Research Week
25 – 29 November 2013

Abstractg 2013

Austin LifeSciences Research Week 2013
Program

Research Week
25 – 29 November 2013

Monday 25 November

12 – 1	Debate "Clinical Trials are a waste of time"	JLLT
1.45 – 3.15	Consumer partnering and awards (includes 40 minutes nursing mini orals)	ELT
3.30 – 4.30	Biogrid Databank extend the power of your study	EP Rm 4.6

Tuesday 26 November

11.30 – 1.30	Dunlop Medical Research Foundation symposium	ELT
2.30 – 3.30	Poster session	EP
4 – 5	Physiotherapy Research Seminar	
	Prof Kim Bennell "Osteoarthritis, Old problem; new perspective"	ELT

Wednesday 27 November

12 – 1.30	AMRF Young Investigator Award presentations and Ingrid Scheffer Distinguished Scientist	JLLT
3.30 – 4.30	Poster session	EP

Thursday 28 November

12 – 1.15	Plenary Session Prof Murray Esler and Awards presentation	JLLT
2.30 – 3.30	Poster session	EP

Friday 29 November

12 – 1	RJ Pierce Symposium: "Anaesthesia and Perioperative Medicine: not just hot (and humidified) air"	
	Prof David Story, Phillip Peyton and Kate Leslie	JLLT

ELT Education Lecture Theatre   **EP** Education Precinct   **JLLT** John Lindell Lecture Theatre

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Austin LifeSciences Research Week 2013

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Austin LifeSciences Research Week 2013

Prize Winners

Recipient	Name of award	For work
Professor J Proietto	AMRF Distinguished Scientist Award	To honour Professor Proietto's contribution to the research community at Austin Health, in both clinical and basic research and his commitment to fostering young people into research and supervision of post-graduate degree students.
Fiona Brownfoot	AMRF Young Investigator Award	Pravastatin quenches oxysterol-induced upregulation of soluble endoglin in primary endothelial cells: a potential therapeutic for preeclampsia
The-Phung To	Allied Health Research Award	Involving consumers as team members in research: The Fasting & Nil By Mouth Project
Kai Mak	Austin Lifesciences Prize for Basic Research	Angiotensin converting enzyme 2 (ACE2) gene therapy attenuates experimental liver fibrosis in mice
Michelle T. Fodero-Tavoletti	FNI Prize for Neuroscience Research	THK523 selectively binds to neurofibrillary tangles and neuropils in Alzheimer's disease subjects
Sem Liew	Ludwig Institute Scholarship	Association of New York-Esophageal Antigen-1 (NY-ESO-1) promoter methylation and survival in stage III non-small cell lung cancer
David Gray	Nursing Research Award	Prioritising care for newly diagnosed men with prostate cancer: development of a supportive care needs risk factor assessment tool.
Melinda Millard	Nursing Encouragement Award	A Model for Facilitating Participant Recruitment in Spinal Clinical Trials in Victoria
Justine Westlake	Rob Pierce Memorial Award	Do shift workers fare as badly as obstructive sleep apnoea patients: investigating sleepiness, mood and performance.

Austin LifeSciences Research Week 2013
Poster Numbers and Titles

Tues 01
S. Iuliano-Burns, T.D.T Vu, C. Chiang, E. Gianatti, E. Hamilton, M. Grossmann, E. Seeman, J. Zajac
Improving management of low trauma fractures in a tertiary hospital. The "Fracture Capture" Project

Tues 02
Sue Berney, Joleen W. Rose, Rinaldo Bellomo, Linda Denehy
Patient activity and environmental enrichment in the intensive care unit

Tues 03
Jenny Healy, Mark Ng Tang Fui, Philippe Dupuis, Mathis Grossmann
Testosterone for prevention of diabetes Type 2 (T4DM)

Tues 04
S. Iuliano, Q.J. Wang, X.F. Wang, R. Zebaze, A. Ghasem Zadeh, Y. Bala, N. Pang, E. Seeman
Cortical bone fragility contributes to fractures in children

Tues 05
Chrysovalantou E. Xirouchaki, Zheng Ruan, Salvatore P. Mangiafico, Jenny Favaloro, Joseph Proietto, Sofianos Andrikopoulos
The impact of muscle-specific deletion of glycogen synthase on glucose tolerance and insulin sensitivity in mice

Tues 06
Gemma Collins, Brooke Chapman & Leonie Pearce
Weight gain and obesity after orthotopic liver transplantation

Tues 07
Shea Edsall, Amy Kaplan, Kellie Draffin and Terrill Bruere
Aggressive feeding protocol safely implemented in a paediatric inpatient eating disorder program

Tues 08
Purcell, K., Sumithran, K., Prendergast, L., Bouniu, C.J., Delbridge, L., Proietto, J.
Personality and social functioning to achieve a pre-determined weight loss target

Tues 09
Selina M Parry, Susan Berney, Catherine L. Granger, Linda Denehy
Functional electrical stimulation cycling in acute traumatic tetraplegia within four days post injury: A Case Report

Tues 10
Selina M Parry, Susan Berney, Catherine L. Granger, Laura Murphy, Danielle L Dunlop, Doa El-Ansary, Renè Koopman, Linda Denehy
A new two-tier approach for measurement of strength in the critically ill patient

Tues 11
Selina M. Parry, Susan Berney, Stephen Warrillow, Doa El-Ansary, Adam L. Bryant, Nicholas Hart, Zudin Puthucheary, Renè Koopman, Linda Denehy
Functional electrical stimulation cycling in the critically ill with sepsis: a pilot case-matched control study

Tues 12
Karen Mardegan, Melodie Heland, Tiffany Whitelock, Robert Millar, Daryl Jones
Improving handover and documentation during Medical Emergency Team review

Tues 13
Chong Tan, Laurence Weinberg, David Story, Phillip Peyton, Larry McNicol, Parameswan Pillai
Try looking another way: 3 non-standard TOE views of the main PA and RVOT

Tues 15
Chong Tan, Laurence Weinberg, David Story, Phillip Peyton, Larry McNicol, Parameswan Pillai
Are non-standard transoesophageal echocardiographic views of the tricuspid annulus feasible?

Tues 16
Chong Tan, Laurence Weinberg, David Story, Phillip Peyton, Larry McNicol, Parameswan Pillai
Seeing is believing: the use of tte to visualise swan-ganz catheter placement in the pulmonary artery

Tues 17
Chong Tan, Chiu Kang
Blocks & breathing: respiratory function after shoulder surgery is unaffected by analgesic technique

Tues 18
Laurence Weinberg, Nick Scurrah, Larry McNicol, Chris Christophi, Mehrdad Nikfarjam
Liberal fluid intervention and positive fluid balance affect length of hospital stay following pancreaticoduodenectomy

Tues 19
Laurence Weinberg , Nick Scurrah , Larry McNicol , Chris Christophi ,
Mehrdad Nikfarjam
*Enhanced recovery after surgery program reduces length of stay following
uncomplicated pancreaticoduodenectomy*

Tues 20
Ping Chia, Linda Gualano, Sathi Seevanayagam, Laurence Weinberg
***Outcomes following fractured neck of femur in an Australian
metropolitan teaching hospital***

Tues 21
Laurence Weinberg, Chong Tan, Nick Scurrah, Guangjun Chen, Larry
McNicol, Mehrdad Nikfarjam
*Analgesia practice for pancreaticoduodenectomy: is it time to reconsider
epidurals?*

Tues 22
Ping Chia, Laurence Weinberg, Chong Tan, Larry McNicol
***Current trend of anaesthesia practice for primary total knee arthroplasty
surgery in an Australian metropolitan teaching hospital***

Tues 23
Laurence Weinberg, Brett Pearce, Richard Sullivan, Lindon Siu, Marie
Backstrom, Nick Scurrah, Mehrdad Nikfarjam, Larry McNicol, Rinaldo
Bellomo, David Story
*A multicentre randomized double-blind controlled non-inferiority multicentre
study of Plasmalyte vs. Compound Lactate Solution (Hartmann's solution) in
patients receiving liver resection (Australian New Zealand Clinical Trials
Registry No: 12610000147088)*

Tues 24
**S. Suzuki, G.M. Eastwood, L. Peck, N.J. Glassford, A.G. Schneider, M.
Garcia, R. Bellomo**
***A pilot before-and-after trial of conservative oxygen therapy in
mechanically ventilated patients***

Tues 25
G.M. Eastwood, S. Suzuki, C. Lluch, A.G. Schneider, R. Bellomo
*Impact of arterial blood gas assessment in patients admitted to intensive care
following non-traumatic cardiac arrest*

Tues 26
G.M. Eastwood, L. Peck, H. Young, S. Suzuki, M.Garcia, R. Bellomo
***Intensive care clinicians' opinion of conservative oxygen therapy (SpO_2
90-92%) for mechanically ventilated patients: a survey***

Tues 27
S. Suzuki, G.M. Eastwood, L. Peck, N.J. Glassford, R. Bellomo
Oxygen management in mechanically venitlated patients: a prospective observational cohort study

Tues 28
John Rogan, Nigel Fealy, Gillian Dunnachie, Stuart Ross, Kristin Majer, Karyn Rutjens, Belinda John, David Thomas, Helen Young, Robyn Best.
Reducing Adverse Events in ICU - Implementation of a NEVER Event program

Tues 29
Patricia K. Russell, Michele V. Clarke, Kristine M. Wiren, Jeffrey D. Zajac, Rachel A. Davey
Androgens act directly via the androgen receptor in proliferating osteoblasts to increase bone size during growth

Tues 30
Lavinia Spain, Marzena Walkiewicz, Simon Knight, Paul Mitchell, Thomas John
Overall survival and smoking status in resectable non-small cell lung cancer

Tues 31
Megan Cotter, Elly Lynch, Martin Delatycki, Alana Jacobs, Agnes Bankier, Matthew Burgess, Alana Jacobs, Thomas John
How frequent is DCIS in families with BRCA1 or BRCA2 mutations? A clinical audit from Austin Health Genetics

Tues 32
N. Anderson, J. Jackson, M. Wada, M. Schneider-Kolsky, M. Rolfo, H. Gan3, K. Kaegi, F. Sneyd, D. Lim Joon, V. Khoo
Creating guidelines for reactive and prophylactic enteral feeding in definitive (Chemo) intensity modulated radiation therapy (IMRT) for head and neck cancer

Tues 33
Marika Ciprotti, Niall C. Tebbutt, Fook T. Lee, Sze T. Lee, Dave C. McKee, Graeme J. O'Keefe, Sylvia J. Gong, Geoffrey Chong, Hui K. Gan, Wendie Hopkins, Bridget Chappell, Nancy Y. Guo, Fiona E. Scott, Archie N. Tse, Mendel Jansen, Manabu Matsumura, Rira Watanabe, Robert A. Beckman, Jon Greenberg, Andrew M. Scott
A phase I imaging and pharmacodynamic trial of CS-1008 in patients (pts) with metastatic colorectal cancer (mCRC)

Tues 34
Mun Sem Liew, Joseph Sia, Maud H.W. Starmans, Ali Tafreshi, Sam Harris, Malcolm Feigen [3], Shane White, Allan Zimet, Philippe Lambin, Paul C. Boutros, Paul Mitchell, Thomas John
Comparison of toxicity and outcomes of concurrent radiotherapy with carboplatin/paclitaxel and cisplatin/etoposide in stage III non-small cell lung cancer

Tues 36
Christopher Hudson, Andreas Behren, Aparna Jayachandran, Matthew Anaka, Sonja McKeown, Jonathan Cebon
Heterogeneity and plasticity in melanoma leads to treatment failure and increased invasiveness that can be blocked by targeting TSP-1 and/or SNAIL

Tues 37
A. Barnett, N. Dhomen, J. Mariadason, A.M. Scott
Potential markers for metformin susceptibility in colorectal cancer

Tues 38
Pu-Han Lo, Aparna Jayachandran, Anderly Chueh, Jonathan Cebon
TKTL1- a promising anti-tumour target in melanomas

Tues 39
D. K. Lau, M. C. Andrews, N. Turner, A.A. Azad, I.D. Davis, J.S. Cebon
A single center experience of patients with metastatic melanoma enrolled in a dabrafenib named patient program

Tues 40
Lars Tögel, Rebecca Nightingale, Anderly C. Chueh, Hoanh Tran, Timothy C. Gahman , Andrew K. Shiau, John M. Mariadason
Evaluation of the efficacy of bromodomain inhibitors for the treatment of colorectal cancer

Tues 41
Simon C-H Tsao, Andreas Behren, Jonathan Cebon, Christopher Christophi
A novel cost- and time-efficient method of enumerating circulating tumour cells

Tues 42
Kheng Soo, Juli Moran
Discharge planning from a palliative care ward to residential aged care using prognostic tools

Tues 43
Uwe Ackermann, Dedrick Song, Shinn Deee Yeoh, Yit Wooi Goh, Henri Tochon-Danguy, Andrew Scott, Jonathan White
Synthesis and evaluation of a pegylated F-18 labelled nitrophenyl sulfoxide for PET imaging of tumor hypoxia

Tues 44
Mun Sem Liew, Anderly C. Chueh, Marzena Walkiewicz, Jonathan Cebon, Paul Mitchell, John Mariadason, Thomas John
Association of New York-Esophageal Antigen-1 (NY-ESO-1) promoter methylation and survival in stage III non-small cell lung cancer

Tues 45
Goh, Yit Wooi, Plougastel, Lucie, Yeoh, Shinn Dee, Sachinidis, John I., Tochon-Danguy, Henri, Poniger, Stan, Scott, Andrew M., Ackermann, Uwe
Fully automated Click radiolabeling and the synthesis and coupling of [^{18}F]FBEM to glutathione using the iPhase Flexlab module

Tues 46
A. Ellis, P.T. Zeglinski, B. Gardiner, A. Mahony, D. Massie, A.G. Frauman, M.L. Grayson
Measurement of fosfomycin in prostate tissue by liquid chromatography tandem mass spectroscopy (LCMSMS)

Tues 47
Celia S.-L. Kuo, Adam Pendlebury, Susan T. Jones, Kerryn F. Ireland-Jenkin
Comparison of conventional cervical cytology with ThinPrep liquid-based cytology (LBC) in a dysplasia clinic setting

Tues 48
Peter J. Wookey, Sebastian G.B. Furness, Angela Kourakis, Patrick M. Sexton, David L. Hare
An anti-calcitonin receptor antibody:fluorophore conjugate that identifies a novel event in apoptosis

Tues 49
Trishe Y-M. Leong, Suzanne Svobodova
EGFR mutation testing pre- and post-establishment of an in-house molecular pathology service

Tues 50
Lin Xiao, Suzana Kovac, Mike Chang, Arthur Shulkes, Graham S. Baldwin and Oneel Patel
Zinc ions up-regulate the hormone gastrin via an E-box motif in the proximal gastrin promoter

Tues 51
Christos N. Joannides, Benjamin J. Lamont, Maria Stathopoulos, Joseph Proietto, Sofianos Andrikopoulos
Glucose toxicity causes a defect in insulin secretion via the K+ATP channel

Tues 52
Mak, K.Y., Jia, Z., Yip, E., Chin, R., Torresi, J., Burrell, L.M., Cunningham, S., Alexander, I., Angus, P.W., Herath, C.B.
Angiotensin converting enzyme 2 (ACE2) gene therapy attenuates experimental liver fibrosis in mice

Tues 53
Xiao Wang, Graham Baldwin, Christopher Christophi, Hong He, Mehrdad Nikfarjam
The potential role of p21-activated kinase 4 (PAK4) in the growth, migration and invasion of pancreatic ductal adenocarcinoma

Tues 54
Paul MacGibbon, Amy Eldridge, Beth Depetro, Dianne Pierce, Mary Harty
Emergency care management plans

Tues 55
Michael J. Pichler
Herpud1 is protective against endoplasmic reticulum stress in diabetic beta-cells

Tues 56
Ada S. Cheung, Anthony Schache, Hans Gray, Philippe Dupuis, Daryl Lim Joon,
Jeffrey D. Zajac, Marcus Pandy, Mathis Grossmann
Decline in functional mobility in men undergoing androgen deprivation therapy

Tues 57
E.J. Gianatti, P. Dupuis, R. Hoermann, J.D. Zajac, M. Grossmann
Effect of testosterone therapy on glucose metabolism in men with Type 2 diabetes: a RCT

Tues 58
Mark Ng Tang Fui, Phuong Nguyen, Emily J. Gianatti, Jeffrey D. Zajac, Mathis Grossmann
Testosterone levels in Type 1, Type 2 diabetic and non-diabetic men

Tues 59
Amanda Leong
Long-term intraindividual variability in albumin excretion rate in patients with type II diabetes

Tues 60
Angela X. Chen, George Jerum, Sara Baqar, Georgina Thomas, Richard J. MacIssac, Christopher O'Callaghan, Elif I. Ekinci
Short-term dietary salt supplementation is not associated with reduced renal function in hypertensive subjects with type 2 diabetes

Tues 62
N.J. Hannan, L. Tuohey, F. Brownfoot, T. Kaitu'u-Lino, K. Onda and S. Tong
Lansoprazole decreases sFlt1 and sEng production in placental and endothelial cells: A potential therapeutic for preeclampsia

Tues 63
A. Sabetghadam, W. Korim, A.J.M. Verberne
A neurophysiological study of the medullary sympathetic pathway to the adrenal gland

Tues 64
Willian S. Korim, Lama Bou-Farah, Simon McMullan, Anthony J.M. Verberne
Glucoprivation of neurons in the perifornical hypothalamus elicits adrenaline release, via an orexinergic relay in the rostral ventrolateral medulla

Tues 65
David Darby, Amy Brodtmann, Michael Woodward, Moacir Neto
The Trajectory-Related Early Alzheimer's Database (TREAD) Study: Initiation

Tues 66
Peter E Batchelor, Peta Skeers, Ana Antonic, Taryn E Wills, David W Howells, Malcolm R Macleod, Emily S. Sena
Systematic review and meta-analysis of therapeutic hypothermia in animal models of spinal cord injury

Tues 67
John Archer, Aaron Warren, David Abbott, Graeme Jackson
Differences in thalamic nuclei responses during epileptiform activity of Lennox Gastaut Syndrome

Tues 68
John Archer, Patrick Carney, Aaron Warren, David Abbott, Graeme Jackson
Primary cortex and pons behave differently during spike-and-wave discharges of Genetic Generalised Epilepsy versus Lennox-Gastaut Syndrome

Tues 69
Johnson George, Dennis Thomas, Billie Bonevski, Simone E. Taylor, Susan Poole, Greg R. Weeks, Michael J. Dooley, Michael J. Abramson
Characteristics of smokers participating in a randomised controlled trial evaluating a system change smoking cessation intervention

Tues 70
Simone E. Taylor, Alana Meaklim, Alice Chow, Melissa Fodera
Medical, nursing and pharmacy staff perceptions of Cerner electronic prescribing implementation for inpatient prescribing

Tues 71
Simon Lau
Cervical Spinal Cord Injury at the Victorian Spinal Cord Injury Service: the Last Decade

Tues 72
J. Grewal, R. Johnston, K. Sanders, R. Rayoo, L. Kearney, R. Lim, G. Smith, P. Srivastava, E. Jones, O. Farouque, A. Al-Fiadh
Ambulatory rapid access chest pain clinic for low to intermediate risk patients – a single centre experience

Tues 73
J. Grewal, A. Al-Fiadh, O. Farouque, E. Jones
Prevalence of patent foramen ovale in patients with acute myocardial infarction and angiographically normal coronary arteries

Tues 74
Therese Thornton, Fergal J. O'Donoghue, Peter D Rochford, Charlie C.L. Xue, John Trinder, Amy S. Jordan
Traditional Chinese Medicine diagnosis of obstructive sleep apnoea

Tues 75
A.Thomson, A. Hilton, C. Christophi, R. Bellomo
An assessment of forearm blood flow by ultrasound Doppler in critically ill patients

Tues 76
D. Wynne, S. N. Kong, C. Christophi, P. Costa
Investigating the effects of kinin receptor inhibition on the progression of colorectal liver metastasis

Tues 77
Catherine S. Hibberd, Gerald M. Y. Quan
Predicting risk of fracture and neurological deficit in patients with spinal metastases

Tues 78
Jonathon Lo, Justin Jedynak, Franklin Pond
Spinal cord ischaemia following endovascular abdominal aneurysm repair: case report

Wed 01
Shahmoradi N, Wang XF, Iuliano-Burns S, Ghasem-Zadeh A, Bjørnerem A and Seeman E
Contributions of lean and fat mass to bone structure: a co-twin study

Wed 02
Melissa J. Hirth, David J. Jacobs, Kate Sleep
Hand-based swing traction splinting for intra-articular proximal interphalangeal joint fractures

Wed 03
Catherine Said, Frances Batchelor, Kathryn Shaw, Jannette Blennerhassett
Preparing people at high risk of falls for discharge home following rehabilitation: Do we meet the guidelines?

Wed 04
Cimoli, M, Oates, J., Greenwood, K., McLaughlin, E., Langmore, S.E.
The use of instrumental swallowing assessments by speech pathologists working in Australia

Wed 05
Tina Griffiths, Liz Pascoe
Evaluation of an education program to facilitate patient adherence, toxicity monitoring and promote safety and wellbeing in the self administration of oral chemotherapy in the home setting

Wed 06
Allison Mo, Andrew Grigg
Metastatic Thymoma and T Acute Lymphoblastic Leukaemia (T-ALL): A Case Report

Wed 07
M. Rolfo, J Jackson, D. Lim Joon, D. Scandurra, N. Anderson, B. Welsh, M. Lawlor, K. Brown, V. Khoo
Simple Segment IMRT: Dosimetric and Resource Implications of an Innovative Rectal Cancer Technique

Wed 08
Heather Leggett, Simone Alford, Chris Hamilton
Dosimetric comparison of sequential electron versus simultaneous integrated boost (SIB) techniques for adjuvant breast radiotherapy

Wed 09
P. Prithviraj, M. Anaka, P. Lo, A. Behren, A. Jayachandran, J. Cebon
Metalloproteinase Pregnancy Associated Plasma Protein-A (PAPP-A) promotes Melanoma progression in vitro

Wed 10
Aparna Jayachandran, Pu-Han Lo, Andreas Behren, Sonja McKeown and Jonathan Cebon
Identifying and targeting regulatory molecules of the melanoma "invasive switch"

Wed 11
S.N. Kong, D. Wynne, C. Christophi, P. Costa
The effects of kinin receptor II blockade and angiotensin converting enzyme inhibition on colorectal cancer liver metastases

Wed 12
Muhammad Asrar ul Haq, Vivek Mutha, Vivek Gupta, David L Hare, Chiew Wong
Interstudy reproducibility of echocardiographic parameters in the serial assessment of left ventricular diastolic function

Wed 13
Muhammad Asrar ul Haq, Vivek Gupta, Chiew Wong, David L Hare
eGFR Can Predict Diastolic Dysfunction In Diabetic Patients

Wed 14
Muhammad Asrar ul Haq , Simon Stewart, Melinda Carrington, David L Hare, Chiew Wong
Asymptomatic Myocardial Disease is Associated with Reduced Functional Capacity in at risk Population

Wed 15
R. Rayoo, D. Patrick, S. Lovibond, J. Grewal, Lu K. Lu, P. Srivastava, P. Calafiore
Predictive Value of Dynamic Left Ventricular Outflow Tract Obstruction During Dobutamine Stress Echocardiography in Patients Undergoing Liver Transplantation

Wed 16
David L. Hare, Andrea Driscoll, Deidre Toia, Samia R. Toukhsati
Pharmacological Restoration of mOod in HEART failure (PRO-HEART): Rationale and Design

Wed 17
Ryan J Spencer, Hari Sugumar, Tina Lin, Darragh Flannery, Paula Rae, David O'Donnell
Non Uniform Ventricular Remodelling Following CRT – Insights from Quadrapolar Leads
Wed 18
Ryan J. Spencer, Jay Ramchand, Dharsh Fernando, David Clark
Achieving Door to Balloon Times (DTBT) <90 minutes Reduces Long Term Mortality in Lower risk ST Elevation MI (STEMI)

Wed 19
Ryan Spencer, Tina Lin, Hariharan Sugumar, Paula Rae, David O'Donnell
Implant Electrical Characteristics Predict Response to Cardiac Resynchronisation Therapy

Wed 20
Darragh Flannery, Paula Rae and David O'Donnell
Coronary sinus dissection during cardiac resynchronization therapy implantation

Wed 21
Darragh Flannery, Tina Lin, Paula Rae, Jasmin Grewal and David O'Donnell
Is the most delayed site the best site for LV lead pacing?

