients with Inferior Vena Cava Filters

Article V. Mohd Rosli R*, Tiong L, Dobbins C, Bautz P

Introduction
Trauma patients are at risk of venous thromboembolic event (VTE) due to a hypercoagulable state induced by trauma. Although risk of VTE can be reduced with anticoagulation medications, in some high risk trauma patients, the administering of blood thinning agents can be contraindicated such as in patients with intracranial bleeding. In this group of patients, insertion of inferior vena cava filters (IVCf) could be considered as another option for VTE prophylaxis. This study aims to investigate the incidence of pulmonary embolus (PE) in high risk trauma patients who had IVCf inserted.

METHODS: A retrospective case series were conducted at the Royal Adelaide Hospital through review of the radiological database of all trauma patients who had IVCf inserted over the last 10 years.

Results
One hundred and thirty seven high risk trauma patients with IVCf were identified. Of these, 107 patients had IVCf inserted prophylactically, and none were found to have clinically significant PE while the IVCf remained in situ. Ninety-two patients had their IVCf removed, of which four were found to have PE after filter removal.

Conclusion
This study shows that IVCf could be useful in preventing PE in high risk trauma patients when anticoagulation is contraindicated.
Virtual Anatomy Dissection Expands Teaching Opportunities in Postgraduate Surgical Education

Article VI. Aitken S, Sivakumaran Y, Kiat A

Introduction
Anatomy knowledge is a perceived deficit for many junior doctors (JMOs). Furthermore, junior doctors participating in postgraduate anatomy education face many barriers, including cost, time and location. This study explores how virtual anatomy dissection, such as using an Anatomage table, can improve the uptake of junior doctors in postgraduate anatomy education.

Methods
An eight-week virtual anatomy course was designed and taught. The course utilised peer-led teaching methods and was facilitated by senior surgical staff. Where possible, adult education learning methods were applied to clinical scenarios. Models, plastinated specimens, high-resolution digital images and medical imaging enhanced the virtual dissection. A questionnaire provided qualitative assessment, whilst quantitative assessment used a standardised pre- and post-multichoice examination.

Results
Four groups (27 students) have participated since the course commenced in 2013. These represent almost a third of the hospital’s JMO workforce. Students demonstrated improved mean examination results by 12% (95%CI: 5 to 19, P=.003) and greater clinical confidence. All students felt anatomy education (especially dissection) was important but 73% were unlikely to participate in offsite anatomy courses. Clinical workload and course length were also perceived barriers. Students stated that mentoring from senior colleagues was an important feature of the course and made it superior to online courses.

Conclusion
Virtual anatomy teaching can be delivered on location within teaching hospitals. It can help overcome the perceived barriers junior doctors experience in furthering postgraduate anatomy education, especially for students unlikely to do courses offered outside the hospital. The small group interactions within the course enhance the learning experience.

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The presenting author, S Aitken, is supported by research grants from the University of Sydney Medical Foundation Chapman Bequest, and the Royal Australian College of Surgeons Senior Lecturer Scholarship.
ARHI is a potential marker in breast cancer

Chakrabarti A\textsuperscript{1*}, Anderson R.L\textsuperscript{1,2}.

1. Peter MacCallum Cancer Centre, Melbourne, Victoria, Australia
2. Sir Peter MacCallum Department of Oncology, The University of Melbourne, Victoria, Australia

Breast cancer is an increasingly diagnosed disease in our society\textsuperscript{1}. The increased prevalence and longevity of cancer survivors results in the emerging issue of recurrence. Currently, we are unable to predict those patients that will have recurrent or progressive disease. This may be the key to stratifying the patients that may benefit from adjuvant therapies.

AIM: To assess the prognostic significance of ARHI

METHOD: An \textit{in silico} analysis was conducted using multiple data sets to assess clinical applicability. The expression of ARHI was then assessed using tissue microarrays and correlated with clinicopathological data.

RESULTS: The loss of the expression of the tumour suppressor gene ARHI may have prognostic significance in predicting recurrence and/or progression of disease.

SUMMARY: The loss of expression of ARHI may indicate an increased risk of recurrence and/or progression of disease and should be followed up accordingly. Patients who have significant expression loss may benefit most from adjuvant treatments.

\textsuperscript{1}Australian Cancer Incidence and Mortality-Breast Cancer 2014

Institution: Peter MacCallum Cancer Centre, St Andrews Pl, East Melbourne
Anannya.chakrabarti@petermac.org

Acknowledgements: Foundation of Surgery, Royal Australasian College of Surgeons, University of Melbourne, Cancer Australia,
# 51st Surgical Research Society Meeting – Evaluation Form

Please fill out this form, tear it out of booklet and return to Registration Desk

*(Please note that it is a requirement of CPD that we produce an evaluation form)*

## Are you? (please circle)
- Research Supervisor
- Research Fellow
- Other

## Questions for all attendees

<table>
<thead>
<tr>
<th>Questions for all attendees</th>
<th>Poor</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Excellent</th>
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<tbody>
<tr>
<td>The venue?</td>
<td>0</td>
<td>1</td>
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<td>5</td>
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<tr>
<td>Value for money?</td>
<td>0</td>
<td>1</td>
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<td>Quality of the program?</td>
<td>0</td>
<td>1</td>
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<tr>
<td>Quality of the questions?</td>
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## Research Supervisor Questions

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<thead>
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<th>3</th>
<th>4</th>
<th>Excellent</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do you rate the SRS Meeting as a forum for young Fellows/Trainees to present at?</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Will you consider attending again?</td>
<td>No</td>
<td>Probably Not</td>
<td>Possibly</td>
<td>Definitely</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Will you send young Fellows/trainees to future SRS meetings?</td>
<td>No</td>
<td>Probably Not</td>
<td>Possibly</td>
<td>Definitely</td>
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</tbody>
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## Research Fellow Questions

<table>
<thead>
<tr>
<th>Research Fellow Questions</th>
<th>No Value</th>
<th>Valuable</th>
</tr>
</thead>
<tbody>
<tr>
<td>How do you rate the overall value of the SRS meeting for you?</td>
<td>0</td>
<td>1</td>
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Any Suggestions/Comments?

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SRS 51st Annual Meeting 2014
MEMBERSHIP APPLICATION FORM

Please return this Form to the Secretariat, Section of Academic Surgery at the address listed above.

TITLE [e.g. Professor, Dr] ____________________________________ DATE ________________

CATEGORY [PLEASE CIRCLE] ACTIVE FELLOW  RETIRED FELLOW  RACS TRAINEE  NON-FELLOW

FULL NAME [PLEASE PRINT CLEARLY] __________________________________________________

PREFERRED POSTAL ADDRESS _________________________________________________________
  __________________________________________________________
  __________________________________________________________

STATE __________ P/CODE __________ COUNTRY ________________________________________

PHONE [BUSINESS HRS] __________________________________

FAX [BUSINESS HRS] __________________________________

MOBILE PHONE ______________________________________

EMAIL [Please note that email and E-Group will be the preferred method of contact and document distribution for the Section]

QUALIFICATIONS [INCLUDING INSTITUTION AND YEAR]

________________________________________________________________________

________________________________________________________________________

ACADEMIC APPOINTMENT

POSITION _____________________________________ INSTITUTION _______________________

THANK YOU FOR YOUR ASSISTANCE

SECRETARIAT, SECTION OF ACADEMIC SURGERY