Wed 22
Elena Velkoska, Karen Griggs, Louise M Burrell
ACE2 activation improves diastolic dysfunction in kidney disease

Wed 23
Susan G. Singh, Gerard Smith, Leighton Kearney, Emma K. Hornsey, Michael Galea, Brenden McColl, Jennifer Shoobridge, Rinku Rayoo, Jasmin Grewal, Jian Xu, Melanie Rayner, George Matalanais, Ruth P. Lim
ECG-Gated Contrast Enhanced CTA of the thoracic aorta versus Non-Contrast Thoracic MRA: A valid alternative?

Wed 24
Angela J. Mountain, Tracy Fuhrmeister, Lewis Lee, Nina J. Paleracio, Mehrdad Nikfarjam, Christopher Christophi, Amber Johns, Andrew Biankin, Carmel Murone
Victorian Pancreatic Cancer Patients Support Genomic Research

Wed 25
Lewis Lee, James Lynam, Angela J. Mountain, Nina J. Paleracio, Pavel Sluka, Ian Davis, Carmel Murone
Biobanking Provides Prostate Tissue for Research

Wed 26
C. Leung, C.B. Herath, J. Zhiyuan, T. Leong, J.M. Forbes, P.W. Angus
Manipulation of dietary advanced glycation end-product (AGE) content influences the progression of fatty liver disease

Wed 27
Elif I. Ekinci, Wei-Ling Chiu, Zhong X. Lu, Ken Sikaris, Intissar Bittar, Que Lam, Nick Crinis, Christine A. Houlihan
A longitudinal study of thyroid autoantibodies in pregnancy

Wed 28
Elif I Ekinci, Wei-Ling Chiu, Zhong X. Lu, Ken Sikaris, Intissar Bittar, Que Lam, Nick Crinis, Christine A. Houlihan
A longitudinal study of TSH-receptor autoantibody in normal pregnancies

Wed 29
Renata Libianto, George Jerums, Scott Baker, Richard MacIsaac, Elif I. Ekinci
Relationship between 24h urinary sodium-to-potassium ratio with blood pressure and renin angiotensin aldosterone activity in people with diabetes

Wed 30
Elif I. Ekinci, Jaquelyne T. Hughes, Mark Chatfield, Paul D. Lawton, Graham R.D. Jones, Andrew G. Ellis, Alan Cass, Wendy E. Hoy, Richard J. MacIsaac, Kerin O'Dea, George Jerums, Louise J. Maple-Brown
Does hyperfiltration exist in Indigenous Australians with and without diabetes?

Wed 31
Natasha E. Holmes, Susan A. Ballard, Margaret M. C. Lam, Paul D.R. Johnson, M. Lindsay Grayson, Timothy P. Stinear, Benjamin P. Howden
Emergence of teicoplanin resistance among vanB vancomycin-resistant Enterococcus faecium isolates in a cluster of solid organ transplant recipients – risk factors and molecular characterisation

Wed 32
Nick. H. Hewitt, Karen. F. Urbancic, Andrew. P. Grigg, M. Lindsay. Grayson
Detailed antifungal stewardship (AFS) is key to achieving excellent plasma levels during oral posaconazole (pcz) prophylaxis in high risk hematology patients

Wed 33
Andrew A Mahony, Elizabeth A. Grabsch, Jenny Wang, Shirley Xie, Susan A. Ballard , M. Lindsay Grayson, Benjamin P. Howden, Paul D.R. Johnson
Enterococcal bloodstream infections in a Melbourne tertiary hospital following an outbreak of Enterococcus faecium ST-203

Wed 34
Bradley J. Gardiner, Andrew A. Mahony, Andrew Ellis, Nathan L. Lawrentschuk, Damien M. Bolton, Philip Zeglinski, Albert G. Frauman, M. Lindsay Grayson
Oral fosfomycin tromethamine (FOS) achieves good intra-prostate levels suggesting it may be a prophylaxis & treatment option for multidrug-resistant (MDR) prostatitis

Wed 35
Miranda Siemienowicz, Anthony Schelleman
Quality Assurance in CT Pulmonary Angiography: Phase 2 and Completed Audit Cycle

Wed 36
Mardiana Lee, Matthew A. Roberts, Maree-Ross Smith, Jason Chuen, Peter F. Mount
Clinical outcomes with early and late arteriovenous fistula creation in chronic kidney disease

Wed 37
Saad A. Khan, Patrick W. Carney, John S. Archer
Asymmetric Tonic Seizures and Diffuse Low Voltage Fast Activity are Characteristic in Mesial Parietal Seizures

Wed 38
Maryam Ejareh Dar, James S. Olver, Richard A.A Kanaan
Cognitive and psychological impact of Androgen Deprivation Therapy: a review

Wed 39
John A. Damiano, Saul A. Mullen, Henrik H. Dahl , Kate Lawrence, Todor Arsov, Susannah Bellows, Michael S. Hildebrand, Ingrid E. Scheffer, Samuel F. Berkovic
Microdeletion and missense mutation at 15q13.3 in a family with genetic generalised epilepsy and neuropsychiatric disorder

Wed 40
Paul A. Yates, Christopher C. Rowe, Victor L. Villemagne, Patricia M. Desmond, Colin L. Masters, David Ames, Lorraine Dennerstein, Philippe Lehert, Kathryn A. Ellis, Cassandra E. Szoeke
Midlife Vascular Risk and Late-life Amyloid Burden: Data from the Women's Healthy Ageing Project (WHAP)

Wed 41
Richard A.J. Masterton, Graeme D. Jackson, David F Abbott
Group analysis of EEG-fMRI using event-related independent components analysis (eICA)

Wed 42
Paul A. Yates, Patricia M. Desmond, Pramit M. Phal, Cassandra E. Szoeke, Victor L. Villemagne, Christopher Steward, Olivier Salvado, Ralph N. Martins, Colin L. Masters, David Ames, Kathryn A. Ellis, Christopher C. Rowe
Cerebral microbleeds and cognitive trajectories: results from AIBL

Wed 43
Patricia M. Desmond, Christopher C. Rowe, Victor L. Villemagne, Christopher Steward, Colin L. Masters, David Ames, Kathryn A. Ellis, Lorraine Dennerstein, Philippe Lehert, Cassandra E. Szoeke
10-year MRI changes and FBB PET: Results from the Women's Healthy Ageing Project (WHAP)

Wed 44
Michelle T. Fodero-Tavoletti, Nobuyuki Okamura, Leanne Taylor, Shozo Furumoto, Catriona McLean, Rachel S. Mulligan, Ian Birchall, Ryuichi Harada, Colin L. Masters, Kazuhiko Yanai, Christopher C. Rowe, Yukitsuka Kudo, Victor L. Villemagne
THK523 selectively binds to neurofibrillary tangles and neuropils in Alzheimer's disease subjects

Wed 45
Lin Hung, Andrew Watt, Rachel S. Mulligan, Shozo Furumoto, Michelle T. Fodero-Tavoletti, Jacky Chan, Kazuhiko Yanai, Colin L. Masters, Yukitsuka Kudo, Christopher C. Rowe, Kevin J. Barnham, Nobuyuki Okamura, Victor L. Villemagne
Detectable levels of white matter PHF-tau in Alzheimer's disease

Wed 46
Xiaoyun Liang, Alan Connelly, Fernando Calamante
Graph analysis of resting-state ASL data reveals nonlinear correlations among CBF and network metrics

Wed 47
Susan M. Palmer, Ayla Barutchu1, E. Low, Gemma Lamp, Leeanne M. Carey
A meta-analysis of brain regions activated during tactile stimulation in healthy individuals

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Kaushik Bhaganagarapu, Graeme D. Jackson, David F. Abbott
An automated method for identifying artefact in Independent Component Analysis of resting-state fMRI

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Susan M. Palmer, Leeanne M. Carey
A meta-analysis of brain areas altered in depressed subjects

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Bladin, C., Moloczij, N., Kung, F., Ermel, S., Cadilhac, D.A., on behalf of the VST Project Investigators
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GLUT1 Mutations are the Only Significant Cause of Generalised Epilepsy Amongst the Major Brain Glucose Metabolism Transporter Genes

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Michael Hildebrand
Unravelling the genetics of the common epilepsies using discordant monozygotic twins

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Harnessing gene expression networks to prioritize candidate epileptic encephalopathy genes

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Targeted resequencing in epileptic encephalopathies reveals marked genetic heterogeneity and novel genes including CHD2 and SYNGAP1

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Changes in acute hospital costs for stroke after clinical facilitators employed to improve stroke care: an Australian case study

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Marion A Simpson, Leeanne Carey, Belinda Bardsley, Richard Macdonell
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Bronwyn E. Grinton, Sarah E. Heron, James T. Pelekanos, Sameer M. Zuberi, Sara Kivity, Zaid Afawi, Tristiana C. Williams, Dan M. Casalaz, Simone Yendle, Ilan Linder, Dorit Lev, Tally Lerman-Sagie, Stephen Malone, Haim Bissan, Hadassa Goldberg-Stern, Thorsten Stanley, Sophie Calvert, Amos D. Korczyn, John C. Mulley, Ingrid E. Scheffer, Samuel F. Berkovic
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Sharon F. Kramer, Toby Cumming, Leonid Churilov, Julie Bernhardt
Measuring activity levels at an acute stroke ward: Comparing observations to a device

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E. L. Roberts, D. A. F. Cossigny and G. M. Y. Quan
The VEGF and TNF-α pathways in prostate cancer metastases to the bony skeleton

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S. Dushyanthen, D.A.F. Cossigny, G.M.Y. Quan.
Osteoblastic and osteoclastic interactions in spinal metastasis of human prostate cancer

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Kenny Rao, Mildred Yim, Damien Bolton, Arthur Shulkes, Graham Baldwin, Oneel Patel
Zinc preconditioning protects the rat kidney against ischemic injury

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Anne E. Holland, Catherine J. Hill, Leona Dowman, Nicole Goh, Glen Westall, Karen Symons, Ian Glaspole
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Danny J. Brazzale, Graham L. Hall and Jeffrey J. Pretto
The effect of adopting the new GLI reference equations on the interpretation of spirometry

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Rebecca L. Smith, Yet H. Khor, Christine McDonald
Suboptimal Management of UFH compared with LMWH in the management of Pulmonary Embolism.

Thur 05
Sue Rochford, Peter Rochford, Michael Sutherland
Does change in symptom score reflect change in lung function FOLLOWING 6 MONTHS OF OMALIZUMAB TREATMENT?

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Marnie Graco, Rachel Schembri, Douglas J Brown, Jeanette Alexander, Melinda Millard, David J Berlowitz
How recruiting to more than one acute clinical trial in spinal cord injury affects recruitment, withdrawal and other trial processes: the COSAQ experience

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Al Matroodi, S.A., McDonald, C.F., Collins, A.L., Darby, I.A., Pouniotis, D.S.
Blood Monocyte Phenotype Is Not Altered In Primary Lung Cancer

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Meaklim, H.J., Berlowitz, D.J, Jackson, G., Brown, D.J., Connelly, A., Farquharson, S., Bilston, L.E., Hatt, A., Cistulli, P.A., Sutherland, K., Skordilis, C. [1], and O'Donoghue, F.
To 3T-MRI or not to 3T-MRI? Issues with the use of 3T-MRI in patients with quadriplegia and obstructive sleep apnoea

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Christian R. Osadnik, Christine F. McDonald, Belinda R. Miller, Catherine Hill, Ben Tarrant , Ranjana Steward, Caroline Chao, Nicole Stodden, Cristino Oliveira, Nadia Gagliardi, Anne E. Holland
A multi-centre, randomised controlled trial of PEP therapy for inpatients with acute exacerbations of COPD.

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Justine Westlake, Gerard Kennedy, Paul Emerson, Philip Swann, Mark Howard
Do shift workers fare as badly as obstructive sleep apnoea patients: investigating sleepiness, mood and performance?

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Mark E. Howard, Michael L. Lee, William J. Horrey, Yulan Liang, Claire Anderson, Michael S. Shreeve, Connor O'Brien, Charles A. Czeisler
Driver awareness of drowsiness and prediction of falling asleep prior to critical driving events during actual motor vehicle driving after actual night shift work
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Jessica Raubenheimer
Investigation into periodic limb movements (PLM) muscle activation patterns and the impact of sensor type on plm detection

Thur 12
Y.H. Khor, J. Tolson, T. Churhward, P. Rochford, C.J. Worsnop
Comparison of estimated and measured sleep latency during home polysomnography among patients with suspected obstructive sleep apnoea

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Kyle G. Smart, Fergal J. O'Donoghue, Christopher J. Worsnop, Allison L Collins, Maree Barnes
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Ali Ghasem-Zadeh, Roger Zebaze, Åshild Bjørnerem, Xiaofang Wang, Yohann Bala, Ego Seeman
Assessing Age, Sex, and Racial Differences in Cortical Porosity Requires Adjustment for Site-Specific Variation in the Selected Region of Interest

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David Story
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Thur 16
Philip Peyton, Christine Wu
Nitrous oxide induced postoperative nausea and vomiting is related to duration of exposure

Thur 17
Philip Peyton, Christine Wu
Poor correlation between meta-analyses and subsequent large randomised controlled trials in anaesthetic literature

Thur 18
Vella, L.J., Pasam, A., Dimopoulos, N., Puaux, A.L., Louahed, J., Andrews, M., Knights, A., Chan, W., Woods, K., Cebon, J.
MEK inhibition, alone or in combination with BRAF inhibition, impairs multiple functions of isolated normal human lymphocytes and dendritic cells

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David Gray, Elizabeth Watt
Prioritising care for newly diagnosed men with prostate cancer: development of a supportive care needs risk factor assessment tool.

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Miles C. Andrews, Dani Tutuka, Andreas Behren, Jonathan Cebon
Newer-generation BRAF inhibitors avoid paradoxical oncogenic effects of targeted therapy in melanoma

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Paul L. Mitchell, Shane Battye, Tom John, Carmel Murone, Simon Knight, Khashayar Asadi
Expression of Mucin 1 in non-small cell lung cancer: Relationship between IHC, tumour characteristics and survival

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Katherine Woods, Anupama Pasam, Ashley Knights, Jonathan Cebon, Catherine Gerard, Anne-Laure Puaux, Sandra Morel, Jamila Louahed
QS21 adjuvant enhances cross presentation of NY-ESO-1 antigen by Dendritic Cells in vitro.

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Dylan King, Dahna Makris, Violeta Spirkoska, Rachael Canfield, Paul Ramsland, William Farrugia, Bruno Catimel, Andrew Scott, Ingrid Burvenich
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Andrew J. Weickhardt, Teresa T. Nguyen, Diego D. Paskulin, Anh T. Le, Dara Aisner, Nathan Schulte, Fiona J.M. Chionh, John Mariadason, Niall C. Tebbutt, Robert C. Doebele, Marileila Varella-Garcia
ALK and ROS1 gene rearrangements detected in colorectal cancer (CRC) by fluorescence in situ hybridization (FISH)

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Association of 18F-FDG Metabolic Tumour Volume and Dysphagia in Head and Neck IMRT as a prophylactic feeding predictor

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Sujitra Detchokul, Melissa J. Davis, Albert G. Frauman
Biomarkers of prostate cancer progression: Evolution of genetic changes and molecular drivers in castrate-resistant prostate cancer (CRPC)

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Paul Ioannidis, John M. Mariadason, Anderly C. Chueh
The role of Protein Kinase C (PKC) in Histone Deacetylase inhibitor (HDACi) induced apoptosis in colon cancer cells

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Anne-Sophie Hatat, Angelo Perani, Bruno Catimel, Harjit Singh, Fiona E. Scott and Andrew M. Scott
Purification of ErbB receptors from Cancer Cell Lines

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Anne-Sophie Hatat, Angelo Perani, Fiona E. Scott and Andrew M. Scott
Determination by Flow Cytometry of ErbB receptor number on Cancer Cell Lines

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Laura J. Vella, Bradley Coleman, Andreas Behren, Andrew F. Hill & Jonathan Cebon
Investigating the role of exosomes in conferring drug resistance in melanoma

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Thomas John, Carmel Murone, Khashayar Asadi, Marzena Walkiewicz, Adrienne Morey, Simon Knight, Paul Mitchell
MET expression, copy number and oncogenic mutations in early stage NSCLC

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Dannel Yeo, Hong He, Christopher Christophi, Graham Baldwin, Arthur Shulkes, Mehrdad Nikfarjam
A Novel p21-Activated Kinase 1 Inhibitor, Glaucarubinone, Combined with Gemcitabine Synergistically Inhibits the Growth of Pancreatic Ductal Adenocarcinoma

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Peter J Wookey, Sebastian G.B. Furness, Karly Sourris, Angela Kourakis, David L. Hare
Development of a unique antibody against human GLP-1 receptor

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K.J. Lu, L.G. Kearney, M. Ord, E. Jones, L.M. Burrell, P.M. Srivastava
Age adjusted Charlson Co-morbidity Index is an Independent Predictor of Mortality over long-term Follow-Up in Infective Endocarditis

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Y. Bala, S. Iuliano, A. Ghasem-Zadeh, X-F. Wang, E. Seeman, R. Zebaze
Distribution of voxel composition of the cortical bone discriminates patients with forearm fragility fractures

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Chee-Yuen Adrienne Lam, Richard Zwar, Brett Ayres
Retrospective audit of outpatient pre-operative chest x-rays and their contribution to pre-operative management in patients who meet and do not meet existing guidelines

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Jan Heng, Stella Liong, Michael Permezel, Gregory Rice, Megan Di Quinzio, Harry Georgiou [2]
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Rachel Cooke, Stephen Valentine, Gerard Hale, Carole L Smith, Raymond Dauer
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Chandran, S., Parker, F., Lontos, S., Vaughan, R., Efthymiou M
Optical diagnosis of diminutive polyp histology with narrow band imaging: Accuracy without optical magnification and the financial impact on the health system

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Chandran, S., Parker, F., Vaughan, R. Efthymiou, M.
The current practice standard for colonoscopy in Australia

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S. Chandran, R. Vaughan, M. Efthymiou, J. Sia, C. Hamilton
A pilot study of EUS guided fiducial insertion for the multidisciplinary management of gastric cancer

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Elevated gastrin levels protect against hypoxia-induced weight loss in mice
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Differences in Cortical and Trabecular Microstructure in Chinese and Caucasian Females originate during Peripubertal Growth

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K. Burton, F. Ciavarella, R. Griffiths
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Thur 50
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Evaluation of clinical care processes using the integrated bedside audit tool (BAT)

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A link between metabolism and renin: renin secretion in mice with mutations of the AMPK/ACC1 pathway

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Matthew R. P. Davies, Marina Katerelos, Kurt Gleich, Scott A. Fraser, Peter F. Mount, David A. Power
Enhanced phosphorylation of NKCC2 by SPAK/OSR1 in a murine model of diet induced obesity

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Jeannette Milgrom, Charlene Schembri, Brian Danaher, John Seeley, Scott Stuart, Milagra Tyler, Jennifer Ericksen, Whitney Lester, Alan Gemmill, Peter Lewinsohn
Web-based intervention for women with postpartum depression: feasibility trial results of MumMoodBooster

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MR-less cortical surface-projection of PET scans with 11C and 18F Labeled radiotracers

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Xiaoyun Liang, Alan Connelly, Fernando Calamante
A novel efficient denoising method for ASL data: Assessment using voxel-wise network analysis

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Robert E. Smith , J-Donald Tournier, Fernando Calamante and Alan Connelly
The effects of SIFT on the reproducibility of the structural connectome

Thur 57
Robert E. Smith, J-Donald Tournier, Fernando Calamante and Alan Connelly
Evidence for the improved biological interpretability of white matter connectivity derived following tractogram filtering using SIFT

Thur 58
S. Farquharson, J-D Tournier, F. Calamante, S. Mandelstam, M. Schneider-Kolsky, S.F. Berkovic , I.E. Scheffer , G. Jackson, A. Connelly
Whole Brain Tractography Mapping Reveals Abnormal Structural Connections in Neuronal Heterotopia

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Konstantine Sfrantzis, Jackie M.Y. How & Daniela M. Sartor
Understanding the mechanisms involved in the aetiology of obesity-related hypertension: implications of diet modification

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Ana Antonic, Mirella Dottori, Jessie Leung, Geoffrey A. Donnan, David W. Howells
NXY-059 does not protect stem cell-derived human neurons: First use of a novel drug screening protocol

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Sharon F. Kramer, Leonid Churilov, Rosalie Kroeders, Marco Y.C. Pang, Julie Bernhardt
Changes in activity levels in the first month after stroke

Thur 62
R. Sheedy N. Shields, L. Churilov, D.A. Cadilhac , J. Bernhardt
Hospital admission for stroke encourages inactivity

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J. Collier, S. Speare, L. Churilov, A. Thrift, R. Lindley, G. Donnan, H. Dewey, P. Langhorne, J. Bernhardt on behalf of the AVERT Trialist Collaboration
What are the main reasons for exclusion from an early rehabilitation trial (AVERT)?

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J. Bernhardt, of behalf of the AVERT Trialist's Collaboration
A Very Early Rehabilitation Trial (AVERT): Update

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Toby Cumming, Emilio Werden, Audrey Raffelt, Renee Lichter, Qi Li, Heath
Pardoe, Amy Brodtmann
*Physical activity is associated with cognition after stroke, but only for tasks
presented visually*

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***Improving the management of oral medications in patients who are
fasting or nil by mouth***

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The-Phung To, David A Story, Jane Booth, Fiona Nielsen, Joanne Sweeney,
Patricia Bruce, Cathy D'Alterio, Melodie Heland, Andrew Hardidge
*Involving consumers as team members in research: The fasting & nil by
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**Dale Christiansen, Effie Mouhtouris, Svjetlana Kireta, Paul Ramsland,
Toby Coates, Frank Ierino, Mauro Sandrin**
Production and Function of Soluble Marmoset ICOS-Ig

Thur 69
Fiona C. Brownfoot, Stephen Tong, Natalie Hannan, Laura Tuohey, Kenji
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*Pravastatin quenches oxysterol-induced upregulation of soluble endoglin in
primary endothelial cells: a potential therapeutic for preeclampsia*

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**Jodie Hahn, Cathy Cooper, Natasha van Zyl, Stephen Flood, Michael
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***Nerve transfers post Spinal Cord Injury: the therapist role in
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Natasha van Zyl, Stephen Flood, Michael Weymouth, Cathy Copper, Jodie
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*The Melbourne Triple Nerve Transfer - Upper limb reanimation in C6
tetraplegia*

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Alexander, J.L., Millard, M.S., Berlowitz, D.J., Graco, M., Schembri, R., Brown, D.J.
A Model for Facilitating Participant Recruitment in Spinal Clinical Trials in Victoria

Thurs 73
S.N.S. Louis [1], J. Siviloglou [2], D. Debono [2], A. G. Frauman [1], K. Garrett [3], D. Liew [4]

Hospital costs of venous thromboembolism and their predictors

TUES 01

S. Iuliano-Burns, T.D.T Vu, C. Chiang, E. Gianatti, E. Hamilton, M. Grossmann, E. Seeman, J. Zajac

Improving Management of Low Trauma Fractures in a Tertiary Hospital The "Fracture Capture" Project

Department of Endocrinology, University of Melbourne, Austin Health

Aim
Follow up after admission for a low trauma fracture is low. An audit of Austin Health in 2003 indicated that <1% of inpatients were discharged with anti-resorptive treatment to reduce fragility fractures, and 6% had follow up investigation. We aimed to determine if a designated fracture capture and treatment program improved management following a low trauma fracture.
Method
Patients admitted through the emergency department (ED) with a low trauma fracture (hip, spine upper and lower limbs) were identified weekly. Inpatients had clinical assessment and biochemical investigations for secondary osteoporosis. Treatment was commenced according to standard guidelines. After discharge, endocrine clinic review was scheduled following outpatient DXA and pathology assessments. Patients discharged directly from the ED were contacted via mail to undergo secondary screening.
Results
From 2009–2013, 1891 females (mean age 73+12yrs) and 642 males (mean age 71+12yrs) with fragility fractures were identified. 1219 were inpatients (700 hip fractures) and 1314 discharged directly from the ED (580 wrist fractures). 70% of inpatients were discharged with treatment or had assessment and clinic review and 46% of those discharged directly from the ED had investigations and clinic review compared to none previously. 13% elected to be treated by their GP or specialist. Of all low trauma fracture admissions, 17% may have been untreated (failed to respond to correspondence).
Conclusion
A dedicated fragility fracture identification and treatment program vastly improves management and treatment of bone fragility. Whether this translates into improved compliance and fracture risk reduction requires further investigation.

TUES 02

Sue Berney [1], Joleen W. Rose [1], Rinaldo Bellomo [2], Linda Denehy [3]

Patient activity and environmental enrichment in the intensive care unit

1. Physiotherapy Department, Austin Health
2. Intensive Care, Austin Health
3. Department of Physiotherapy, University of Melbourne

Aim
Increased physical activity levels in the intensive care unit (ICU) are associated with improved short and long term outcomes. However, the baseline activity of longer stay critically ill patients has not been systematically evaluated. We aimed to document the activity levels and environmental enrichment of patients who are critically ill.
Method
Patients requiring at least 48 hours of mechanical ventilation and staying at least 96 hours in intensive care were observed between the hours of 08:00-17:00. Included patients were observed for one minute every ten minutes except for four randomly selected 10-minute breaks for eight hours. At each time-point patient location, physical activity and any person attending the patient were recorded. Physiotherapists completed treatment records.
Results
Forty-one patients were observed on 54 occasions, a total of 2214 observations. Over the eight hour period 83% (6.64 hours) was spent in bed and 34% (2.7 hours) alone. For the patients observed that were awake, alert and cooperative (n=24) they spent 76% of the observation period (6 hours) in bed. Patients who were able to walk with or without assistance (n=6) spent 4.2 hours in bed (52% of observed time). Physiotherapists were involved in the first instance of mobilisation of every patient.
Conclusion
Despite being able to mobilise patients remain in bed for the majority of the day. This study provides baseline data for the investigation of future strategies to improved physical activity levels of critically ill patients and will be important in ensuring separation is achieved in future trials.

TUES 03

Jenny Healy [2]**, Mark Ng Tang Fui** [1, 2]**, Philippe Dupuis** [1, 2]**, Mathis Grossmann** [1, 2]

Testosterone For Prevention Of Diabetes Type 2 (T4DM)

1. Department of Endocrinology, Austin Health
2. Department of Medicine, University of Melbourne

Testosterone For Prevention Of Diabetes Type 2 (T4DM) Type 2 diabetes mellitus (T2DM) is associated with lower testosterone (T) levels in men. Although directional cause-and-effect relationships remain unclear, there is evidence that low T may be a rectifiable factor to reduce the risk of pre-diabetes progressing to T2DM.

Our local data, from our diabetes clinics showed that 43% of men with T2DM had low T levels and multiple other studies have shown that men with low T are more likely to be overweight and obese which is the main risk factor for developing T2DM. T treatment is known to reduce fat mass and increase muscle mass. Short-term studies indicate that, in men with low T and T2DM, T treatment ameliorates insulin resistance and improves glucose and HbA1c. Although lifestyle modification has been shown to prevent T2DM it is difficult to achieve and sustain. T supplementation may, therefore, be an attractive therapeutic option. However, no large-scale, long-term studies have assessed the benefits and risks of T therapy for preventing T2DM.

We are undertaking a multicentre, double-blinded placebo-controlled trial that aims to determine whether, in 1500 overweight or obese men aged 50-74yrs with pre-diabetes, intramuscular T replacement over two years will prevent progression to T2DM. All men are enrolled in a lifestyle management program provided by Weight Watchers. Secondary outcome measures include body composition, psychosocial factors and motivation to comply with the lifestyle program.

We will discuss the challenges of performing a multi site randomised clinical trial.

TUES 04

S. Iuliano[1], Q.J. Wang [1], X.F. Wang [1], R. Zebaze [1], A. Ghasem Zadeh [1], Y. Bala [1], N. Pang [2], E. Seeman [1]

Cortical Bone Fragility Contributes to Fractures in Children

1. Department of Endocrinology, University of Melbourne, Austin Health
2. Austin Health

Aim
About 50% of children sustain fractures during their growth. The highest incidence coincides with puberty, when there is a transient reduction in volumetric vBMD and cortical thickness. We hypothesize that deficits in cortical thickness and increased cortical porosity are present in children with fractures.

Method
We recruited 54 children (52% males) with low-trauma fractures and imaged their distal contralateral radius using high-resolution pQCT. Cortical porosity, degree of mineralization (tissue mineralization density), and transitional zone dimensions (area between compact-appearing cortex and trabecular bone) were determined using StrAx1.0. Fracture cases were compared to 54 age- (11.9±2.9 vs. 11.7±2.8yrs), height- (152.4±16.7 vs. 150.7±15.2cm) weight- (46.6±15.6 vs. 45.8±15.3kg) and maturity-matched controls.

Results
Bone cross-sectional area was similar in cases and controls (224±66 v 208±59mm2). Cortical vBMD was 5% lower in cases (773±114 vs. 819±135mgHA/cm3, $p<0.05$) due to their 6% higher porosity (53±8 vs. 50±9%, $p<0.05$) and 3% lower tissue mineralization density (61±3 vs. 63±3%, $p<0.0001$). Differences were most evident in pre-pubertal boys (n=26) in whom fracture cases had 26% thinner cortices (0.30±0.07 vs. 0.41±0.12mm, $p<0.01$), and 9% wider transitional zone (2.77±0.19 vs. 2.55±0.30μm, $p<0.05$) than controls. Fracture cases had greater medullary area (107±27 vs. 84±28mm2, $p<0.05$) with thicker (0.08±0.01 vs. 0.07±0.0mm, $p<0.01$), and fewer (1.8±0.2 vs. 2.1±0.31/mm, $p<0.01$) and more separated trabeculae (0.49±0.08 vs. 0.41±0.06mm, $p<0.01$) than controls.

Conclusion
We infer that cortical material and structural abnormalities contribute to bone fragility during growth predisposing to fractures should a fall occur.

TUES 05

Chrysovalantou E. Xirouchaki, Zheng Ruan, Salvatore P. Mangiafico, Jenny Favaloro, Joseph Proietto, Sofianos Andrikopoulos

The impact of muscle-specific deletion of glycogen synthase on glucose tolerance and insulin sensitivity in mice.

Department of Medicine, University of Melbourne, Austin Health

Aim:
Impaired glucose storage is a defect that contributes to peripheral insulin resistance in Type 2 Diabetes. The aim of the present study was to examine the effects of muscle-specific deletion of the Glycogen Synthase (gys1) gene on glucose metabolism, using an optimized mouse model generated via conditional, tamoxifen-inducible Cre-LoxP system.
Method :
Muscle-specific MerCreMer mice were bred with gys1 floxed (Gyslox) mice to generate animals with a Gyslox+/+/Cre+/- (knockout) and Gyslox+/+/Cre-/- (control) genotype. 10 week-old mice were fed a diet containing 1 mg/g tamoxifen for 8 weeks followed by a recovery period of 1-4 weeks on chow diet. Oral glucose tolerance tests, Insulin tolerance tests, basal glucose turnover, and hyperinsulinaemic-euglycaemic clamps followed by measurement of insulin-stimulated 2-deoxy-glucose uptake were performed.
Results:
Knockout mice presented >80% deletion of muscle GS protein levels, preserved for 1-4 weeks following tamoxifen withdrawal. These mice were glucose intolerant (insulin AUC Compared with the control mice: control 67.6±4.4 vs gys1-knockout 83.6±8.5 ng/mlx120min, $P<0.05$). Under basal conditions, the metabolic clearance rate of Gyslox+/+/Cre+/- knockout mice was significantly lower than control mice (gys1ko: 8.46±0.67 ml/min/kg vs control: 11.96±1.01 ml/min/kg $P<0.05$). Under insulin-stimulated conditions, knockout mice showed reduced glucose uptake in heart, muscle and white adipose tissue, indicative of insulin resistance. No statistically significant differences in body weight rate were identified between the two groups over the eight weeks. The recovery successfully reversed the tamoxifen-induced weight loss.
Conclusion:
An optimized inducible muscle specific-deletion of glycogen synthase in adult mice results in glucose intolerance associated with insulin resistance in muscle.

TUES 06

Gemma Collins, Brooke Chapman & Leonie Pearce

Weight gain and obesity after orthotopic liver transplantation

Department of Nutrition and Dietetics, Austin Health

Aim:
Weight gain after orthotopic liver transplantation (OLTx) is well documented, and obesity increases morbidity and mortality in this population. Increasing numbers of OLTx's and improved survival means long-term consequences of OLTx are becoming more evident. For the first time at Austin Health, we assessed the extent of weight gain and prevalence of overweight and obesity in patients following OLTx.
Methods:
Weight and body mass index (BMI) were collected retrospectively in all patients transplanted between July 2009 and December 2011. Dry weight was assessed at transplant, and 3-, 6-, 12- and 24-months post OLTx.
Results:
110 patients were assessed (73% male, average age 48.1 years, range 17-67 years). Ninety-five percent of patients were transplanted for chronic liver disease. The most common causes of liver failure were primary sclerosing cholangitis (PSC) and primary biliary cirrhosis (PBC) (22%), hepatoma (20%), Hepatitis C (19%) and alcoholic liver disease (11%). At OLTx, 31 and 19% of patients were overweight and obese, respectively. This increased significantly to 45% (overweight) and 26% (obese) by 24 months post OLTx (p=0.02). Weight trends showed there was an initial weight loss of 2kg at 3 months post OLTx, with average increases of 0.9kg, 3.5kg and 6.2kg at 6, 12 and 24 months, respectively.
Conclusion:
The prevalence of overweight and obesity is high in patients following OLTx. Patients experience weight gain from 6 months post transplant, which progressively increases up to 24 months. Targeted interventions including dietary advice should be implemented at 6 months post transplant to prevent excessive weight gain.

TUES 07

Shea Edsall, Amy Kaplan, Kellie Draffin and Terrill Bruere

Aggressive feeding protocol safely implemented in a paediatric inpatient eating disorder program

Department of Nutrition and Dietetics, Austin Health

Aim:
This study evaluated outcomes following the introduction of an aggressive feeding protocol in an inpatient paediatric eating disorder program. Historically, a cautious approach to feeding has occurred due to the risk of refeeding syndrome.
The aggressive feeding protocol implemented in May 2012, included inpatients commencing a meal plan at a higher energy level, with more rapid energy increases and macronutrient manipulation, while maintaining a food based approach.
Method:
A retrospective audit of 38 patients admitted to the paediatric ward between June 2012 and January 2013 was completed, with data collected from the medical record. These patients were admitted for medical stabilisation of their eating disorder, using the aggressive feeding protocol. Results were compared to an audit conducted prior to the introduction of the aggressive feeding protocol.
Results:
37 patients (97%) were commenced on a meal plan of 8.2 megajoules (MJ) or more and increased to 11 MJ within one week of admission. Previously, 23 patients (60%) had commenced on 6.8 MJ or less.   With more aggressive feeding 30 patients (79%) reached the target weight gain of 1 to 1.5 kilograms per week throughout admission (only 35% previously). Hypophosphatemia was identified and treated in only 2 patients (5%), and 2 other patients (5%) were identified as being at high risk of refeeding syndrome and received prophylactic phosphate supplementation.
Conclusion:
Aggressive feeding was achieved safely with a food based approach in this patient group during an inpatient stay. Patients achieved weight gain targets without any adverse effects associated with refeeding syndrome.

TUES 08

Purcell, K. [1], Sumithran, K. [1], Prendergast, L. [2], Bouniu, C.J. [1], Delbridge, L. [3], Proietto, J. [1]

Personality and social functioning to achieve a pre-determined weight loss target

1. Department of Medicine, University of Melbourne, Austin Health
2. La Trobe University
3. Department of Physiology, University of Melbourne

Introduction:
Outcomes for individual participants who undergo any given weight loss treatment vary considerably (1, 2); some participants lose little or nothing while others achieve impressive losses. This project aims to identify any subject characteristics that predict successful weight loss on different types of weight loss programs.
Methods:
The study is a randomised dietary intervention trial. Initial baseline testing was performed then 200 participants were randomised to:
A.   Rapid Weight Loss (RWL) Group- participants were instructed bi-weekly by a dietitian to follow a VLCD over three months;
B.   Gradual Weight Loss (GWL) Group- participants were instructed bi-weekly by a dietitian to lose weight gradually over a 9-month period.
Participants were deemed successful if they lost 15% of their body weight.
Results:
In the GWL group, baseline hunger level was positively related to weight loss success ($p<0.05$). Seeking social support was also related to weight loss success in the GWL group; each additional point on the Ways of Coping Checklist- Revised subscale 'Seeks Social Support' increased the odds of weight loss success by 270% ($p<0.05$). In the RWL group, being less preoccupied with food at baseline was related to weight loss success; such that each additional centimetre placed on the VAS following the question 'How much are you preoccupied by thoughts of food?' was associated with a 32% reduction in the odds of weight loss success ($p<0.05$). The personality trait 'agreeableness' was positively associated with weight loss success on the RWL program ($p<0.05$).
Conclusion:
Agreeable obese individuals who are less preoccupied with food are more successful at losing weight rapidly than individuals who are less agreeable and more preoccupied with food. In contrast, individuals who are hungrier and seek social support when needed are more likely to be successful at losing weight gradually than those who are less hungry and seek social support less frequently.
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2. Palmeira A, et al. Predicting short-term weight loss using four leading health behavior change theories. Int J Behav Nutr Physical Activ 2007; 4: 14-14.

TUES 09
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TUES 10
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TUES 11
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TUES 12
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TUES 13

Chong Tan [1], Laurence Weinberg [1], David Story [1], Phillip Peyton [2] Larry McNicol [2], Parameswan Pillai 2

TRY LOOKING ANOTHER WAY: 3 NON-STANDARD TOE VIEWS OF THE MAIN PA AND RVOT

1. Consultant Anaesthetist, Austin Health
2. Department of Anesthetics, Austin Health

AIMS:
Transoesophageal echocardiographic (TOE) imaging of the main pulmonary artery (MPA) and right ventricular outflow tract (RVOT) is important for right heart assessment. We compared the feasibility of image capture of these structures between American Society of Echocardiographers (ASE)/ Society of Cardiovascular Anesthesiologists (SCA) standard views and 3 non-standard TOE views.
METHODS:
30 patients undergoing cardiac surgery were recruited. The frequency of image capture of the aortic arch short axis view (AoA SAX) and ascending aorta short axis view (AscAo SAX) was compared to that of the deep transgastric right ventricular inflow-outflow view (DTG RVIO), transgastric right ventricular outflow view (TG RVO), and mid-oesophageal pulmonary artery long axis view (MOPA LAX).
RESULTS:
There was a trend towards more reliable image capture in the non-standard views compared with the ASE/ SCA standard views (See Table 1) that did not reach statistical significance ($p = 0.11$, chi-squared test for trend).

TABLE 1

TOE VIEW	FREQUENCY (%)	95% CI
AoA SAX	70	51 – 83%
AscAo SAX	90	74 – 97%
MOPA LAX	83	66 – 93%
DTG RVIO	93	78 – 99%
TG RVO	87	70 – 85%

CONCLUSION:
ASE/ SCA non-standard views of the RVOT and MPA are at least as reliably captured as standard views. In cases where standard views are not available, use of non-standard views may offer visualisation of these structures.

TUES 15

Chong Tan [1], Laurence Weinberg [1], David Story [1], Phillip Peyton [2] Larry McNicol [2], Parameswan Pillai [2]

ARE NON-STANDARD TRANSOESOPHAGEAL ECHOCARDIOGRAPHIC VIEWS OF THE TRICUSPID ANNULUS FEASIBLE?

1. Consultant Anaesthetist, Austin Health
2. Department of Anesthetics, Austin Health

AIMS:
The commonly used mid-oesophageal 4-chamber view (ME4Ch), an American Society of Echocardiographers (ASE)/ Society of Cardiovascular Anesthesiologists (SCA) standard view, has been shown to understimate the true long-axis diameter of the tricuspid annulus (TA) when planning tricuspid annuloplasty. We investigated the reliability of image capture of several non-standard TOE views, which assess the TA at multiple angles.

METHODS:
30 patients undergoing cardiac surgery were recruited. The frequency of image capture of the 0o lower oesophageal coronary sinus view (LECS), 90O tricuspid valve "2-chamber" view (TV2Ch), 120o modified bicaval view (MBC), 120o lower oesophageal coronary sinus view (LE120CS), and deep transgastric right ventricular inflow-outflow view (DTGRVIO) was calculated.

RESULTS:
All proposed non-standard views were captured in most patients (See Table 1).

TABLE 1

TOE VIEW	SECTOR SCAN ROTATION	FREQUENCY (%)	95% CI
LECS	0o	100	87 – 100%
TV2Ch	90o	83	66 – 93%
MBC	120o	67	49 – 81%
LE120CS	120o	78	62 – 91%
DTG RVIO	120o	93	78 – 99%

CONCLUSION:
ASE/ SCA non-standard views of the TA are reliably captured. These views should be used when assessing the TA in anticipation of tricuspid annuloplasty, as standard views underestimate TA long axis length.

TUES 16

Chong Tan [1], Laurence Weinberg [1], David Story [1], Phillip Peyton [2] Larry McNicol [2], Parameswan Pillai [2]

SEEING IS BELIEVING: THE USE OF TTE TO VISUALISE SWAN-GANZ CATHETER PLACEMENT IN THE PULMONARY ARTERY

1. Consultant Anaesthetist, Austin Health
2. Department of Anesthetics, Austin Health

AIMS:
Although the most commonly used technique to guide swan-ganz catheter placement, pressure waveform analysis may be occasionally confounded by artefacts. Incorrect placement beyond the pulmonary artery carries a 1:650 – 1:4,300 risk of mortality. We hypothesized that transthoracic echocardiography (TTE) assists confirmation of correct placement.
METHODS:
100 patients requiring swan-ganz catheter insertion for cardiac surgery were recruited. TTE was used to confirm placement after conventional placement with pressure waveform analysis. The parasternal short axis right ventricular inflow-outflow view (PSRVIO), subcostal right ventricular inflow-outflow view (SCRVIO) and parasternal ascending aorta short axis view (PSAscAo) were used in preferential order until visualisation was successful. The proportion of catheters placed in the main or right pulmonary arteries were compared.
RESULTS:
Placement of the PAC balloon within the MPA or RPA was confirmed by TTE in 98 patients [sensitivity 98%,(95%CI 93-100%)], and its absence correctly established in 100 patients [specificity 100% (95-100%)]. TTE was in excellent agreement with pressure waveform guidance [Cohen's Kappa 0.97, (95%CI 0.94 – 1.0)]. The successful view used and final catheter positions are shown in Table 1.

PARAMETER		Number (95% CI of proportion) and p-value	
Final PAC position in MPA		81 (72-88%)	p = < 0.0001
Final PAC position in RPA		19 (13-29%)	
TTE view in whichPAC was seen	PSRVIO	53 (43-63%)	p = < 0.0001
	SCRVIO	35 (26-45%)	
	PSAscAo	13 (6-24%)	

CONCLUSION:
TTE is a highly sensitive and specific adjunct to pressure waveform guided PAC insertion and should assist in reducing complications related to PAC malposition.

Chong Tan, Chiu Kang

BLOCKS & BREATHING: RESPIRATORY FUNCTION AFTER SHOULDER SURGERY IS UNAFFECTED BY ANALGESIC TECHNIQUE

Department of Anaesthesia, Austin Health

AIMS
Pain following shoulder surgery is known to be severe. Interscalene brachial plexus blockade offers ideal analgesia for 24 hours but is known to cause hemidiaphragmatic paralysis. Opioid analgesia impairs oxygenation by multiple mechanisms, particularly in older patients. We aimed to explore the differences in effect on respiratory function between the two analgesic techniques.
METHODS
The hospital records of 90 patients over the age of 50 who had undergone such surgery within the last 3 years in a tertiary centre were examined. We compared postoperative fall in the partial pressure of arterial oxygen: fraction inspired oxygen ($PaO_2{:}FiO_2$) ratios of patients receiving interscalene block versus opioid analgesia in the 24hr postoperative period.
RESULTS
68 patients received single dose interscalene brachial plexus blockade (Group ISB) versus 22 who did not (Group OP). Opioid analgesics administered intraoperatively and in recovery (morphine equivalents, mg/kg) were significantly higher in Group OP (mean difference 0.2mg/ kg, $p = 0.01$). Patients in group ISB experienced a fall in Pa:FiO_2 ratio of [mean (95% CI)] [188, (148-228)] compared with patients in group Op [165, (136-193)], $p = 0.48$. Patient demographics (age, sex, BMI, ASA status) and prevalence of premorbid disease (COAD, CCF, hypertension, serum creatinine and eGFR) were not significantly different between groups.
CONCLUSIONS
There does not appear to be any significant difference in the effect on oxygenation between interscalene brachial plexus and opioid analsgesia. V/Q matching is significantly impaired after shoulder surgery regardless of analgesic technique.

TUES 18

Laurence Weinberg [1]**, Nick Scurrah** [1]**, Larry McNicol** [1]**, Chris Christophi** [2]**, Mehrdad Nikfarjam** [2]

Liberal fluid intervention and positive fluid balance affect length of hospital stay following pancreaticoduodenectomy

1. Department of Anaesthesia, Austin Health
2. Department of Surgery, Austin Health

Introduction:
The effects on detailed fluid intervention on perioperative complications and length of hospital stay (LOS) after pancreaticoduodenectomy have not been reported. We hypothesized that patients undergoing pancreaticoduodenectomy treated with a liberal fluid regime would have a longer LOS compared to those managed with a restrictive regime.
Methods:
We conducted a retrospective analysis of patients undergoing pancreaticoduodenectomy in a University hospital, expert in hepatobiliary surgery and liver transplantation. Demographic data, operative details, detailed fluid prescription, complications and outcomes were retrieved from medical records. Prognostic predictors for LOS were determined.
Results:
Data for 150 consecutive patients undergoing pancreaticoduodenectomy between 2004-2012 was collected. Mean age: 66 years; Male gender: 59%, Mean weight: 74kg, ASA Class 3: 75%. Average volume of intravenous fluid administered on postoperative days (POD) 1 to 3 was 3.0L (range: 0.9-14.1), 2.1L (range: 0.3-6.1), and 1.7L (range: 0-6.0) respectively. 50 patients (33%) experienced at least one major complication; 66 patients (44%) at least one minor complication. Common complications: sepsis (22%), anastomotic leak (20%), pneumonia (17%), delayed gastric emptying (17%), myocardial infarction (8%), pulmonary oedema (6%). 30-day mortality: 2%. Median LOS: 17 days (range: 7-140 days). Patients experiencing complications received more fluid intraoperatively, and on POD 1-3 (P=0.02). Positive fluid balance was a strong independent predictor of hospital morbidity. On multivariate analysis, factors independently associated with a LOS of <14 days were complications (OR 0.1, 95% CI:0.0-0.3;P<0.001) and >3L fluid on POD 1 (OR 3.0, 95% CI:1.1-8.3;P<0.003).
Conclusions: Liberal perioperative fluid intervention and a positive fluid balance adversely affect LOS stay following pancreaticoduodenectomy.

TUES 19

Laurence Weinberg [1]**, Nick Scurrah** [1]**, Larry McNicol** [1]**, Chris Christophi** [2]**, Mehrdad Nikfarjam** [2]

Enhanced Recovery After Surgery Program Reduces Length of Stay Following Uncomplicated Pancreaticoduodenectomy

1. Department of Anaesthesia, Austin Health
2. Department of Surgery, Austin Health

Introduction
Factors affecting length of hospital stay after uncomplicated pancreaticoduodenectomy have not been reported. We hypothesized that patients undergoing uncomplicated pancreaticoduodenectomy treated by an Enhanced Recovery After Surgery (ERAS) program would have a shorter length of hospital stay compared to those managed by standard care.
Methods
Patients without surgical or medical complications following pancreaticoduodenectomy managed by ERAS or standard programs between 2005 and 2011, were identified and prognostic predictors for length of hospital stay determined.
Results
Forty-one patients treated by pancreaticoduodenectomy had no medical or surgical complications during this period. Of these patients, 20 underwent ERAS program compared to 21 who underwent standard care. Median postoperative length of stay was shorter in the ERAS group (8 days, range: 7-16 days) versus 14 days, range:8-29 days; P<0.001). There were three readmissions in the ERAS 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 fast track recovery program group (median 9 days, range: 7-17 days versus median14 days, range: 8-29 days;P<0.001). Patients in the standard group were more likely to have a feeding jejunostomy tube (P<0.001), pylorus preserving procedure (P=0.001) and a nasogastric tube in place longer than 24 hours postoperatively (P<0.001). There were no significant differences in discharge destination between groups. On multivariate analysis, the only factor independently associated with postoperative discharge by day 8 was ERAS program (OR: 37.1, 95% CI: 4.08-338;P<0.001).
Conclusion
ERAS program achieved significantly shorter length of stay following uncomplicated pancreaticoduodenectomy.

TUES 20

Ping Chia [1], **Dr Linda Gualano** [2], **Sathi Seevanayagam** [2], **Laurence Weinberg** [1]

Outcomes following fractured neck of femur in an Australian metropolitan teaching hospital

1. Department of Anaesthesia, Austin Health
2. Department of Anaesthesia, Northern Health

Objectives
To determine the morbidity and mortality outcomes of patients presenting with a fractured neck of femur in an Australian context. Peri-operative variables related to unfavourable outcomes were identified to allow planning of intervention strategies for improving peri-operative care.

Methods
We performed a retrospective observational study of 185 consecutive adult patients admitted to an Australian metropolitan teaching hospital with fractured neck of femur between 2009 and 2010. The main outcome measures were 30-day and one-year mortality rates, major complications and factors influencing mortality.

Results
The majority of patients were elderly female with multiple comorbidities. Multiple perioperative medical complications were observed, including pre-operative hypoxia (17%), post-operative delirium (25%), anaemia requiring blood transfusion (28%), representation within 30 days of discharge (18%), congestive cardiac failure (14%), acute renal impairment (12%) and myocardial infarction (4%). Mortality rates were 8.1% at 30 days and 21.6% at one year. Factors predictive of one-year mortality were American Society of Anesthesiologists (ASA) score (odds ratio (OR) 4.2 (95% confidence interval (CI) 1.5 to 12.2)), general anaesthesia (OR 3.1 (95% CI 1.1 to 8.5)), age > 90 years (OR 4.5 (95% CI 1.5 to 13.1)) and post-operative oliguria (OR 3.6 (95% CI 1.1 to 11.7)).

Conclusions
Results from an Australian metropolitan teaching hospital confirm the persistently high morbidity and mortality in patients presenting with a fractured neck of femur. Efforts should be aimed at medically optimising patients pre-operatively and correction of pre-operative hypoxia. This study provides planning data for future interventional studies.

TUES 21

Laurence Weinberg [1], Chong Tan [1], Nick Scurrah [1], Guangjun Chen [1], Larry McNicol [1], Mehrdad Nikfarjam [2]

Analgesia practice for pancreaticoduodenectomy: is it time to reconsider epidurals?

1. Department of Anaesthesia, Austin Health
2. Department of Surgery, Austin Health

Introduction:
The efficacy of routine epidural use for major pancreatic surgery has recently been questioned[1,2,3]. This study examined epidural failure rates and complications in patients undergoing pancreaticoduodenectomy in an Australian tertiary centre with a dedicated hepatobiliary-pancreatic service, including liver transplantation.

Methods:
We conducted retrospective analyses of the use of epidurals in patients undergoing pancreaticoduodenectomy. Demographic data, operative details, anaesthesia/analgesia regimes and complications were retrieved from hospital medical records.

Results:
Data for 150 consecutive patients undergoing pancreaticoduodenectomy between 2004-2012 was collected. Mean age: 66 years (range: 38-84 years). 59% of patients were male. Mean weight: 74kg (SD+13); 24% were ASA Class 2; 75% Class 3. Epidurals were attempted in 84 patients (56%). Epidurals were successful (good pain control for 48 hours without complications) in 31 patients (37%). Epidural failure rate (conversion to opioid analgesia, or epidural related complication) was 63%. The most common reason for epidural failure was inadequate block (48%), followed by inability to insert (5%), postoperative hypotension requiring medical intervention (7%), dislodgement (5%), and leakage (1%). There were no epidural related neurological complications. There was no difference in hospital length of stay between patients who received epidurals and those who did not (16 days vs. 18 days, p=0.293).

Conclusions:
This study supports published literature that questions the utilization of epidurals as the "ideal" method of controlling pain in patients undergoing pancreaticoduodenectomy.

References:
1. Choi et al. Pancreas 2010;39:492-97.
2. Pratt et al. Journal of Gastrointestinal Surgery 2008;12:1207-20.
3. Sakowska et al. World Journal of Surgery 2009;33:1802-8.

TUES 22

Ping Chia, Laurence Weinberg, Chong Tan, Larry McNicol

Current trend of anaesthesia practice for primary total knee arthroplasty surgery in an Australian metropolitan teaching hospital

Department of Anaesthesia, Austin Health

Introduction

In a report identifying 14,000 patients undergoing primary total knee arthroplasty (TKA), spinal anaesthesia was associated with reduced complications compared with general anaesthesia (GA)1. The purpose of this study was to examine recent trends of choice of anaesthesia technique in an Australian tertiary centre.

Methods

With ethics approval, we conducted a retrospective analysis of choice of anaesthesia technique utilized for adult patients undergoing TKA. Patient data were retrieved from hospital medical records.

Results

Data for 205 consecutive patients undergoing TKA between 2010-2011 was collected. Mean age was 70 years; 64% were female. 53% had ASA Class 3 and 43% ASA Class 2. Spinal anaesthesia was used in 90 patients (44%), followed by GA in 71 patients (35%), and combined general-spinal anaesthesia in 43 patients (21%). Overall, 135 patients (66%) received a peripheral nerve block: femoral nerve (67%), fascia iliaca (23%), combined femoral/sciatic nerve (9%), and lumbar plexus (1%). In the GA group, 59 patients (83%) received a peripheral nerve block.

Conclusions

In a single centre university teaching hospital there is a divergence away from recent trends supporting the benefits of spinal anaesthesia in reducing complications following TKA. Our results reflect a mixed use of anaesthesia modality. Whilst there is a slight preference for spinal anaesthesia, there is an emerging trend toward multimodal analgesia using peripheral nerve blockage, especially in patients undergoing GA.

Reference

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TUES 23

Laurence Weinberg [1], Brett Pearce [1], Richard Sullivan [2], Lindon Siu [3], Marie Backstrom [3], Nick Scurrah [1], Mehrdad Nikfarjam [4], Larry McNicol [1], Rinaldo Bellomo [5], David Story [1]

A multicentre randomized double-blind controlled non-inferiority multicentre study of Plasmalyte vs. Compound Lactate Solution (Hartmann's solution) in patients receiving liver resection (Australian New Zealand Clinical Trials Registry No: 12610000147088)

1. Department of Anaesthesia, Austin Health
2. Department of Anaesthesia, Peter MaCallum Medical Centre
3. Department of Anaesthesia, Monash Medical Centre
4. Department of Surgery, Austin Health
5. Department of Intensive Care, Austin Health

Introduction:
Acid-base disorders frequently occur in patients undergoing liver resection. We hypothesized that patients undergoing liver resection will have equivalent or improved acid-base haemostasis if Plasmalyte is used for fluid intervention compared to Hartmann's solution.
Methods:
Design: prospective, blinded randomized non-inferiority trial in patients undergoing liver resection. Participants were randomized to Plasmalyte or Hartmann's solution for intraoperative fluid intervention. Primary outcome: base-excess immediately after surgery. Secondary outcomes: lactate levels, strong-ion-difference (SID), total weak acids, net-unmeasured-ions, changes in liver enzymes, perioperative complications and duration of hospital stay.
Results:
60 participants were recruited from 4 tertiary-level hospitals. Both groups were matched according to baseline characteristics, extent of resection, and surgery duration. There were no differences in the volume of trial fluid used, perioperative fluid balance, or urine output. Plasmalyte was not inferior to Hartmann's for the primary endpoint. Plasmalyte base-excess was 0.8mmol/L greater (95%CI: -0.4 to 2.0;P=0.18). This was associated with hyperchloraemia (Difference 1.7mmol/L, 95%CI: 0.2 to 3.2mmol/L, p=0.03) and hyperlactaemia (Difference 0.8mmol/L, 95%CI: 0.2 to 1.3mmol/L;P=0.01) in the Hartmann's group. In the Hartmann's group 23 patients (77%) had a lactate above the reference range compared to 14 patients (47%) in the Plasmalyte group, P=0.02. Complications were more frequent in the Hartmann's Group (56% vs. 20%, 95%CI: 1.3 to 6.1;P=0.007). Median length of hospital stay: 5.9 days vs. 7.8 days (P=0.041) favouring Plasmalyte group.
Conclusion:
For patients undergoing liver resection use of Plasmalyte solution resulted in improved acid base haemostasis, less hyperlactaemia, reduced perioperative complications and a shorter length of hospital stay compared to patients receiving Hartmann's solution.

TUES 24

S. Suzuki, G.M. Eastwood, L. Peck, N.J. Glassford, A.G. Schneider, M. Garcia, R. Bellomo

A PILOT BEFORE-AND-AFTER TRIAL OF CONSERVATIVE OXYGEN THERAPY IN MECHANICALLY VENTILATED PATIENTS

Department of Intensive Care, Austin Health

Aim:
We sought to assess the feasibility and safety of targeting SpO_2 of 90% to 92% in mechanically ventilated ICU patients. Studies indicate that the dominant approach to oxygen therapy in ICU patients receiving mechanical ventilation (MV) is to target SpO_2 levels >96%. A more conservative approach may be possible and perhaps desirable.
Methods
A prospective before-and-after trial was performed. Adult patients who needed MV for more than 48 hours were eligible. We screened all consecutive admissions during a 3.5-month before (conventional oxygen therapy) period and during a 3-month intervention (conservative oxygen therapy) period.
Results
We enrolled 51 patients during the "conventional" before period and 54 after a change to "conservative" oxygen therapy. During conservative oxygen therapy the median time-weighted average SpO_2 during MV was 95.5% [IQR 94.0-97.3] vs. 98.4% [IQR 97.3-99.1] (p<0.001) during conventional therapy and the median PaO_2 was 83 mmHg [IQR 71-94] vs. 107 mmHg [IQR 94-131] (p<0.001) with a change to a median FIO_2 of 0.27 [IQR 0.24-0.30] vs. 0.40 [IQR 0.35-0.44] (p<0.001). Conservative oxygen therapy decreased the total amount of oxygen delivered during MV by about two-thirds (5122 L [1837-10499] vs. 15580 L [8263-29351], p<0.001). The evolution of the PaO_2/FIO_2 ratio was similar during the two periods and there were no difference in any other biochemical or clinical outcomes.
Conclusions
Conservative oxygen therapy in mechanically ventilated ICU patients was feasible and free of adverse biochemical, physiological or clinical outcomes while allowing a marked decrease in excess oxygen exposure.

TUES 25

G.M. Eastwood[1], S. Suzuki[1], C. Lluch[1], A.G. Schneider[2], R. Bellomo[1]

IMPACT OF ARTERIAL BLOOD GAS ASSESSMENT IN PATIENTS ADMITTED TO INTENSIVE CARE FOLLOWING NON-TRAUMATIC CARDIAC ARREST

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2. Intensive Care Medicine, Universite de Lausanne, Lausanne, Switzerland

Introduction:
Resuscitated cardiac arrest (CA) patients are typically receive moderate therapeutic hypothermia and arterial blood gases (ABG) are assessed based on values corrected to 37oC (alpha-stat). However, the impact of assessing ABG according to the patient's actual body temperature (pH stat) has not been studied.
Objectives:
To compare alpha-stat and pH-stat methods of ABG analysis for non-traumatic CA patients.
Methods:
We performed a retrospective comparative study of ABG data obtained during the first 24 hours of ICU admission. We enrolled all non-traumatic CA patients admitted to our ICU between June 2010 and December 2011. For each ABG analysis method, we determined the physiologic changes in pH, PaO_2, and $PaCO_2$ according to alpha-stat and pH-stat assessment for the overall cohort and those treated with therapeutic hypothermia (TH).
Results:
We examined 1013 ABGs from 120 patients; 89 patients (74%) received TH. For the overall cohort, the alpha-stat median [IQR] pH was 7.33 [7.25-7.41], PaO_2 122 [95-156](mmHg) and $PaCO_2$ 39 [34-46](mmHg), compared to the pH-stat pH of 7.37 [7.29-7.44], PaO2 107 [82-143](mmHg) and $PaCO_2$ 35 [30-41](mmHg)(p <0.01). For patients treated with TH, 210 of 365 observations (58%) classified as 'normocapnic' ($PaCO_2$ 35-45mmHg) with alpha-stat were reclassified as 'hypocapnic' ($PaCO_2$ <35mmHg) with pH-stat; and, 125 of 416 observations (30%) classified as 'hyperoxaemic' (PaO_2 >120mmHg) with alpha-stat were 'normoxaemic' (PaO_2 60-120mmHg) with pH-stat compared with 8 (8%) and 11 observations (11%) for patients not treated with TH, respectively.
Conclusions:
There is a clinically important discrepancy in pH, carbon dioxide and oxygenation status in ABG between with alpha-stat and pH-stat during the early management of resuscitated CA patients treated with TH.

TUES 26

G.M. Eastwood, L. Peck, H. Young, S. Suzuki, M.Garcia, R. Bellomo

INTENSIVE CARE CLINICIANS' OPINION OF CONSERVATIVE OXYGEN THERAPY (SpO2 90-92%) FOR MECHANICALLY VENTILATED PATIENTS: A SURVEY

Department of Intensive Care, Austin Health

Aim
We sought to explore intensive care clinicians' opinion of conservative oxygen therapy for mechanically ventilated adult patients. Administering more oxygen than necessary may be injurious to lung tissue and systemically associated with hyperoxia. To reduce exposure to hyperoxia a conservative oxygen therapy protocol (targeted SpO_2 90-92% using lowest FiO_2) for mechanically ventilated patients was introduced in a single tertiary ICU in September, 2012.
Methods
A structured multi-choice questionnaire of intensive care clinicians was conducted between February-March 2013. Institutional ethics committee approval was obtained.
Results
Responses were received from 90 staff members: 81 intensive care nurses and nine medical doctors. A majority of respondents (60.7%) considered oxygen related lung injury as 'a major concern'. Most respondents (81/89; 91.1%) felt conservative oxygen therapy was easy to perform and few respondents (6/88; 8%) considered performing conservative oxygen therapy to be stressful. Most respondents (58%) reported not performing more arterial blood gases to monitor PaO_2 during conservative oxygen therapy and 90% (81/90) of respondents indicated a desire to continue conservative oxygen therapy. Free text comments a paradigm shift yet more education and research to elucidate the benefits/harm of lower SpO_2 targeting is needed.
Conclusions
Intensive care clinicians readily incorporated conservative oxygen therapy into their practice. Most respondents found conservative oxygen therapy easy and not stressful to perform. Further evaluation of intensive care clinician's administration and management of oxygen therapy and possible impact on outcome for mechanically ventilated patients appears desirable.

TUES 27

S. Suzuki, G.M. Eastwood, L. Peck, N.J. Glassford, R. Bellomo

OXYGEN MANAGEMENT IN MECHANICALLY VENITLATED PATIENTS: A PROSPECTIVE OBSERVATIONAL COHORT STUDY

Department of Intensive Care, Austin Health

Aim

The aim of this study was to describe current oxygen administration and titration in such patients in our academic intensive care unit. Oxygen therapy is universally applied to mechanically ventilated patients but oxygen targets and dose are poorly understood.

Methods

Prospective observational cohort study conducted between March and June 2012. Consecutive adult patients that were mechanically ventilated for =48 hours were included. For each patient we recorded the FiO_2, PaO_2 and SpO_2 every six hours until extubation. We calculated the amount of excess oxygen delivery (SpO_2 >98% with FiO_2 >0.21) and assessed the Intensivists' response to hyperoxaemia (SpO_2 >98%). Institutional ethics committee approval was obtained.

Results

We examined 358 mechanical ventilation days in 51 critically ill patients. Patients spent the majority of time with their SpO_2 >98% (59% [29-83]) and PaO_2 between 80-120 mmHg (59% [38-72]). Half of all observations were classified as hyperoxaemia and 4% were severe hyperoxaemia (PaO_2 >202.5 mmHg). The total calculated amount of excess oxygen delivered was 263,841 L, with a median excess of 3472 L per patient. Seventy-one per cent of the total calculated excess oxygen occurred with a FiO_2 between 0.3-0.4. When hyperoxaemia occurred with a FiO_2 between 0.3-0.4, 88% of the episodes had no subsequent FiO_2 adjustment made.

Conclusions

Excess oxygen delivery and liberal oxygen therapy were common in mechanically ventilated patients. Current oxygen therapy practice may be suboptimal and expose patients to unnecessary episodes of hyperoxaemia. Further evaluation of oxygen, its management and impact on outcome for mechanically ventilated patients appears desirable.

TUES 28

John Rogan, Nigel Fealy, Gillian Dunnachie, Stuart Ross, Kristin Majer, Karyn Rutjens, Belinda John, David Thomas, Helen Young, Robyn Best.

Reducing Adverse Events in ICU - Implementation of a NEVER Event program.

Department of Intensive Care, Austin Health

Introduction:
As an extension of our incident monitoring program, we identified three frequently occurring incidents and aimed to reduce their frequency to zero: A Never Event (NE).
In our 20-bed adult ICU we set out to eliminate the occurrence of: Inadvertent airway loss, sacral pressure injury and patient physical aggression towards ICU staff.
Method:
The ICU staff ranked 10 adverse events to identify the top three. A team was established for each of these, with key interventions towards the NE identified and subsequently communicated to all ICU staff. A 12-month period was allowed for the NE interventions to be established into the ICU standards of care. Incidents were reported via the RiskMan incident reporting tool. We compared data collected over a nine-month period to that from the 12 months prior to starting the NE interventions.
Results:
Pre / post NE's per month:
Inadvertent airway loss; 0.66 to 0.33.
Patient physical aggression; 0.92 to 0.66.
Sacral pressure injury; 0.66 to 1.33.
The reduction of inadvertent airway loss by 50% and patient physical aggression by 30% were advances toward a NE. Sacral pressure injury events increased by 100% and clearly require further and new interventions.
Conclusion:
Whilst the NE program may not have reduced these events to 'zero' within a nine-month period, the process improvements implemented may yield further achievement of our long-term aims
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TUES 29

Patricia K. Russell [1], **Michele V. Clarke** [1], **Kristine M. Wiren** [2,3], **Jeffrey D. Zajac** [1], **Rachel A. Davey** [1]

ANDROGENS ACT DIRECTLY VIA THE ANDROGEN RECEPTOR IN PROLIFERATING OSTEOBLASTS TO INCREASE BONE SIZE DURING GROWTH.

1. Department of Medicine, University of Melbourne, Austin Health
2. Bone and Mineral Research Unit, Portland Veterans Affairs Medical Center, Oregon, USA
3. Department of Medicine, Oregon Health and Science University, Portland, Oregon, USA

Aim:
The aim of this study was to elucidate the actions of androgens on osteoblasts, the bone forming cells, at two stages of their maturation, the 1) proliferative and 2) mineralisation stages.
Method:
We used the innovative approach of generating two genetically modified mouse lines in which we replaced the AR only in osteoblasts of global-ARKOs, which have no AR expression in any tissue, at the 1) proliferative (pOBLAR-Replacement) or 2) mineralisation stage (mOBLAR-Replacement) of osteoblast maturation, and characterised their bone phenotype by microCT and histomorphometry at 6 and 12 weeks of age.
Results:
Deletion of the AR in all tissues in male mice (global-ARKOs) results in bones of reduced size and volume compared to controls. Replacement of the AR specifically in proliferating, but not mineralising osteoblasts of global-ARKOs restored bone size as measured by periosteal circumference at 6 weeks of age in pOBLAR-Replacement and mOBLAR-Replacement, respectively. Trabecular bone volume was fully restored in pOBLAR-Replacements to levels observed in controls, whilst restoration of BV/TV was partial in mOBLAR-Replacements. Trabecular number was increased in pOBLAR-Replacement and mOBLAR-Replacements compared to global-ARKOs ($P<0.05$), suggesting an inhibitory effect of androgens on bone resorption via the AR on osteoblasts.
Conclusion:
Androgen action directly via the AR in osteoblasts, is dependent on the stage of osteoblast maturation. Understanding the central role androgens play in regulating bone formation and breakdown has potential to provide new avenues for therapies which target the specific actions of androgens via the AR, within specific bone cell types, thereby improving bone health.

TUES 30

Lavinia Spain [1], **Marzena Walkiewicz** [2], **Simon Knight** [3], **Paul Mitchell** [4], **Thomas John** [4]

OVERALL SURVIVAL AND SMOKING STATUS IN RESECTABLE NON-SMALL CELL LUNG CANCER

1. Oncology Unit, Austin Health
2. Ludwig Institute for Cancer Research, Austin Health
3. Thoracic Surgical Unit, Austin Health
4. Joint Austin Ludwig Oncology Unit, Austin Health

Aim

The impact of quantitative smoking history on overall survival in resectable tumours has not been well described. We analysed the impact of increasing number of pack years of smoking on stage, histology, mutation status and overall survival in an Australian population. We specifically focused on patients without nodal involvement (N0) as they were less likely to have received neoadjuvant or adjuvant therapy.

Methods

Data was extracted from a large single institution database containing information on patients who underwent curative resection of non-small cell lung cancer from 1992 to 2012. Statistical analysis was performed using Chi-square tests and the Kaplan Meier method for survival.

Results

Information on pack year smoking status was available for 470 patients. This included 311 (66%) pathological N0 (pN0), 64 (14%) pN1 and 95 (20%) pN2. Smoking history ranged between 0 (never smokers N=32, 7%) and 180 pack years, with a median of 45 and mean of 48. Frequencies of mutations were as follows: KRAS 21%, TP53 10%, EGFR 5%, PIK3CA 4%. Increased pack year history of smoking was not associated with overall survival. In the pN0 wild type population, no association with smoking and survival was seen. In the pN0 mutation group (Figure 1) those with a <25 pack year history had significantly better overall survival than heavier smokers (HR 0.61, 95% CI 0.40-0.92).

Conclusion

Smoking status was not associated with overall survival across the entire cohort. In patients whose tumour harboured a mutation, increased smoking was associated with a less favourable mutation profile including in KRAS, TP53 and PIK3CA. In patients with pN0 disease a significant difference in overall survival was observed favouring light smokers. The presence of mutations in association with heavy smoking negatively impacts overall survival.

TUES 31

Megan Cotter [1], **Elly Lynch** [1], **Martin Delatycki** [1,2], **Alana Jacobs** [1,3], **Agnes Bankier** [1,] **Matthew Burgess** [1], **Alana Jacobs** [1,3], **Thomas John** [1,4]

How frequent is DCIS in families with BRCA1 or BRCA2 mutations? A clinical audit from Austin Health Genetics

1. Austin Health Clinical Genetics Service
2. Bruce Lefroy Centre for Genetic Health Research, Murdoch Childrens Research Institute
3. Ludwig Institute of Medical Research
4. Imperial College, London

Early studies suggested that ductal carcinoma in situ (DCIS) of the breast was infrequently diagnosed in patients with BRCA1 or BRCA2 mutations [1,2]. In 2007, Hwang et al [3] reported that high grade DCIS is equally as prevalent in patients with deleterious BRCA mutations as in high risk women who are non-carriers and that women with BRCA mutations develop earlier onset of DCIS than comparable women who are BRCA-negative.

As part of a larger audit of individuals tested at Austin Health Clinical Genetics between 2009 and 2012, the pathology of the breast cancer in index cases was noted, including the presence or absence of DCIS. In total, there were 42 families with mutations in BRCA1 or BRCA2.

We will present the results of that audit, including how frequently DCIS was found in mutation carriers, either in association with an invasive cancer diagnosis or as an isolated diagnosis. We will also report on the grade of the DCIS reported, the gene in which the mutation was detected and the BRCApro scores of those tested.

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2.Lakhani SR et al. Multifactorial analysis of differences between sporadic breast cancers and cancers involving BRCA1 and BRCA2 mutations. J Natl Cancer Inst 90:1138-1145, 1998
3.Hwang ES et al. Ductal Carcinoma in Situ in BRCA Mutation Carriers. Journal of Clinical Oncology 25:6; 642-647

TUES 32

N. Anderson[1], J. Jackson[1], M. Wada[1], M. Schneider-Kolsky[2], M. Rolfo[1], H. Gan[3], K. Kaegi[1], F. Sneyd[1], D. Lim Joon[1], V. Khoo[4]

Creating Guidelines for Reactive and Prophylactic Enteral Feeding in Definitive (Chemo) Intensity Modulated Radiation Therapy (IMRT) for Head and Neck Cancer

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2. Faculty of Medical Imaging & Medical Radiations Sciences, Monash University
3. Ludwig Institute for Cancer Research, Austin Health
4. Department of Clinical Oncology, Royal Marsden NHS, Chelsea, UK

Purpose/Objectives:
Enteral feeding tubes (FT) are commonly utilized in patients undergoing intensity modulated radiotherapy (IMRT) for head and neck cancer to assist nutritional maintenance. Enteral feeding (EF) protocols vary between institutions: prophylactic centers (PC) insert FTs prior acute toxicity onset in most patients and reactive centers (RC) generally insert FTs upon failure of adequate oral nutrition. Numerous nutritional guidelines recommend a prophylactic FT if EF is likely to persist for more than 4 to 6 weeks. This study examined several pre-treatment factors that could predict the likelihood of inadequate oral intake, with the aim of creating guidelines for identifying patients who should receive prophylactic FTs and those who could be treated reactively.
Methods/Materials:
This study identified 115 patients treated with definitive IMRT in a PC between 2007 and 2012. Gross disease was treated to 70Gy/35 fractions and bilateral, elective necks to 56Gy. EF duration and intensity was gleaned from a prospective nutritional database to identify patients as: a) low feeding (LF) - using a FT for 25-75% of dietary needs for < 4 weeks OR b) high feeding (HF) - using a FT for ≥ 75% of needs for > 6 weeks. Differences in frequency distributions of demographics, use of chemotherapy, disease site, stage, and volume were analyzed.
Results:
Table 1 displays univariate predictors of LF and HF. Both LF and HF were associated with advanced disease and chemotherapy use. While nodal stage was a significant discriminator of LF, only the primary tumor extent was significant for HF. The same pattern was observed in relation to PTV 70Gy length. This may be a product of the conformality of the high risk volume and the steeper dose gradient achieved around nodal volumes, sparing the pharyngeal axis with IMRT. Oropharyngeal primaries were larger than those in the larynx (mean 41.1 vs. 7.8cc; p=0<0.001) and EF rates reflect this. No patient factors, including malnutrition, morbidity and substance use, predicted EF outcomes.
Conclusion:
Irrespective of institutional philosophy, these findings legitimize reactive FTs in patients with low volume primary and nodal disease, treated without chemotherapy, and prophylactic FTs in patients with advanced primary tumors, treated with chemotherapy, regardless of neck disease. The apparent pharyngeal sparing of IMRT despite advanced nodal disease warrants further dosimetric investigation.

TUES 33

Marika Ciprotti [1]**, Niall C. Tebbutt** [1]**, Fook T. Lee** [1]**, Sze T. Lee** [1]**, Dave C. McKee** [2]**, Graeme J. O'Keefe** [2]**, Sylvia J. Gong** [2]**, Geoffrey Chong** [2]**, Hui K. Gan** [1]**, Wendie Hopkins** [1]**, Bridget Chappell** [2]**, Nancy Y. Guo** [1]**, Fiona E. Scott** [1]**, Archie N. Tse** [3]**, Mendel Jansen** [3]**, Manabu Matsumura** [3]**, Rira Watanabe** [3]**, Robert A. Beckman** [3]**, Jon Greenberg** [3]**, Andrew M. Scott** [1]

A phase I imaging and pharmacodynamic trial of CS-1008 in patients (pts) with metastatic colorectal cancer (mCRC)

1. Ludwig Institute for Cancer Research, Austin Health
2. Austin Health
3. Daiichi Sankyo Co., Ltd.

Background:
Death receptor 5 (DR5) is a member of the TNFR superfamily that initiates the extrinsic apoptotic pathway. CS-1008 is a humanised, monoclonal IgG1 agonistic antibody (Ab) to human DR5 created by CDR grafting of the murine Ab TRA-8.
Methods:
Pts with mCRC were treated with weekly IV CS-1008 in 5 non-sequential cohorts. Different loading doses were used on days 1 and 8 (0.2-6 mg/kg), followed by weekly CS-1008 (2 mg/kg). D1 and D36 doses were trace-labeled with 111In. Primary endpoints: biodistribution, pharmacokinetic (PK) and tumour uptake following single infusion and after sequential doses. Secondary endpoints: tumour response; changes in tumour metabolism; serum apoptosis biomarkers and tumour response markers.
Results:
19 pts were enrolled. Tumour uptake was variable: 7 pts had no uptake, 11 pts had uptake in all measurable lesions except liver. Tumour uptake and PK were not affected by dose or repeated drug administration. No anti-CS-1008 Ab responses were detected. DR5 expression in archived samples did not correlate with uptake or response. ^{111}In-CS-1008 biodistribution showed gradual blood pool clearance and no abnormal uptake in normal tissue. There were 8 SD, 1 PR and 10 PD. Duration of PR was 3.7 months (mo). Mean duration of SD was 4 mo. Disease control rate (SD+PR) in pts with uptake was 58% vs 28% of pts with no uptake.
Conclusions:
Tumour DR5 expression, assessed by 111In-CS-1008 imaging, revealed real-time heterogeneous DR5 expression and appeared to be a promising predictive imaging biomarker of clinical benefit in pts with mCRC receiving CS-1008.

Mun Sem Liew, [#1,2,6]**, Joseph Sia** [#3]**, Maud H.W. Starmans** [4,5]**, Ali Tafreshi** [1]**, Sam Harris** [1]**, Malcolm Feigen** [3]**, Shane White** [1]**, Allan Zimet** [1]**, Philippe Lambin** [5]**, Paul C. Boutros** [4]**, Paul Mitchell** [1]**, Thomas John** [1,2]

Comparison of toxicity and outcomes of concurrent radiotherapy with carboplatin/paclitaxel and cisplatin/etoposide in stage III non-small cell lung cancer

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2. Ludwig Institute for Cancer Research, Austin Health
3. Department of Radiation Oncology, Olivia Newton-John Cancer & Wellness Centre, Austin Health
4. Informatics and Biocomputing Platform, Ontario Institute for Cancer Research, Toronto, Canada.
5. Department of Radiation Oncology (Maastro), GROW-School for Oncology and Developmental Biology, Maastricht University Medical Center, Maastricht, The Netherlands.
6. Department of Medicine, University of Melbourne, Austin Health.
 # MSL and JS contributed equally as first authors

Background :
Concurrent chemoradiotherapy (CCRT) has become the standard of care for patients with unresectable stage III non-small cell lung cancer (NSCLC). The comparative merits of two widely used regimens: carboplatin/paclitaxel (PC) and cisplatin/etoposide (PE), each given with concurrent radiotherapy, remain largely undefined.
Methods:
Records for consecutive patients with stage III NSCLC treated with PC or PE and =60Gy chest radiotherapy between 2000-2011 were reviewed for outcomes and toxicity. Survival was estimated using the Kaplan-Meier method and Cox modeling with the Wald test. Comparison across groups was done using the student t and chi-squared tests.
Results:
75 (PC: 44, PE: 31) patients were analyzed. PC patients were older (median 71 vs 63 years; p=0.0006). Other characteristics were comparable between groups. With PE, there was significantly increased grade =3 neutropenia (39% vs 14%, p=0.024) and thrombocytopenia (10% vs 0%, p=0.039). Radiation pneumonitis was more common with PC (66% vs 38%, p=0.033). Five treatment related deaths occurred (PC: 3 vs PE: 2, p=1.000). With a median follow up of 51.6 months, there were no significant differences in relapse free survival (median PC 12.0 vs PE 11.5 months, p=0.700) or overall survival (median PC 20.7 vs PE 13.7 months; p=0.989). In multivariate analyses, no factors predicted for improved survival for either regimen.
Conclusions:
PC was more likely to be used in elderly patients. Despite this, PC resulted in significantly less hematological toxicity but achieved similar survival outcomes as PE. PC is an acceptable CCRT regimen, especially in older patients with multiple comorbidities.

TUES 36

Christopher Hudson[1,2], Andreas Behren[1,2,] Aparna Jayachandran[1,2,]
Matthew Anaka[1,2], Sonja McKeown[3], Jonathan Cebon[1,2,3]

Heterogeneity and plasticity in melanoma leads to treatment failure and increased invasiveness that can be blocked by targeting TSP-1 and/or SNAIL

1.Ludwig Institute for Cancer Research, Heidelberg, Vic., Australia;
2.Olivia Newton John Cancer and Wellness Centre,Heidelberg, Vic., Australia;
3.University of Melbourne

Introduction
We investigated emergent resistance to kinase inhibitors by assessing cellular heterogeneity and plasticity; which can both yield resistant cells either stochastically or under the selective pressure of therapy.
Methods
Cellular heterogeneity was evaluated in vitro with functional assays including the use of a membrane dye, CM-Dil, which identified a slow-cycling cell subpopulation within lines and xenografts. Cells were evaluated for migration in Boyden chamber assays and in vivo in the neural tube of the developing chick embryo. Chemoresistance was assessed following exposure to cytotoxic agents and the BRAF inhibitors PLX4720 and dabrafenib. Genome-wide gene expression was analysed with Illumina HT12 arrays. Label-retaining cells (LRC) were identified in multiple cell lines. Targets of interest were assessed by gene inhibition with siRNA.
Results
The LRC were more resistant to cytotoxic drugs and more invasive. Gene expression profiling identified a network of overexpressed genes related to epithelial-to-mesenchymal transition (EMT). Resistance to BRAF inhibitors was associated with a phenotypic switch, reduced differentiation and increased invasiveness with acquisition of the LRC gene signature. This was characterised by thrombospondin-1 (TSP-1), a transforming-growth factor beta (TGFb) activating enzyme, as well as TGFb-induced (TGFBI) and a variety of other molecules which code for extracellular proteins. Targeted knockdown of SNAIL or TSP-1 resulted in migration inhibition in vitro and in vivo.
Conclusion
The LRC genotype links treatment failure, cellular plasticity, EMT and invasiveness. The plastic switch in vivo was blocked by inhibition of TSP-1 or SNAIL. These insights inform the identification of targets for overcoming disease progression.

TUES 37
This abstract has not been included at the request of the author

TUES 38

Pu-Han Lo, Aparna Jayachandran, Anderly Chueh, Jonathan Cebon

TKTL1- a promising anti-tumour target in melanomas

Cancer Immunobiology Laboratory, Ludwig Institute for Cancer Research, Austin Health

Enhanced glucose consumption is the most consistent hallmark of cancers. Unlike normal differentiated cells, most cancer cells produce energy by fermenting glucose to lactate in the cytosol even in the presence of oxygen, a phenomena known as aerobic glycolysis or the Warburg Effect. The transketolase-like protein 1 (TKTL1) has been suggested as a key enzyme and its over-expression has been reported in a variety of human cancer tissues. The strong correlation between high TKTL1 expression and poor patient survival as well as tumor progression has also been shown in different types of cancers. Over-expression of TKTL1 was observed in melanoma by quantitative RT-PCR assays and immunohistochemistry using a panel of melanoma cell lines and normal tissues. Expression of TKTL1 correlated with promoter methylation was determined by quantitative MS-PCR. Re-expression of TKTL1 was observed in melanoma cells upon treatment using DNA methylation inhibitor, 5-Aza, suggesting DNA methylation regulates the expression of TKTL1 at the transcription level. In order to investigate the functional role of TKTL1 in melanoma, studies using small molecule TKTL1 inhibitors, oxythiamine, and siRNA-mediated knockdown were performed on human melanoma cell lines. TKTL1 suppression altered glucose consumption and L-lactic acid production. G1 arrest was found in siRNA-mediated TKTL1-suppressed cells. This suggests TKTL1 plays a role in cell cycle and metabolism in melanoma cells. This data provides new evidence for the role of TKTL1 in melanoma and indicates that TKTL1 is not only a tumor marker but also as a good target for anticancer therapy.

TUES 39

D. K. Lau [1], M. C. Andrews [1], N. Turner [1], A.A. Azad [1], I.D. Davis [1,2], J.S. Cebon [1]

A single center experience of patients with metastatic melanoma enrolled in a dabrafenib named patient program

1. Ludwig Institute for Cancer Research and Joint Ludwig-Austin Medical Oncology Unit, Austin Health
2. Eastern Health Clinical School, Monash University, Box Hill

Background
We studied the efficacy, tolerability and clinical courses of dabrafenib-treated patients with metastatic melanoma who were ineligible for enrolment in a clinical trial.

Methods
Between July 2011 and May 2013, patients with unresectable stage III or stage IV, V600-mutated metastatic melanoma who were not eligible for clinical trials were offered treatment with dabrafenib through a named patient program. Routine efficacy and toxicity data were collected throughout treatment and studied retrospectively. The endpoints were progression free survival, overall survival and best overall response.

Results
Thirty-one patients commenced dabrafenib including six individuals who had progressed on a prior BRAF inhibitor treatment. The majority of patients had cerebral metastases (n=17) and/or poor performance status (ECOG =2, n=11). Median overall survival was 5.6 months (range 0.1-22). Median progression-free survival was 3.3 months (range 0.1-21) and was similar despite performance status. One patient had a complete response and there were eight partial responses to treatment. Patients with cerebral metastases (n=17) had a median progression free survival of 4.6 months. Five patients (16%) had dose-limiting toxicities.

Conclusions
Despite several poor-prognostic features, dabrafenib is a safe and effective treatment in the community setting, with occasional impressive outcomes.
Keywords: metastatic melanoma, BRAF inhibitor, dabrafenib, cerebral metastasis, named patient program.

TUES 40

This abstract has not been included at the request of the author

TUES 41

Simon C-H Tsao, Andreas Behren, Jonathan Cebon, Christopher Christophi

A novel cost- and time-efficient method of enumerating circulating tumour cells.

Ludwig Institute for Cancer Research, Austin Health
Department of Surgery, University of Melbourne, Austin Health

The ability to enumerate circulating tumour cells (CTC) has long been confirmed to have significant diagnostic and prognostic values. However, CTC measurement has not been cooperated into routine clinical practice. One of the major obstacles is the high cost associated with purchasing the technology and their consumables. The average cost of a single test ranges from $500 to more than $1000 and the samples are required to be sent away with a long turn over time. We have developed a filtration-based method to detect the presence of CTC that will allow the cost to be reduced to less than $1 per sample and providing a result in under 12 hours. This method utilises the size differentials of CTC from other systemic cells to isolate them, and subsequently labelled with tumour-specific-immunofluorescence antibody to confirm their identity. The method is cheap and easy to set up and is very simple to operate. It has the potential to be adopted widely in clinical practice.

TUES 42

Kheng Soo, Juli Moran

Discharge planning from a palliative care ward to residential aged care using prognostic tools.

Department of Palliative Care, Austin Health

Aim:
Accurate prognostication is important when considering discharge from a Palliative Care Unit (PCU). This retrospective study evaluates the discharge planning process from a PCU to residential aged care facility (RACF). Factors assessed include time taken for each step, outcomes and whether prognostic tools can be used to improve decision-making.
Methods:
All inpatients referred to the Aged Care Assessment Service (ACAS) between 1st July 2011 and 30th June 2012 at Austin Health PCU were identified from social work records. Electronic medical records were reviewed for demographic information, diagnosis, time-lines and outcomes. Prognostic tool information was collected at time of admission, decision for placement and ACAS review. Prognostic tools evaluated were Palliative Prognostic Index (PPI), modified Palliative Prognostic (mPaP) Score and modified Prognosis in Palliative Care Study (mPiPs) prognosticator.
Results:
Twenty patients were analysed. Overall success rate for discharge was 55%. Average time from admission to discharge was 30.7 days. Presence of malignancy was associated with a shorter process compared with non-malignant diagnoses (28 days versus 48 days, P=0.007). Only PPI was substantially correlated with survival time (Spearman coefficient -0.5378, P=0.039). PPI with a high cut-off score of 7.5 demonstrated a sensitivity of 40% and specificity of 90% for predicting death during discharge planning.
Conclusions:
This retrospective study provides valuable information regarding discharge planning from a PCU to RACF. This information can be used to facilitate planning and delivery of service. In addition, a potential role was identified for the use of the Palliative Prognostic Index (PPI) in this process.

TUES 43

Uwe Ackermann [1,2,3], Dedrick Song [4], Shinn Deee Yeoh [1,4], Yit Wooi Goh [1,4], Henri Tochon-Danguy [1,2,3], Andrew Scott [1,2,3], Jonathan White [4]

Synthesis and evaluation of a pegylated F-18 labelled nitrophenyl sulfoxide for PET imaging of tumor hypoxia

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3. Ludwig Institute for Cancer Research, Austin Health
4. Bio21 Institute, University of Melbourne, Parkville

Objectives:
Confirming the presence of hypoxia in tumors is of huge importance for the planning of radiotherapy and chemotherapy[1]. Imaging of tumor hypoxia using Positron Emission Tomography (PET) has proven to be a useful tool for this purpose. Due to the unfavourable pharmacokinetics of 2-nitroimidazole based tracers, we have synthesised a series of F-18 labelled nitrophenyl sulfoxides and investigated their suitability as hypoxia imaging agents[2,3]. In this abstract we describe the synthesis and evaluation of an F-18 labelled pegylated nitrophenyl sulfoxide.
Methods:
Ethyl bromoacetate was conjugated to 4-nitrophenylthioaniline using K2CO3, followed by reaction with 2-(2-(2-(prop-2-yn-1-yloxy)ethoxy)ethoxy)ethyl trifluoromethanesulfonate and oxidation with NaIO4 to form the radiolabelling precursor. Radiolabelling of the acetylene moiety was achieved via click chemistry using fluoroethyl azide. Radiotracer stability was checked using a S9 liver fraction assay and in vivo evaluation was performed using BALB/c nude mice bearing SK-RC-52 tumors.
Results:
The radiotracer was purified using semi-preparative HPLC with a decay corrected radiochemical yield of 25-35% based on free fluoride. The compound showed high stability in our S9 liver fraction assay with 80% of the radiotracer intact after 2 h of incubation. Dynamic imaging over a 2 h period has revealed that the tracer accumulates in hypoxic tumors and clears rapidly from muscle. A tumor to muscle ratio of 1 was observed at 45 min post injection, which increased to 2.5 at 2 h post injection.
Conclusion:
We have synthesised a new nitrophenyl sulfoxide with improved pharmacokinetics using click chemistry. The good radiolabelling yields, stability in our S9 liver fraction assay as well as high tumor to muscle ratio suggest that this compound may be a promising radiotracer for hypoxia imaging.

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TUES 44

Mun Sem Liew [1,2,*]**, Anderly C. Chueh** [2,*]**, Marzena Walkiewicz** [2]**, Jonathan Cebon** [1,2]**, Paul Mitchell** [1,2]**, John Mariadason** [2]**, Thomas John** [1,2]
***MSL and AC contributed equally to this work**

Association of New York-Esophageal Antigen-1 (NY-ESO-1) promoter methylation and survival in stage III non-small cell lung cancer

1. Austin-Ludwig Oncology Unit, Austin Health
2. Ludwig Institute for Cancer Research, Olivia-Newton John Cancer Centre, Austin Health

Background:
Cancer-Testis antigens (CTAs) are immunogenic molecules exclusively expressed in normal testes but with aberrant expression in up to 30% of NSCLC. NY-ESO-1, is a CTA whose expression is associated with poorer survival but improved response to chemotherapy.1 The promoter regions for many CTA genes contain CpG islands which are predominantly methylated in most tissues. In cancer, hypomethylation of CTA gene promoters have been shown to be determining factor for the frequent re-expression of these genes. Herein we sought to correlate NY-ESO-1 promoter methylation (PM) with protein expression in lung cancers and test whether methylation status can be used as a predictive and prognostic marker in NSCLC.
Methods:
We revieed the clinicopathological data for patients with pathological N2 NSCLC treated with surgical resection followed by either observation or adjuvant chemotherapy, if treated after 2004. Genomic DNA from formalin fixed paraffin embedded (FFPE) samples were purified and bisulfite converted according to the manufacturer's (QIAGEN) instructions. Mutational status was determined in genomic DNA using Sequenom's Oncocarta panel v1.0. Tumour samples were cut and stained with NY-ESO-1 antibody (E978). Previously described protocols for methylation-specific NY-ESO-1 primers2 and beta-actin3 control probes were used. Using real-time quantitative methylation-specific polymerase chain reaction (qMS-PCR), the level of NY-ESO-1 methylation was determined and expressed as the ratio of methylated to unmethylated molecules (M/UM). We used a cut-off fold-difference of 5 (Log2, M/UM) to separate tumour samples into hypomethylated and hypermethylated groups. Survival estimates were obtained using the Kaplan-Meier method. Comparison across groups was performed using the Chi-squared or Fisher's test.
Results:
NY-ESO-1 PM MS-PCR was successful in 92/100 (92%) of specimens. NY-ESO-1 was hypermethylated in 86% (79/92) of samples. Age, smoking history, gender, histology and oncogenic mutations were not associated with presence of NY-ESO-1 PM. NY-ESO-1 hypomethylation was associated with protein expression (p<0.0001). In multivariate analysis, hypomethylation of the NY-ESO-1 promoter was an independent poorer prognostic marker in patients not treated with chemotherapy (HR 2.97, 95%CI 1.06-8.29, p=0.038), after adjusting for age, gender, stage IIIA/B and histology. Conversely, in patients treated with chemotherapy there were no differences in survival associated with NY-ESO-1 PM, suggesting hypomethylated tumours remain chemosensitive.
Conclusions:
NY-ESO-1 hypomethylation was an independent adverse prognostic marker in patients not treated with chemotherapy. Given their poorer outcome, association with chemosensitivity and known immunogenicity, CTAs may make attractive targets for immunotherapy, demethylating agents and immune checkpoint inhibition.
References:
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Goh, Yit Wooi [1], **Plougastel, Lucie** [1,4,]; **Yeoh, Shinn, Dee** [1], **Sachinidis, John I.**[1], **Tochon-Danguy, Henri** [1,2], **Poniger, Stan** [1,3], **Scott, Andrew M.** [1,2,3], **Ackermann, Uwe** [1,2,3*]

Fully automated Click radiolabeling and the synthesis and coupling of [18F]FBEM to glutathione using the iPhase Flexlab module

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2. The University of Melbourne, Parkville
3. Ludwig Institute for Cancer Research, Austin Health
4. École Nationale Supérieure de Chimie de Rennes, Rennes, France

Objectives:
Both Click radiolabeling and the radiolabeling of peptides or antibodies through a thiol-reactive prosthetic groups, such as N-[2-(4-18F-fluorobenzamido)ethyl]maleimide ([18F]FBEM, 1) [1], have become increasing important in radiopharmaceutical science, despite the involvement of multi-step reactions and purification of radioactive intermediates.

In order to minimize radiation exposure and allow for more reliable and practical routine preparation, we have developed fully automated procedures for Click radiolabeling and the production and peptide/antibody conjugation of 1 using the commercially available dual reactors iPhase Flexlab module

Methods:
Flexlab module is a dual reactors system with a series of vials for the addition of reagents or solvents and the purification and reformulation of intermediates and products. Temperature in each reactor can be independently controlled within a range of 1-255°C and is equipped with separate HPLC column and dedicated loop vial that allows HPLC purification of the intermediate and final product.

The Click radiolabeling synthesis of [18F]fluoroethyltriazolylthymidine analog (2) occurred when 2-[18F]fluoroethylazide (3) was obtained from nucleophilic fluorination of 2-azidoethyl-4-toluene sulfonate (4) in reactor 1 and purified by distillation to reactor 2. Click reaction between 3 and ethynyldeoxyuridine (5) with Cu(I) as catalyst was performed in reactor 2 to give 2 and purified by HPLC 2.

The preparation of 1 occurred when the (4-ethoxycarbonylphenyl)trimethyl ammonium triflate (6) was converted to 4-[18F]fluorobenzoic acid (7) in reactor 1 and purified with C18 seppak. It was then transferred to the loop vial 1 and coupled with N-(2-aminoethyl)maleimide to form 1 and purified by HPLC 1. As a model system for future couplings to suitably modified single chain antibodies, the coupling of 1 with glutathione was carried out in reactor 2 and purified by HPLC 2.

Results:
Fully automated two steps Click radiolabeling synthesis of 2 have been sucessfully carried out in iPhase Flexlab module with comparable yield to the previously developed manual method [2] and overall synthesis time reduced by 45 mins. The synthesis and purification of 1 has also been achieved in this fully automated synthesis module with radiochemical yield of 20%. The subsequent coupling to the sulfhydryl group of glutathione was found to be quantitative with a total synthesis time of 2 hours.

Conclusions:
The Flexlab module allowed fully automated Click chemistry and the preparation and coupling of [18F]FBEM (1) to glutathione in high radiochemical yields and shorter synthesis time.

TUES 46

A. Ellis [1,2]**, P.T. Zeglinski** [2]**, B. Gardiner** [1]**, A. Mahony** [1]**, D. Massie** [1,] **A.G. Frauman** [1,2] **and M.L. Grayson** [1,2]

MEASUREMENT OF FOSFOMYCIN IN PROSTATE TISSUE BY LIQUID CHROMATOGRAPHY TANDEM MASS SPECTROSCOPY (LCMSMS)

1. Austin Health
2. University of Melbourne, Clinical Pharmacology and Therapeutics, and Department of Medicine, Austin Health

Introduction
Multi-drug resistant gram-negative bacterial (MDR-GNB) infections are a problem complicating trans-rectal prostate biopsy and urinary tract sepsis. Fosfomycin (FOS) has in vitro and urinary activity against MDR-GNBs. A sensitive method to measure FOS is required to assess the levels in plasma, urine and prostate tissue to evaluate the use of FOS for treatment of infection associated with prostatic or urological procedures.

Methods
A method was developed to measure FOS in these matrices. It included small volume homogenization of tissue and methanol precipitation of sample protein after the addition of 13C3-fosfomycin. Analysis by LCMSMS with electrospray ionisation in negative ion mode and monitoring of the following transitions (m-/z): fosfomycin 137.1->79.1 and 13C3-fosfomycin 140.1->79.1. The method was used to measure levels after oral FOS administration prior to transurethral resection of the prostate.

Results
Range of linearity of the standard curve was 0.1–200 µg/mL, $r2>0.998$. Accuracy data (% bias from nominal, n≥6 each at lower concentration levels) for each of the matrices was: ±0.5% in plasma at 5 µg/mL, ±3.2% in urine at 100 µg/mL, and ±14.6% at 1.0 µg/mL in tissue from different patients and a range of tissue sample sizes. Precision data (CV%, n≥5) for each matrix were: 5.1% in plasma, 9.8% in urine and 6.4% in tissue from different patients and a range of tissue sample sizes.
Application of the assay to study samples revealed relatively high levels in plasma and urine of 11.4±7.6 µg/mL and 571±418 µg/mL respectively. Prostate tissue levels were 6.5±4.9 µg/g (range: 0.7-22.1 µg/g) with 70% of patients achieving levels ≥4 µg/g.

Conclusion
An LCMSMS assay appropriate for the measurement of FOS levels in human plasma, urine and prostate tissue was developed. The method was successfully applied in a prospective clinical study and reasonable levels were attained in all matrices following oral administration.

TUES 47

Celia S.-L. Kuo [1], Adam Pendlebury [2], Susan T. Jones [1], Kerryn F. Ireland-Jenkin [1]

Comparison of conventional cervical cytology with ThinPrep liquid-based cytology (LBC) in a dysplasia clinic setting

Austin Pathology, Austin Health and Mercy Hospital for Women

Aim:
Austin Pathology successfully utilises LBC for a range of non-gynaecologic cytology, with a lower rate of LBC in cervical cytology, due to patient out-of-pocket cost in the public hospital setting. LBC has largely replaced conventional cervical cytology in some countries (1), mainly due to utility for location guided screening (2), and HPV testing, rather than increased sensitivity for detecting CIN2+ (3). Our aim was to compare conventional and LBC of split samples from a dysplasia clinic; a different setting to community screening.
Methods:
During September - October 2012, split samples were collected from 93 consecutive dysplasia clinic patients (MHW), and reported at Austin Pathology. Conventional and ThinPrep Pap tests were assessed independently, but slides later assessed side by side in the post-test analysis phase.
Results:
As a result of finding additional abnormal material in the LBC slides, an additional 6 high-grade lesions (squamous and glandular) were reported (which represented an increase of 43% detection of definite high grade lesions). However, it should be noted that most of these were from the Possible HSIL and Possible High grade glandular groups, with only two cases being derived from the negative and unsatisfactory groups. If only these latter were considered true new detections, this would equate to an increased detection rate of 14%. In the six cases there was both more diagnostic material, and better-preserved material, with less air-drying and cytolysis. There were no cases where the LBC yielded less diagnostic material than the conventional smear.
Conclusion:
The rate of detection of high-grade lesions was higher on LBC than conventional cytology in this complex clinical setting. These were later histologically confirmed, with three cases regarded as clinically significant.

Peter J Wookey [1]**, Sebastian G.B. Furness** [2]**, Angela Kourakis** [1]**, Patrick M. Sexton** [2]**, David L. Hare** [1]

An anti-calcitonin receptor antibody:fluorophore conjugate that identifies a novel event in apoptosis

1. Department of Medicine, University of Melbourne, Austin Health
2. Monash Institute of Pharmaceutical Science, Monash University, Parkville

Aim:
Apoptosis is a form of programmed cell death, and the recognized events of extrinsic apoptosis include activation (cleavage) of caspase 8/caspase 3, shunting of phosphatidylserine to the cell surface (detected by annexin V binding), chromatin condensation and DNA fragmentation. A novel reagent (antibody conjugate) to monitor a previously undescribed event in apoptosis is characterised in this study.
Method:
Using a unique antibody:fluorophore conjugate that recognises an extracellular epitope of human calcitonin receptor (CTR), we demonstrate high fluorescence events (HFEs) associated with apoptopic cells using confocal microscopy, and in real time, InCell analysis.
Results:
HFEs follow annexin V binding to the plasma membrane (InCell analysis) and appear concurrent with activation of caspase 3 (confocal microscopy). The rate of cell death induced with staurosporine was quantified (cell death [mean value +/- standard error] versus time) by InCell analysis using the antibody:fluorophore conjugate.
Conclusion:
An HFE results from mobilisation of CTR from intracellular compartments in response to cytotoxin, exposure on the plasma membrane and is followed by rapid internalisation of the antibody:fluorophore with apoptosis. This discovery is relevant to our understanding of apoptosis generally and the novel reagent presents diagnostic opportunities (imaging) for human diseases such as cardiovascular diseases and cancers.

TUES 49

Trishe Y-M. Leong & Suzanne Svobodova

EGFR mutation testing pre- and post-establishment of an in-house molecular pathology service

Austin Health

Background:
Molecular testing of tumours is a rapidly growing area. In addition to the expense of the test itself, the retrieval and preparation of material for testing may be both time-consuming and labour-intensive. Limited information exists in the literature regarding adherence to guidelines, and without this information it is difficult to determine if the additional workload is justified. Aims:
To determine the timing, appropriateness and rates of EGFR mutation testing at the Austin and to identify any changes to these measures following establishment of an in-house service. Method: For EGFR mutation testing, specimen type, average request rates, turnaround times and test failure rates were determined for the three-month period from October to December 2012. Following the establishment of in-house EGFR mutation testing, these rates were determined for the three month period of January to March 2013. Results:
EGFR tests were confined to cases of primary or metastatic lung adenocarcinoma only. Turnaround times improved significantly following introduction of in-house testing (average TAT time pre-introduction: 34.5 days, average TAT post-introduction: 6.9 days, p<0.01). Request rates increased following introduction of in-house testing. Failure rates remained unchanged. Conclusions:
At the Austin, moving to an in-house molecular service has resulted in significant reductions in turnaround time that can only be of benefit to patient care. Although EGFR testing may have additional unaccounted-for costs for laboratories, these costs appear justified at our institution by clinically-appropriate testing. Our data indicates increasing request rates although the exact reasons for this are beyond the scope of this study.

TUES 50

Lin Xiao, Suzana Kovac, Mike Chang, Arthur Shulkes, Graham S. Baldwin and Oneel Patel

Zinc ions up-regulate the hormone gastrin via an E-box motif in the proximal gastrin promoter

Department of Surgery, University of Melbourne, Austin Health

Background:
Gastrin and its precursors act as growth factors for the normal and neoplastic gastrointestinal mucosa. Previously we demonstrated for the first time that hypoxia (1% O2) up-regulated the gastrin expression in AGS cells via HIF-independent pathway. The gastrin up-regulation induced by hypoxia mimetic cobalt chloride (CoCl2) was much higher at all three levels of regulation (promoter activity, mRNA and protein) compared to 1% O2.
This study was therefore extended to investigate if other metal ions were able to regulate gastrin expression and the possible mechanisms of up-regulation.
Methods:
Gastrin mRNA was measured by real-time PCR, gastrin peptides by radioimmunoassay, and gastrin promoter activity by dual-luciferase reporter assay.
Results:
Exposure to Zn^{2+} ions increased gastrin mRNA concentrations in the human gastric adenocarcinoma cell line AGS in a dose-dependent manner, with a maximum stimulation of 55 $\oplus$ 14 fold at 100 μM ($P < 0.05$). Significant stimulation was also observed with Cd^{2+} and Cu^{2+}, but not with Ca^{2+}, Mg^{2+}, Ni^{2+} or Fe^{3+} ions. Activation of mitogen-activated protein kinase and phosphatidylinositol 3-kinase pathways are necessary but not sufficient in gastrin induction by Zn^{2+}. Deletional mutation of gastrin promoter identified an 11bp DNA sequence which contained an E-box motif as necessary for Zn^{2+}-dependent gastrin induction.
Conclusions:
E-box binding transcription factors play a crucial role in the epithelial-mesenchymal transition (EMT), together with our observation that Zn^{2+} ions up-regulate the gastrin in AGS cells in an E-box-dependent mechanism, suggests that Zn^{2+} ions may induce an EMT, and that gastrin may be involved in the transition.

TUES 51

Christos N Joannides, Benjamin J Lamont, Maria Stathopoulos, Joseph Proietto and Sofianos Andrikopoulos

Glucose toxicity causes a defect in insulin secretion via the K+ATP channel

Department of Medicine, University of Melbourne, Austin Health

Insulin resistance and impaired insulin secretion are hallmark features associated with fasting hyperglycemia and impaired glucose tolerance in Type 2 diabetes. Although both abnormalities are linked, it is generally thought that most individuals develop insulin resistance long before beta-cell dysfunction occurs. However, the mechanisms underlying progressive beta-cell dysfunction in the presence of insulin resistance remain unclear.

We have previously published that an impairment in glucose-mediated insulin secretion develops in 12 week-old obese and glucose intolerant PEPCK transgenic rats which have a primary defect causing hepatic insulin resistance. Furthermore, tolbutamide-induced insulin secretion was also impaired in PEPCK transgenic rats suggesting that this defect may lie at the level of the K+ATP channel.

The aims of this study were to (i) confirm the impairment in insulin secretion ex vivo; (ii) determine whether this secretory defect was secondary to obesity; and (iii) determine the expression levels of the components of the K+ATP channel in islets.

Our results show that (i) compared to lean control islets, PEPCK transgenic islets had similar insulin secretion at 2.8mM glucose but impaired secretion at 20mM glucose; (ii) pair-feeding PEPCK transgenic rats to the lean control resulted in matched body weights, but did not rescue glucose-mediated insulin secretion; and (iii) Real-time PCR analysis of islet mRNA showed reduced levels of Abbc8 and Kcnj11.

We conclude that the impaired insulin secretion in the PEPCK transgenic rat is not associated with obesity, but rather, may be caused by glucose toxicity associated with a reduction of the components of the K+ATP channel.

TUES 52

This abstract has not been included at the request of the author

TUES 53

Xiao Wang, Graham Baldwin, Christopher Christophi, Hong He and Mehrdad Nikfarjam

The Potential Role of p21-activated kinase 4 (PAK4) in the Growth, Migration and Invasion of Pancreatic Ductal Adenocarcinoma

Department of Surgery, University of Melbourne, Austin Health

Background:
Pancreatic Ductal Adenocarcinoma (PDAC) is one of the most aggressive forms of cancer. The overall 5-year survival rate is less than 5% after diagnosis, even with the best current treatment options. Increased expression of p21-activated kinase 4 (PAK4) has been implicated in PDAC; however, better understanding of the mechanisms involved is required.
This project aims at determining the potential role of PAK4 on the growth, migration, and survival of PDAC in vitro, and the combined effect of PAK4 inhibition with the current standard chemotherapy gemcitabine.
Methods:
The role of PAK4 in pancreatic cancer growth, migration and survival was examined in vitro, using a PAK4 inhibitor (PF-3758309) and three pancreatic cancer cell lines - two human (PANC-1 and MiaPaCa-2) and one murine (PAN02). Cell proliferation was measured using a 3H-thymidine incorporation assay, cell migration/invasion was measured using a Transwell Boyden Chamber assay, and cell survival/toxicity was measured using a 3H-thymidine withdrawal assay. The combined effect of the PAK4 inhibitor and gemcitabine were evaluated on cell proliferation.
Results:
PAK4 inhibition reduced the proliferation and migration/invasion in all cell lines with no toxic effects. IC50 values for proliferation of MiaPaCa-2, PANC-1 and PAN02 cells were 86.7nM, 500nM, and 505nM, respectively, and for migration were 60.1nM, 141nM, and 1.25µM, respectively. In combination with gemcitabine, the PAK4 inhibitor further reduced cell proliferation.
Conclusion:
PAK4 inhibition by PF-3758309 suppressed pancreatic cell growth and metastasis in vitro, and demonstrated synergistic effects with gemcitabine. PAK4 inhibition may be a promising therapeutic option for treatment of PDAC.

TUES 54

Paul MacGibbon [1], Amy Eldridge [1], Beth Depetro [1], Dianne Pierce [2], - Project and Quality Coordinator, Mary Harty [3]

Emergency Care Management Plans

1. Emergency Care Coordination Team, Austin Health
2. Medical and Emergency CSU, Austin Health
3. Emergency Department, Austin Health

Aim:
To ensure best practice care is provided to complex, frequent presenters of the Austin Health Emergency Department (ED) through the implementation of care plans to reduce presentations and Length of stay.

Methods:
Through the use of a working group and in consultation with the ED Quality Committee, a system for developing ED Care Management Plans was implemented for patients that frequently present.

The ED Quality Committee provides governance for the development and maintenance of plans.

A retrospective audit of all patients for whom a care plan had been in place and in use for a 12 month period was completed. Data collected examined the number of emergency department presentations for these patients and looked at the total length of stay over these presentations. Data was then compared to the 12 months prior to care plan implementation.

Results:
13 plans have been completed of which 3 have been in use for over 12 months

The median number of presentations to the Emergency department over the 365 days prior to and post care plan implementation decreased from 25 to 16.6

The median length of stay in ED over 365 days prior to and post care plan implementation decreased from 313 to 212 minutes.

Patient	Care plan start date	Presentations prior 365 days	Average LOS mins prior 365 days	Presentations post 365 days	Average LOS mins post 365 days
A	9/4/2012	32	439	5	279
B	11/4/2012	28	229	31	155
C	2/5/2012	15	271	14	201

Conclusion:
Data from the first year post implementation of the ED care plans show promising results indicating evidence for decreased length of stay and ED presentations.

Michael J. Pichler

Herpud1 is protective against endoplasmic reticulum stress in diabetic beta-cells

Department of Medicine

Endoplasmic reticulum (ER) stress in pancreatic beta-cells can lead to beta-cell failure and type 2 diabetes. ER stress can occur in beta-cells when a chronic nutrient overload stimulates an increase in insulin production that exceeds the folding capacity of the ER. ER stress can result in reduced insulin secretory function and beta-cell death. Herpud1 encodes Herp, which is an ER membrane-associated protein that mediates ER-associated degradation of misfolded proteins. Normal Herp function may help relieve ER stress and thus protect the beta cell.

Here, we show that Herpud1 expression increases in response to incubation of MIN6 cells for 96 hours in media containing high glucose (40mM), 1mM palmitate and a combination of both, potentially acting as a protective mechanism against glucolipotoxicity.

After treatment with a combination of glucose and palmitate (40mM and 1mM respectively), we find reduced expression of the apoptotic factor caspase 3 and observe a trend for a reduction in x-box binding protein 1 (XBP1). In contrast, there were no changes in C/EBP homologous protein (CHOP) and binding immunoglobulin protein (BiP) expression.

In previous studies we have shown that knockdown of Herpud1 results in reduced glucose stimulated insulin secretion in mouse islets ex vivo.

Further experiments will determine whether knockdown of Herpud1 affects markers of ER stress and cell viability in MIN6 beta-cells. These studies will help determine a role of Herpud1 in relieving ER stress in beta-cells and potentially unveil a novel target for reducing beta-cell failure in type 2 diabetes.

TUES 56

This abstract has not been included at the request of the author

TUES 57

E.J. Gianatti [1,2], **P. Dupuis** [1,2], **R. Hoermann** [2], **J.D. Zajac** [1,2], **M. Grossmann** [1,2]

Effect of testosterone therapy on glucose metabolism in men with Type 2 diabetes: a RCT

1. Department of Endocrinology, Austin Health
2. Department of Medicine, University of Melbourne, Austin Health

Aim:
Up to 50% of men with type 2 diabetes (T2D) have lowered testosterone levels. Cause and effect are debated and whether testosterone therapy improves glucose metabolism is not well established. The aim of this trial is to assess the effect of testosterone therapy on glucose metabolism.
Methods:
We conducted a randomised, double blind, placebo-controlled, 40-week trial of intramuscular testosterone undecanoate in men with T2D, with glycated haemoglobin (HbAlc) ≤8.5% and a serum total testosterone (TT) of ≤ 12nmol/L (ClinicalTrials.gov, number NCT00613782).
Results:
88 men were randomised and 75 completed the study. In the testosterone (T) group at 40 weeks, TT increased (+4.6nmol/L $p<0.001$ IQR [0.7,8.8]) while there was no significant change in the placebo group. Testosterone therapy had no significant effect on HOMA-IR (40 week adjusted between group difference -0.08 $p=0.23$ CI [-0.31, 0.47]) or HbA1c (+0.36 $p=0.05$ CI [0, 0.7]). There were no significant changes in either group in fasting glucose, dynamic insulin resistance as measured by oral glucose tolerance test, anthropometry, lipid profile, blood pressure or change in the prevalence of metabolic syndrome. In the T group, changes in circulating TT during treatment correlated inversely with change in total body fat mass ($r=-0.36$, $p=0.02$) while there was no correlation with HOMA-IR ($r=0.13$, $p=0.47$).
Conclusions:
In men with T2D and lowered serum testosterone, testosterone therapy was not associated with significant improvements in measures of glucose metabolism or the metabolic syndrome despite altering body composition in a metabolically favourable manner.

TUES 58

Mark Ng Tang Fui [1]**, Phuong Nguyen** [2]**, Emily J. Gianatti** [1, 2]**, Jeffrey D. Zajac** [1, 2]**, Mathis Grossmann** [1, 2]

Testosterone levels in Type 1, Type 2 diabetic and non-diabetic men

1. Department of Endocrinology, Austin Health
2. Department of Medicine, University of Melbourne

Introduction:
Population-based studies consistent show high rates of low testosterone (T) in men with type 2 diabetes. The prevalence of low T in type 1 diabetic men is less clear. The significance of ageing and obesity on low T levels in these men remains to be determined. Our aim was to determine the prevalence of low T levels in men with type 1 diabetes, compared to men with type 2 diabetes and non-diabetic men.
Methods:
Morning fasting serum testosterone levels were measured in patients with type 1 diabetes presenting to clinic from January '07-'11, in patients with type 2 diabetes and men without diabetes. Anthropometric data was also collected.
Results:
We analysed 80 men in each cohort. 5% of type 1 diabetics (mean age 47y, mean BMI 27kg/m2), 25% of type 2 diabetics (mean age 56y, mean BMI 31kg/m2) and 15% of non-diabetics (mean age 57y, mean BMI 28kg/m2) had low T as defined T <10nmol/L (P<0.05 between groups). In all three cohorts, T declined as BMI increased. Low testosterone was independently associated with BMI, advancing age and diabetes type.
Conclusion:
Low testosterone is common in diabetic men however increasing age and BMI are significant contributors to this.

TUES 59

Amanda Leong

Long-term Intraindividual Variability in Albumin Excretion Rate in Patients with Type II Diabetes

Austin Clinical School, University of Melbourne, Austin Health

Aims:
There is paucity of data on the long-term variability of Albumin Excretion Rate (AER) in patients with type II diabetes. This study aimed to determine the variability of AER and factors that influence it, in type II diabetic patients.
Methods:
Consecutive AER measurements from 1999-2012 of 497 type II diabetic patients were recorded in a cohort study. Coefficient of variation (CV) was used as a measure of intraindividual AER variability. The first three AER measurements were used to classify individuals into normo-, micro- and macroalbuminuria groups at baseline. Linear regression examined the effects of baseline demographic variables on the AER CV: AER group, HbA1c, age, gender, duration of diabetes, total cholesterol, HDL, systolic BP, BMI, ACEi/ARB use at baseline and smoking. A logarithmic transformation was applied to CV prior to analyses.
Results:
The intraindividual variability in AER was compared between treated (ACEi/ARB use in 2000, n=312) and untreated(n=185) patients. The CV was higher in those treated than those untreated(p=0.003). There was no evidence of a relationship between the AER CV and baseline characteristics. Linear regression of log CV in treated and untreated groups and AER groups was used. After adjustment for AER groups, the difference in mean CV between the treated and untreated groups remained significant(p=0.013). After adjustment for ACEi/ARB use, the mean CV in the microalbuminuria group was 1.27 times that of the normoalbuminuria group, 1.15 times greater in macroalbuminuria compared to the normoalbuminuria, with no difference for micro- versus macroalbuminuria groups. Overall, p<0.001.
Conclusion:
Patients with type II diabetes and micro- or macroalbuminuria have a greater AER CV than those with normoalbuminuria at baseline. There was a greater intraindividual CV in those treated with ACEi/ARB indicating greater changes in AER over time in these patients. These results emphasize the need for serial AER measurements in assessing AER trajectory.

TUES 60

Angela X. Chen [1]**, George Jerums** [1,2]**, Sara Baqar** [1]**, Georgina Thomas** [1]**, Richard J. MacIssac** [2,3]**, Christopher O'Callaghan** [2,4]**, Elif I. Ekinci** [1,2,5]

Short-term dietary salt supplementation is not associated with reduced renal function in hypertensive subjects with type 2 diabetes

1. Department of Endocrinology, Austin Health
2. Department of Medicine, University of Melbourne
3. Department of Endocrinology, St Vincent's Health
4. Department of Clinical Pharmacology, Austin Health
5. Menzies School of Public Health, Darwin

Background:
Guidelines recommend low dietary salt intake in people with diabetes to reduce blood pressure. However low salt intake is associated with increased mortality and renin angiotensin aldosterone system (RAAS) activity in patients with diabetes. Randomised controlled studies on the effects of salt supplementation on RAAS and eGFR in diabetes are presently limited.
Aims:
The aim of the study was to examine the effect of dietary sodium chloride (NaCl) supplementation on estimated glomerular filtration rate (eGFR), mean arterial blood pressure (MAP), plasma renin activity (PRA) and serum aldosterone in hypertensive patients with type 2 diabetes.
Method:
In a randomised, double blind, controlled study (RCT), patients with type 2 diabetes (n=28), treated with 40mg of telmisartan (angiotensin II receptor blocker) received two weeks of placebo or NaCl capsules (100mmol/24hr). The protocol was then repeated in reverse, allowing subjects to act as their own controls. 24h urinary sodium excretion (24hUNa), ambulatory blood pressure monitoring and blood tests were performed to determine eGFR, MAP, PRA and serum aldosterone. Repeated one-way ANOVA was performed to assess the effects of NaCl versus placebo supplementation.
Results:
NaCl supplementation significantly increased eGFR and MAP, but reduced PRA and serum aldosterone in the presence of angiotensin II receptor antagonists (Table).
Conclusion:
The results from this RCT demonstrate a reduction in RAAS activity following NaCl supplementation, with no evidence of adverse effects on eGFR in the short-term.

TUES 62

This abstract is not included at the request of the author

TUES 63

A. Sabetghadam, W. Korim. and A.J.M. Verberne

A neurophysiological study of the medullary sympathetic pathway to the adrenal gland

Clinical Pharmacology and Therapeutics Unit, Department of Medicine, University of Melbourne, Austin Health

INTRODUCTION:
Our laboratory has identified a role for the rostral ventrolateral medulla (RVLM) in the control of adrenaline secretion from the adrenal gland and its role in glucose homeostasis. In this study, we have examined sympathetic evoked responses recorded from the adrenal sympathetic nerve in response to intermittent stimulation of the RVLM.
METHODS:
All experiments were performed using isoflurane/urethane-anaesthetised, artificially-ventilated, paralysed, male Sprague-Dawley rats. The RVLM pressor region was first identified by extracellular single unit recording combined with field potential mapping of the facial motor nucleus. We compared the latencies of the evoked adrenal sympathetic response to that recorded from the lumbar sympathetic nerve upon electrical stimulation of the RVLM (0.5 Hz, 1 ms pulse width, 50-300 µA) after conversion to urethane anaesthesia (1.4 g/kg, i.v.) and induction of neuromuscular paralysis (pancuronium bromide, 1 mg/kg, i.v.).
RESULTS:
RVLM stimulation elicited an evoked sympathetic response in the adrenal nerve that depended on whether the recording was primarily pre- or post-ganglionic activity as judged by the effect of the ganglion blocker hexamethonium. When mostly pre-ganglionic, several peaks of activity were noted: an early peak (latency - 79 ± 9 ms, n=4) and a late peak (latency - 149 ± 6 ms). In contrast, lumbar sympathetic nerve activity exhibited a prominent early peak (latency - 87 ± 7 ms; n = 5) that was eliminated by Hex (20-40 mg/kg, i.v.). Pre-ganglionic ASNA was reduced by 62 % after intrathecal injection of a glutamate receptor antagonist (kynurenate; 0.5 µmole/10 µl; $P<0.01$, late peak, n=3).
CONCLUSION:
These data suggest that the early peak represents sympathetic vasomotor activity in both the adrenal and lumbar sympathetic nerves. However, the late sympathetic response noted in the adrenal nerve may be involved in the control of catecholamine secretion from adrenal chromaffin cells
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TUES 64

This abstract has not been included at the request of the author

TUES 65

David Darby [1-4]**, Amy Brodtmann** [1]**, Michael Woodward** [4]**, Moacir Neto** [1,5,6]

The Trajectory-Related Early Alzheimer's Database (TREAD) Study: Initiation

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2. Centre for Neuroscience, University of Melbourne
3. CogState Ltd, Melbourne
4. Austin Health
5. Centro de Medicina Preventiva e Esportiva (CEMPRE), Brazilia, Brazil.
6. Hospital de Basa - DF (HBDF), Brazilia, Brazil

Background:
Early detection of Alzheimer's disease (AD) in the prodromal stages is now critical to test promising disease modifying therapies at a time when single mechanism therapies are likely to be most effective. Identification of such early prodromal patients is problematic. Serial computerized cognitive testing is a potentially cost-effective community screening approach. Methods: The TREAD study is a Melbourne-based initiative that aims to recruit 10,000 community dwelling volunteers age 50 and over, who are willing to perform internet-based remote computerized cognitive testing serially in order to detect decline in episodic memory. When detected, they are offered medical evaluation for identifiable causes, and if none are detected, then are offered biomarker (CSF, amyloid-PET) and benchmarking (neuropsychological, MRI, FDG-PET) evaluations to obtain baseline measures for future trials (and determination of pre-trial trajectories). Such well-characterized volunteers are then made available for clinical trial recruitment.
Results:
Recruitment started on 21 Dec 2012 with a single radio interview, with over 520 registered participants by Feb 2013. Baseline demographic data: Mean age 60.0 years (SD 0.32), mean education 13.5 years (SD 0.15), males 36%, family history of AD 26%, right handed 89%. Mean Penn State Worry Questionnaire-15 29.2/90 (SD 0.62) suggestive of at most mild anxiety. Mean Patient Health Questionnaire-9 2.4/27 (SD 0.12) indicative of no depression. Subjective memory complaints mean 2.1/10 (SD 0.1) consistent with minimal complaints. Testing used both various software engines - 72% could test using a FLASH-based engine, 95% could use a javascript-based engine.
Conclusions:
Interest is high amongst community dwelling participants for memory screening despite being forewarned that they will be told if found to be declining. Browser and technical issues have dominated early adoption of this approach but appear to be surmountable. Target recruitment of much larger numbers appears feasible and will be attempted over the next months.

TUES 66

Peter E Batchelor [1, 2], **Peta Skeers** [1, 2], **Ana Antonic** [1, 2], **Taryn E Wills** [1, 2], **David W Howells** [1], **Malcolm R Macleod** [3], **Emily S Sena** [1, 3]

Systematic review and meta-analysis of therapeutic hypothermia in animal models of spinal cord injury

1. Florey Institute of Neuroscience and Mental Health, Austin Health
2. Department of Medicine, University of Melbourne
3. Division of Clinical Neurosciences, University of Edinburgh, Edinburgh

Introduction:
Therapeutic hypothermia is a clinically useful neuroprotective therapy for cardiac arrest and neonatal hypoxic ischemic encephalopathy, and may potentially be useful for the treatment of other neurological conditions including traumatic spinal cord injury (SCI). The pre-clinical studies evaluating the effectiveness of hypothermia in acute SCI broadly utilise either systemic hypothermia or cooling regional to the site of injury. The literature has not been uniformly positive with conflicting studies of varying quality, some performed decades previously.
Methods:
In this study, we systematically review and meta-analyse the literature to determine the efficacy of systemic and regional hypothermia in traumatic SCI, the experimental conditions influencing this efficacy, and the influence of study quality on outcome. Our inclusion criteria consisted of the (i) reporting of efficacy of hypothermia on functional outcome (ii) number of animals and (iii) mean outcome and variance in each group.
Results:
Systemic hypothermia improved behavioural outcomes by 24.5% and a similar magnitude of improvement was seen across a number of high quality studies. The overall behavioural improvement with regional hypothermia was 26.2%, but the variance was wide. Sufficient heterogeneity was present between studies of regional hypothermia to reveal a number of factors potentially influencing efficacy, including depth and duration of hypothermia, animal species, and neurobehavioural assessment. However, these factors could reflect the influence of earlier lower quality literature.
Conclusion:
Systemic hypothermia appears to be a promising potential method of treating acute SCI on the basis of meta-analysis of the pre-clinical literature and the results of high quality animal studies.

TUES 67

This abstract has not been included at the request of the author

TUES 68

This abstract has not been included at the request of the author

TUES 69

Johnson George [1], **Dennis Thomas** [1], **Billie Bonevski** [2], **Simone E. Taylor, Susan Poole** [1,4], **Greg R. Weeks** [1,5], **Michael J. Dooley** [1,4], **Michael J. Abramson** [6],

Characteristics of smokers participating in a randomised controlled trial evaluating a system change smoking cessation intervention

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2. School of Medicine and Public Health, University of Newcastle
3. Pharmacy Department, Austin Health\
4. Pharmacy Department, The Alfred Hospital
5. Pharmacy Department, Barwon Health, Geelong
6.Department of Epidemiology and Preventive Medicine, Faculty of Medicine, Nursing and Health Sciences, Monash University, The Alfred Hospital

Background:
Intensive smoking cessation interventions initiated during hospitalisation are effective, but currently underused.
Methods:
A randomised controlled trial is underway at three Victorian public hospitals comparing GIVE UP FOR GOOD© – an intensive system change smoking cessation intervention delivered by a trained pharmacist – to standard care. The primary outcomes are carbon monoxide validated abstinence at six and 12 months.
Results:
A total of 600 participants have been recruited – mean (±SD) age 51±14 years and 64% male. The baseline median (IQR) confidence to quit was low 5 (3 – 8), however the motivation to quit was very high 9 (6.5 – 10). The majority of participants were either in the preparation (intended to change in one month [23%]) or action (already made changes [53%]) stage on the 'readiness to quit ladder'. Majority were daily smokers, started smoking before the age of 18, and had smokers in their social circle or at home. Many of them reported quit attempts in the previous 12 months; almost half of them preferred to quit with the help of medicines in their future quit attempts.
Conclusion:
GIVE UP FOR GOOD© has the potential to increase abstinence rates in hospitalised smokers and if effective, could be considered for wider implementation.

TUES 70

Simone E. Taylor [1], Alana Meaklim [1], Alice Chow [1,2], Melissa Fodera [2]

Medical, nursing and pharmacy staff perceptions of Cerner electronic prescribing implementation for inpatient prescribing.

1. Pharmacy Department, Austin Health
2. Clinical Systems Project Group, Austin Health

Aims:
To evaluate front-line clinical staff perceptions of user-friendliness, impact on work-flow and training strategy as Cerner was implemented across an acute-care hospital.
Methods:
A questionnaire, including likert-scale and open-ended questions, was distributed six months after electronic inpatient prescribing went live. All ward pharmacists, junior doctors and five nurses on each acute ward were invited to participate.
Results:
The questionnaire was completed by 42 nurses, 16 junior doctors and 22 pharmacists (response rate 62%); 98% of respondents used Cerner multiple times daily. Overall feeling towards Cerner was scored as 7.1±1.9 (0='hate it', 10='love it'). Whilst the majority found Cerner to be user-friendly and were pleased to be involved in 'pioneering' work, there was greater variability in responses around work-load and attitudes towards helping others. Three quarters of staff were neutral or agreed that they were well prepared and knew what to expect during implementation. Recommendations for improved implementation were for training sessions to be shorter but more frequent, ensuring training was relevant to staff workflow and including specific examples. Nurses and pharmacists felt more doctor training was needed. Implementation elements that were well done were availability of ward super-users, to help with trouble shooting. Many respondents identified that initially Cerner slowed down their workflow but once familiar, it is more efficient than the paper-based system.
Conclusions:
Overall, Cerner has been well accepted by front-line clinical staff. Super-users on the wards were important when the system initially went live, but content and duration of tutorials could be improved.

TUES 71
Simon Lau

Cervical Spinal Cord Injury at the Victorian Spinal Cord Injury Service: the Last Decade

Surgery, Austin Health.

INTRODUCTION
Cervical Spinal Cord Injury (CSCI) is a significant medical and socioeconomic problem. In Victoria, Australia, there has been limited research into the incidence of CSCI. The Austin Hospital and Victorian Spinal Cord Injury Service (VSCIS) is a tertiary referral hospital that accepts referrals for surgical management and ongoing neurological rehabilitation for south eastern Australia.
METHODS
This was a retrospective review of medical records from January 2000 to January 2010 of all patients who underwent surgical management of acute CSCI in the VSCIS catchment region. Outcome measures included: demographics, method of injury and associated factors (like alcohol) and neurological status
RESULTS
Men were much more likely to have CSCI than women with a 4:1 ratio, and the highest incidence of CSCI for men was in their 20s, who were at greater risk of complete injury. The most common cause of CSCI was transport related (51%), followed by falls (20%) and water-related incidents (16%). Falls were more prevalent among those >50 years. Alcohol was associated in 22% of all CSCIs, including 42% of water related injuries. Water related injuries only involved people 50 years who suffer falls from height.

Public awareness campaigns should target these groups to lower incidence of CSCI.

TUES 72

J. Grewal [1], R. Johnston [1], K. Sanders [1], R. Rayoo [1], L. Kearney [1], R. Lim [3], G. Smith [3], P. Srivastava [1,2], E. Jones [1], O. Farouque [1,2], A Al-Fiadh [1,2]

Ambulatory Rapid Access Chest Pain Clinic for Low to Intermediate Risk Patients – A Single Centre Experience

1. Department of Cardiology, Austin Health
2. Department of Medicine, University of Melbourne, Austin Health
3. Department of Radiology, Austin Health

Background :
Our Emergency Department (ED) reviews >1500 chest pain presentations annually. Due to high service demand, patients with stable chest pain syndromes referred to the outpatient Cardiology service wait 3-4 months for an appointment. To improve service access for low-intermediate risk chest pain patients referred from ED, Chest Pain Clinic was introduced with rapid access to diagnostic investigations i.e. CT coronary angiogram (CTCA), stress echocardiography (SE) and invasive coronary angiogram (ICA).
Aims :
An audit to assess the feasibility and short-term outcomes of the Chest Pain Clinic. Low to intermediate risk patients were defined as having =15% 5-year risk of cardiovascular disease using the Framingham Risk Equation. Eligible patients were aged 60mL/min/1.73m2.
Results :
Over 5 months, 121 patients were referred (mean age 52 ± 10 years; 57% male). Mean time from ED discharge to clinic review was 11 ± 4 days. CTCA SE ICA No. of patients (%) 101 (82.6%) 20 (16.6%) 1 (0.8%) Mean time from review to Ix (days) 4 ± 5 23 ± 22 15 Of patients undergoing CTCA, 8% had severe coronary artery disease (CAD) and underwent ICA. Of these, 25% proceeded to percutaneous intervention and 12.5% to coronary artery bypass grafting. There were no procedural complications or major adverse cardiovascular outcomes. Revascularisation rate was 2.5%.
Conclusion :.
In our experience, this model safely improves service provision, enabling rapid and definitive assessment of chest pain syndromes.

TUES 73

J. Grewal [1]**, A. Al-Fiadh** [1,2]**, O. Farouque** [1,2]**, E. Jones** [1]

Prevalence of Patent Foramen Ovale in Patients with Acute Myocardial Infarction and Angiographically Normal Coronary Arteries

1. Department of Cardiology, Austin Health
2. Department of Medicine, University of Melbourne, Austin Health

Background :
The prevalence of patent foramen ovale (PFO) is about 25% in the general population, but increases to 40% in patients with cryptogenic stroke. We hypothesise that paradoxical embolism via PFO could be an alternative cause for acute myocardial infarction (AMI) in patients with angiographically normal coronary arteries.
Methods :
We recruited patients aged 21-80 years with symptoms of AMI and elevated cardiac enzymes who underwent coronary angiography within 3 days of admission. Patients with angiographically normal coronary arteries comprised the study group (n=20); patients with obstructive coronary artery disease comprised the control group (n=20). The study and control groups were age-matched. All patients underwent transthoracic echocardiography with agitated intravenous saline contrast for detection of PFO.
Results :
The collected data were analysed using paired t-test. Study group Control group p-value Mean age (years) 57 +/- 13 58 +/- 14 0.77 Male gender 35% 85% 0.0016 PFO 45% 10% 0.0047 Current smoker 25% 30% 0.71 Hypertension 40% 65% 0.13 Diabetes 0% 25% 0.02 Dyslipidaemia 45% 55% 0.57 FHx of IHD 35% 25% 0.54
Conclusion :
Paradoxical embolism should be considered a potential alternative cause for AMI in patients with normal coronary arteries. However, the role of PFO closure in this population is unclear.

TUES 74

Therese Thornton [1,2], **Fergal J. O'Donoghue** [2], **Peter D Rochford** [2], **Charlie C.L. Xue** [3], **John Trinder** [1], **Amy S. Jordan** [1,2]

Traditional Chinese Medicine diagnosis of obstructive sleep apnoea

1. School of Psychological Sciences, The University of Melbourne
2. The Institute for Breathing and Sleep, Austin Health
3. School of Health Sciences, RMIT University

Aim
This study aimed to identify the most common TCM pattern shown by OSA patients in an Australian sleep laboratory. A previous trial has demonstrated that acupuncture reduced the severity of Obstructive Sleep Apnoea (OSA). The same treatment was applied to all patients regardless of their Traditional Chinese Medicine (TCM) diagnosis and despite overall improvement across the group, several patients showed no improvement. There have been 4 TCM disease mechanisms suggested to underlie OSA identified in several case studies reported in China.
Method
Forty (40) patients undergoing polysomnographic (PSG) investigation for OSA were given a TCM diagnosis immediately prior to PSG. It was predicted that patients diagnosed with OSA through PSG investigation would be diagnosed with one of the proposed TCM patterns.
Results
Results showed that Spleen-Qi Deficiency with Phlegm-Dampness appeared concurrently with Liver-Lung Fire in 41.03% of cases, and concurrently with Yin-Deficiency-Fire in 17.95% of cases. Other combinations of the 4 TCM patterns were rare, as were cases with a single pattern diagnosis.
Conclusions
The identification of these patterns suggests that in order for acupuncture treatment to be more clearly supported as an effective treatment for OSA, treatment protocols need to address the specific TCM patterns. A clinical trial of acupuncture treatment for OSA, designed to address the most common TCM disease pattern identified by the present study, is currently underway.

TUES 75

A.Thomson [1]**, A. Hilton** [2]**, C. Christophi** [1]**, R. Bellomo** [2]

An assessment of forearm blood flow by ultrasound Doppler in critically ill patients

1. Department of Surgery, University of Melbourne, Austin Health
2. Intensive Care Unit, Austin Health

Aim:
Monitoring of post-cardiac surgery patients in Intensive Care Units (ICU) has traditionally focused on central haemodynamic variables, including cardiac index (CI) and mean arterial pressure. Keeping these variables at normal or supraphysiological levels is thought to result in better patient outcomes. However, the relationship between central and regional haemodynamics is not fully understood. This study aimed to assess this relationship.
Method:
We studied 20 patients undergoing elective cardiac surgery. Data were collected prior to surgery, following admission to ICU and the following morning. Measurements of the patient's central haemodynamics were made using their pulmonary artery catheter. Ultrasound scans of the brachial artery were taken to measure regional/forearm blood flow.
Results:
There was no statistical difference ($p > 0.05$) in forearm haemodynamics between right and left arms and between dominant and non-dominant arms. There was no correlation between CI and indexed forearm blood flow (FBF), or between the systemic vascular resistance index and the brachial artery resistance index (Spearman's rank test $p > 0.05$). FBF between time points was not related (one-way ANOVA p0.05).
Conclusion:
There appears to be no relationship between central haemodynamics and forearm blood flow. Additional analysis is needed to determine the effect of confounders and if this disconnect extends to other vascular beds, including internal organs and the brain.

TUES 76

D. Wynne, S. N. Kong, C. Christophi, P. Costa

Investigating the effects of kinin receptor inhibition on the progression of colorectal liver metastasis

Department of Surgery, University of Melbourne, Austin Health

Aim:
The liver is the dominant metastatic site in patients with colorectal cancer (CRC). Although well-established treatment options exist, high rates of tumour recurrence and low rates of survival persist. A novel treatment option may exist in the inhibition of kinin/kinin-receptor binding. This study investigates the effects of kinin receptor inhibition in a murine model of colorectal liver metastasis.
Methods:
The proliferative ability of mouse colorectal cancer (MoCR) cells treated with kinins (Bradykinin or desArg9-Bradykinin), and/or the antagonists SSR240612 and FR173657 (kinin receptor 1 and kinin receptor 2 antagonists respectively), was analyzed in vitro using the H3-thymidine incorporation assay. In vivo study incorporated 3 groups - control, FR173657 and SSR240612 - of 6 CBA mice. Tumour induction was achieved via the intrasplenic injection of tumour cells into anesthetized mice. Mice were administered drug daily (15 mg/kg/day of FR173657 and 10 mg/kg/day of SSR240612) via oral gavage. Percent tumour volume of liver was used to assess the extent of tumour growth.
Results:
Bradykinin, at concentrations of $0.001\mu M$ ($p<0.05$), $0.1\mu M$ ($p<0.01$) and $1.0\mu M$ ($p<0.001$), increased MoCR cell proliferation in vitro. The enhanced proliferation observed using $0.1\mu M$ of Bradykinin and desArg9-Bradykinin, was attenuated with administration of $1\mu M$ of FR173657 ($p<0.0001$) and SSR240612 ($p<0.0001$) respectively. Pilot in vivo results suggest mice treated with FR173657 and SSR240612 may possess a decreased tumour burden compared to control, though not statistically significant. Higher doses of antagonists will be tested.
Conclusion:
Kinin receptor antagonism appears likely to disrupt, in some capacity, the development of CRC liver metastasis in mice.

TUES 77

This abstract has not been included at the request of the author

TUES 78

Jonathon Lo, Justin Jedynak, Franklin Pond

Spinal cord ischaemia following endovascular abdominal aneurysm repair: case report

Vascular Unit, Austin Health

Paraplegia from spinal cord ischaemia is an extremely rare and devastating complication of abdominal aortic surgery. We report a case of postoperative paraplegia immediately following endovascular abdominal aneurysm repair (EVAR). A cerebrospinal fluid drain was inserted and steroid therapy commenced with improvement in sensation but no change to the motor deficit. We examine the mechanisms of spinal cord ischaemia and important implications for perioperative management.

WED 01

Shahmoradi N, Wang XF, Iuliano-Burns S, Ghasem-Zadeh A, Bjørnerem A and Seeman E

Contributions of lean and fat mass to bone structure: a co-twin study

Depts of Endocrinology and Medicine. Austin Health, University of Melbourne

Background:
We examined the association between total body lean mass (LM) and fat mass (FM) and bone microstructure in healthy female twin pairs.
We hypothesis that lean mass, not fat mass, is associated with total cross sectional area but fat mass not lean mass is associated with medullary cross sectional area.
Methods:
We measured the macro- and microarchitecture of the distal radial and distal tibial metaphysis using high-resolution peripheral quantitative computed tomography (HR-pQCT). Lean and fat mass were determined by dual-energy X-ray absorptiometry (DXA, Lunar, GE Prodigy). Relationships between within-pair differences in lean mass or fat mass and within-pair differences in bone structure were tested using linear regression analysis.
Results:
Of 112 twin pairs aged 44 to 65 years (mean 53 years), 18% were premenopausal, 20% perimenopausal and 62% postmenopausal. Within-pair differences in lean mass controlling for fat mass, were associated with total CSA as well as medullary and cortical CSA at the tibia but not radius (r ranging from 0.23-0.44, P<.005).
After controlling for lean mass, within-pair differences in fat mass were associated with within-pair differences in total vBMD at the tibia only (r=0.26, P=0.02).

WED 02

Melissa J. Hirth [1]**, David J. Jacobs** [1]**, Kate Sleep** [2]

Hand-based swing traction splinting for intra-articular proximal interphalangeal joint fractures

1. Department of Occupational Therapy, Austin Health
2. Malvern Hand Therapy

Introduction.
Acute intra-articular fractures of the proximal interphalangeal (PIP) joint have always presented as a difficult injury to manage for the treating surgeon and therapist. Traction management enabling ligamentotaxis and motion is a popular method to manage these injuries. This case series presents the design and results of hand-based swing traction splinting which is less cumbersome for patients than other forms of traction splinting.
Methods.
Five patients presenting with intra-articular PIP joint fractures underwent surgery whereby a transverse K-wire was inserted across the middle phalanx. The treating Occupational Therapist fabricated a hand-based swing traction splint to provide a distraction force from the K-wire to the splint. Range of motion and patient satisfaction were the primary outcome measures.
Results.
All five patients reported satisfaction with their hand function following therapy involving swing traction splinting. Furthermore, range of motion was comparable to other forms of traction management reported in the literature with an 88° mean arc of motion at the PIP joint.
Conclusion.
This case series demonstrates that hand-based swing traction splinting is a viable treatment option for the management of intra-articular PIP joint fractures. With similar outcomes to other forms of distraction that enable early movement, such as the Pins and Rubber Traction System, this design is an alternative. The less cumbersome splint design is the main advantage over other splinting methods that apply distraction whilst also enabling early motion.

WED 03

This abstract has not been included at the request of the author

WED 04

Cimoli, M, Oates, J., Greenwood, K., McLaughlin, E., Langmore, S.E.

The use of instrumental swallowing assessments by speech pathologists working in Australia

Speech Pathology

Fibreoptic Endoscopic Evaluation of Swallowing (FEES) is an instrumental swallowing assessment used by speech pathologists to evaluate swallowing. Historically, considered to be an alternative assessment to the Videofluoroscopic Swallowing Study (VFSS), the scientific evidence supporting the use of FEES in different clinical contexts and with different populations is growing. However, there is limited research available to describe how speech pathologists actually use FEES in clinical practice.
This study was designed to obtain information about how widely FEES is used in Australia. The methods used to conduct and interpret the examination, and types of FEES training undertaken by speech pathologists, were also examined. A 44-item questionnaire was developed, and delivered as a web-based survey to practising members of Speech Pathology Australia currently working in Australia with adult patients who have dysphagia.
A total of 68 speech pathologists responded (17.4% participation rate). There was some variation in the completeness of responses with 86.4% of responses being complete. In addition to questions relating to FEES practice, the survey also included items relating to VFSS practice. As a well-established instrumental swallowing assessment, the methods used by speech pathologists in their use of VFSS provided some opportunities for comparing approaches used in conducting these two examinations.
Data regarding frequency of use, assessment and procedural elements included in these examinations, as well as clinical experience and training were collected.
The results of this study provide valuable information about current approaches to FEES practice and training, and identified some areas of variation in practice.

WED 05

Tina Griffiths [1,] **Liz Pascoe** [2]

Evaluation of an education program to facilitate patient adherence, toxicity monitoring and promote safety and wellbeing in the self administration of oral chemotherapy in the home setting

1. Olivia Newton-John Cancer & Wellness Centre, Austin Health
2. Faculty of Health Sciences, La Trobe University

Introduction:
The use of oral chemotherapy as a cancer treatment is increasing (Hede 2009), with patients expected to self-administer them (Goodin et al. 2007). While self- administration in the home setting offers advantages to patients (Simchowitch et al. 2010), it poses significant challenges for health care professionals, many of which revolve around adherence, toxicity monitoring and safety issues (Halfdanarson & Jotoi 2010).
In this study, patients prescribed oral chemotherapy, received education and follow-up support from the Chemotherapy Nurse Coordinator (CNC) at the Olivia Newton-John Cancer and Wellness Centre, Melbourne Victoria.
Aim:
Evaluate an education program to facilitate patient adherence, toxicity monitoring and promote safety and wellbeing of oral chemotherapy in the home setting.
Methodology:
Cancer patients (N =15) prescribed oral chemotherapy received education about their treatment using a teaching tool developed by The Multinational Association of Supportive Care in Cancer (MASCC) ™. The patient's supportive care needs were assessed using the Distress Thermometer (DT). A modified version of the MASCC questionnaire was administered pre and post education to assess the patient's knowledge about oral chemotherapy, safe storage and handling, and associated toxicity issues. A follow up phone call to the patient one week later addressed issues relating to the education program. The patient also completed the DT.
Results:
Data was analysed using descriptive statistics. Education program highlighted the importance in patients' knowledge and understanding around key issues pertaining to oral chemotherapy. Limitations are small sample size.
Conclusion:
Tailored education programs may facilitate medication adherence, toxicity management and enhance patient's well-being.

WED 06

Allison Mo, Andrew Grigg

Metastatic Thymoma and T Acute Lymphoblastic Leukaemia (T-ALL): A Case Report

Haematology Department Austin Hospital

BACKGROUND:
Rare reports have described T-ALL concurrent with thymoma, with poor outcomes. We describe the first case of a patient achieving complete remission (CR) of both T-ALL and pre-existing refractory metastatic malignant thymoma following anti-leukaemia treatment.
CASE REPORT:
A 53 year old man was diagnosed with TypeB2(cortical) malignant thymoma in August 2010 after presenting with a mediastinal mass. After tumour resection, chemotherapy (cyclophosphamide, adriamycin, cisplatin) and mediastinal radiotherapy were given. Biopsy-confirmed thymoma progression occurred in October 2011, with new pleural nodules. He failed to respond to ABT-806i (anti-EGFR monoclonal-antibody), and treatment ceased in June 2012. In October 2012, he developed hepatosplenomegaly and fevers. Bone marrow biopsy confirmed T-ALL. He was given T- ALL chemotherapy (cyclophosphamide, L-asparaginase, vincristine, daunorubin, Ara-C, teniposide, 6-MP, prednisolone). Marrow biopsies (November 2012 and March 2013) showed CR. PET/CT (January and April 2013) showed no metabolically active tumour. He is currently on oral maintenance, 41 weeks following ALL diagnosis.
CONCLUSION:
The underlying pathogenesis of concurrent T-ALL with thymoma, and why the latter achieved remission despite prior chemorefractoriness, is unknown. Malignant transformation in a common precursor cell is unlikely, as thymomas (arising from thymic epithelial cells) and thymocytes have different embryonic origins. Hypotheses include that the precipitant for thymoma also triggers the development of clonal T-lymphoblasts. Alternatively, the immunological milieu of the thymoma epithelium, additionally stimulated by chemoradiotherapy, predisposes thymocytes to malignant transformation. A recent report describes molecular transformation of polyclonal non-malignant thymocytes into monoclonal T-ALL, nine years after thymoma treatment.(Ertel 2013)

WED 07

M. Rolfo [1], **J Jackson** [1], **D. Lim Joon** [1], **D. Scandurra** [1], **N. Anderson** [1], **B. Welsh** [1], **M. Lawlor** [1], **K. Brown** [1], **V. Khoo** [1,2]

Simple Segment IMRT: Dosimetric and Resource Implications of an Innovative Rectal Cancer Technique

1. Olivia Newton John Cancer and Wellness Centre, Austin Health
2. The Royal Marsden NHS Foundation Trust (Radiation Oncology), London, United Kingdom

Purpose/Objectives:
Intensity Modulated Radiotherapy (IMRT) can reduce the volume of small bowel irradiated to high-dose in neoadjuvant radiotherapy (RT) for rectal cancer. Patients treated with this technique may experience lower rates of late intestinal toxicity. However, IMRT is associated with higher integral dose and potentially more low-dose bowel exposure than three-dimensional conformal RT (3D). The long term implications of this exposure are unknown. IMRT requires extended delivery time and quality assurance (QA) checks which are resource intensive. This planning study investigates the dosimetric and resource implications of a hybrid technique with large, simple segments - Simple Segment IMRT (SS), compared to 3D and 7 field IMRT (IMRT7).

Methods/Materials:
Ten patients (5 male: 5 Female) with MRI stage T3N0 rectal cancer were planned in the supine position for preoperative (chemo) radiotherapy. Target volumes, bladder, and intestinal cavity (IC) were defined and 3 plans were generated for each patient: 3 field 3D using XIO planning system, IMRT7 (38, 92, 143, 194, 245, 296, 347°) and 5 field SS (80,150, 180, 210, 280° with minimum segment size set to 16cm2) both planned on Monaco Version 3.2. The 3DCRT were planned as 2 phase 50.4/45Gy in 1.8Gy per fraction and the IMRT were both delivered via synchronous in field boost at 1.8/1.68Gy per fraction. Dose plane gamma analysis was performed on all SS and IMRT7 plans and delivery times were recorded.
Results: The SS plans delivered significantly lower IC V45 than 3D (mean 53.6 vs. 87.9cc; p=0.021) but were comparable to IMRT7 (mean 43.4cc; p=0.51). SS had lower IC V15, V20 and V30 than IMRT7 (767.3 vs. 989.2, 506.1 vs. 837.2, and 294.3 vs. 367.5cc; p=0.002, 0.0001, and 0.018) and lower V15 than 3D (767.3 vs. 911.8cc; p=0.010). Total monitor units were lower in SS than 3D and IMRT7 (304.9 vs. 914.1 and 506.6; p=0.0001 and 0.0001) as were total segments vs. IMRT7 (mean 24.5 vs. 64.4; p=0.0001). Integral dose was lower in SS than 3D and IMRT7 at V10 and V15 (40.0 vs. 42.1 and 42.7, 33.2 vs. 36.0 and 37.8cc and; p=0.022 and 0.009, 0.0006 and 0.001).

WED 08

Heather Leggett [1], Simone Alford [2], Chris Hamilton [2]

Dosimetric comparison of sequential electron versus simultaneous integrated boost (SIB) techniques for adjuvant breast radiotherapy

1. Ballarat Austin Radiation Oncology Centre, Ballarat Regional Integrated Cancer Centre.
2. Olivia Newton-John Cancer and Wellness Centre, Austin Health

Aim:
To compare the relative planning target volume (PTV) and clinical target volume (CTV) coverage and organ at risk (OAR) avoidance using sequential electron and SIB technique.
Method:
The plans of 20 patients with 10 right and 10 left sided tumours were de-identified. OAR and CTV/PTV delineation was defined and/or reviewed by the treating Radiation Oncologist. The SIB technique consisted of a forward-planned conformal boost to the tumour bed PTV to 60Gy in 25 fractions, concurrently treating the whole breast PTV to 45Gy in 25 fractions. The sequential technique simulated a dose of 50Gy in 25fractions to the whole breast, followed by a 10Gy boost to the tumour bed PTV using a direct electron field. CTV and PTV coverage for the two techniques was assessed based on V95 and V100, as were doses to the heart, lung and contralateral breast with descriptive statistics and paired t-tests.
Results:
Coverage of Breast PTV V95% was 90.49% for SIB compared with 86.80% for sequential ($p<0.05$). Boost CTV coverage was superior with an SIB approach with V95% of 99.95 compared with 94.29 for sequential ($p<0.05$). Doses to the heart and lungs were similar, however the maximum and mean doses to the contralateral breast were slightly higher for the SIB, 5.48 versus 0.12Gy ($p=0.48$) and 0.55 versus 0.14Gy ($p=0.42$) respectively.
Conclusions:
The SIB approach in adjuvant radiotherapy for early-stage breast cancer results in a dosimetric advantage with respect to PTV coverage when compared to a sequential electron boost. OAR avoidance is not compromised. However dose to the contralateral breast is higher using this technique than a sequential electron boost.

WED 09

P. Prithviraj, M. Anaka, P. Lo, A. Behren, A. Jayachandran, J. Cebon
Cancer Immunobiology Laboratory, Ludwig Institute for Cancer Research, Austin Health

Metalloproteinase Pregnancy Associated Plasma Protein-A (PAPP-A) promotes Melanoma progression in vitro

Ludwig Insitute for Cancer Research/Melbourne University

Background:
Melanoma is a common and highly aggressive form of skin cancer with a high propensity to metastasise. Insulin-like Growth Factor (IGF1) promotes melanoma metastasis and plays an important role in disease progression. Bioavailability of IGF1 is known to be regulated by IGF-binding proteins (IGFBPs). IGFBP4 forms a complex with IGF1 and inhibits release of active IGF1. IGFBP4 is cleaved by metalloproteinase Pregnancy-Associated Plasma Protein-A (PAPP-A) resulting in release of bioactive IGF1.
In this study, we addressed the role of PAPP-A in melanoma progression.
Methods:
PAPP-A mRNA expression was analysed by quantitative RT-PCR in forty-eight metastatic melanoma patient tumour samples, and in thirty-eight melanoma cell lines established in our institute. PAPP-A secretion was quantified by commercial ELISA in twenty-one melanoma patient sera and eleven melanoma cell lines. Efficient knockdown of PAPP-A expression and secretion (down to <90%, $p<0.01$) was achieved with siRNA transfection lasting for 72 hrs. Functional studies at various time points were performed post PAPP-A siRNA knockdown, which included proliferation (MTS), invasion (matrigel) and migration (wound healing assay). PAPP-A gene expression was analyzed in melanoma cells resistant to BRAF inhibitor (BRAFi) and cytotoxic chemotherapy (cisplatin & paclitaxel).
Results:
PAPP-A was noted to be widely and variably expressed in tumour tissue samples and melanoma cell lines, with some melanoma cell lines expressing PAPP-A as high as 900 copies/105 copies of Bactin and PAPP-A protein was found to be secreted in varying concentration by melanoma cell lines. Quantification of PAPP-A in metastatic melanoma patient sera did not reveal elevated levels as compared to normal. PAPP-A knockdown resulted in significant decrease in invasive capability of melanoma cells (paired t-test, p value<0.01), associated with marked inhibition in migration. Proliferative ability of melanoma cells did not change with PAPP-A knockdown. A significant increase in PAPP-A expression was noted in melanoma cells resistant to cytotoxic chemotherapy (upto 20 fold), and in BRAFi resistant cells (upto 3 fold). This was accompanied by up-regulation in expression of IGF1 receptor (IGFR1) and IGF receptor substrates (IRS1 & IRS2).
Conclusion:
Our data suggests that PAPP-A plays a role in melanoma progression and treatment resistance to BRAF inhibitors. Targeting PAPP-A could be a novel therapeutic strategy to limit disease progression and holds a promise in overcoming resistance to BRAFi in melanoma patients. In addition, PAPP-A has a potential to be an important biomarker for IGF targeted therapy

WED 10

This abstract has not been included at the request of the author

WED 11

S.N. Kong, D. Wynne, C. Christophi, P. Costa

THE EFFECTS OF KININ RECEPTOR II BLOCKADE AND ANGIOTENSIN CONVERTING ENZYME INHIBITION ON COLORECTAL CANCER LIVER METASTASES

Department of Surgery, University of Melbourne, Austin Health

Aim:
To determine if combined kinin receptor II (B2R) blockade by FR173657 and angiotensin converting enzyme (ACE) inhibition by captopril could result in greater inhibition of colorectal cancer liver metastases (CRLM) than either treatment alone. Inhibition of ACE reduces tumour growth in a murine model of CRLM. ACE metabolizes bradykinin into inactive metabolites and converts angiotensin I to angiotensin II. B2R, receptor of bradykinin, has been identified as a potential anti-cancer agent.
Method:
Tube formation assays were performed with human umbilical vein endothelial cells (HUVECs) in the presence of FR (10 µM) and/or captopril (1 µM). The in vitro invasiveness of MOCR murine colorectal cancer cells treated with captopril (0.01mM and 1mM) was assessed in fibronectin-coated transwells assay. For in vivo study, tumour cells were injected into the spleen of CBA mice, followed by splenectomy, which leads to the formation of liver metastases. Treatments (FR 30 mg/kg/day, per oral gavage and captopril 300mg/kg/day, IP injection) were administered daily for 21 days. Tumour burden was assessed by liver-to-body weight ratio and stereology.
Results:
Single treatment of FR and captopril decreased tube formation (p<0.0001) and combined FR and captopril enhanced this effect (p<0.0001). Captopril inhibited cell invasion (p=0.0087). Combined treatment showed reduced liver-to-body weight ratio (p=0.0081) and tumour burden (p=0.0479) in CRLM mice compared to control or FR, but not compared with captopril.
Conclusion:
Blockade of B2R reduces angiogenesis and ACE inhibition decreases both cell invasion and angiogenesis. Combined treatment with FR does not improved captopril's inhibition of liver metastases in vivo.

WED 12

Muhammad Asrar ul Haq [1, 2, 3], **Vivek Mutha** [1, 2], **Vivek Gupta** [2, 3], **David L Hare** [1, 3], **Chiew Wong** [1, 2, 3, 4]

Interstudy reproducibility of echocardiographic parameters in the serial assessment of left ventricular diastolic function

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2. The Northern Hospital
3. Austin Health
4. Department of CCVT, Western Health

Background:
Serial monitoring of left ventricular (LV) diastolic function using echocardiography remains a challenge and carries prognostic value. We examine the interstudy variations of echo parameters for myocardial function to assess their test-retest reliability.
Methods:
We studied 620 patients recruited for interventional trial in a tertiary hospital who had common antecedents of Chronic Heart Failure(CHF) including pre-existing cardiovascular disease but no clinical diagnosis of CHF. Detailed transthoracic echocardiogram studies were performed whilst in clinically stable state at baseline and 18 months performed blinded of the earlier studies.
Results:
68% male with mean age 67 ± 11 years and mean BMI 27 ± 7. The Bland-Altman graphs of interstudy differences (second minus first study measurements) plotted against average values comparing baseline and 18 months showed a good interstudy reproducibility of deceleration time(DT) and left atrial pressure(E/e') while tissue Doppler velocity (e') was highly reproducible with least variability and a mean interstudy difference of 0.01 ± 0.01 cm/s (CI 0.14-0.16). Interclass correlations of e' (r=0.74; CI 0.67-0.8) and E/e' (r=0.87; CI 0.83-0.9) were very high. Interstudy reproducibility of left atrial volume(LA) and ejection fraction(LVEF) was modest only with relatively large 95% CI; LA (-7.6 cm2 - 6.8 cm2) and LVEF(-16.3% - 12.9%). There were no significant relations among interstudy differences of various echo measurements as well as with change in BMI and age to suggest any true change to account for the variations.
Conclusion:
Echocardiographic parameters DT (load dependent), and e' and E/e' (less load dependent) have acceptable interstudy variance and may provide a useful and reliable assessment of LV diastolic function in serial studies.

WED 13

Muhammad Asrar ul Haq [1, 2, 3], **Vivek Gupta** [1, 2, 3], **Chiew Wong** [1, 2, 3, 4], **David L Hare** [1, 3]

eGFR Can Predict Diastolic Dysfunction In Diabetic Patients

1. University of Melbourne, Austin Health
2. The Northern Hospital
3. Austin Health
4. Department of CCVT, Western Health

Aims:
Type 2 diabetes(DM2) is an established risk factor for diastolic dysfunction (DD). Although the connection between renal impairment and adverse cardiovascular events has been well established, the association between renal function and asymptomatic DD in diabetic patients has not been fully examined.

Methods:
We studied 105 patients with DM2 but no previous or current diagnosis of Chronic Heart Failure(CHF) recruited for a randomized intervention study. Echocardiography was performed whilst patients in clinically stable state 30 days after discharge. All measures of Doppler function were obtained. Multivariate analysis was performed using linear regression and subgroup analysis by analysis of variance(ANOVA). Chronic Kidney Disease(CKD 1-3) was categorised according to their estimated glomerular filtration rate(eGFR) of >90, 60-90, and 30-59ml/min/1.73m2 respectively and left ventricular hypertrophy(LVH) based on the American Society of Echocardiography.

Results:
Overall, 75% were male with mean age of 65±10, mean weight 92±21kg and mean BMI 31±6. Impaired renal function expressed in eGFR was significantly proportional to impaired LV relaxation e'(r=0.25,p<0.05) and elevated filling pressure E/e'(r=-0.25,p<0.05) adjusted for age, body mass index(BMI) and LV Mass Index(LVMI). Neither HbA1c nor BMI were significantly associated with DD. Subgroup analysis showed CKD severity stage from 1 to 3 was significantly associated with reduced e'(6 ± 1.8, p<0.001) and elevated E/e'(14 ± 5.4, p<0.001).

Conclusion:
Mild to moderately reduced eGFR can predict asymptomatic diastolic dysfunction in diabetic patients independent of age, BMI and LVH suggesting a relationship between renal failure and diastolic dysfunction that is not dependent on preload.

WED 14

Muhammad Asrar ul Haq [1, 2, 5]**, Simon Stewart** [3]**, Melinda Carrington** [3]**, David L Hare** [1, 5]**, Chiew Wong** [1, 2, 4, 5]

Asymptomatic Myocardial Disease is Associated with Reduced Functional Capacity in at risk Population

1. University of Melbourne, Austin and Northern Health
2 The Northern Hospital
3 Preventative Cardiology, Baker IDI Heart & Diabetes Research Institute
4 Department of CCVT, Western Health
5 Austin Health

Objectives:
Diastolic dysfunction or heart falure with normal ejection fraction (HFNEF) as diagnosed by echocardiography carries a negative prognostic value. Asymptomatic myocardial disease is prevalent in at risk population. We investigate the determinants of functional capacity as assessed by 6-minute walk test (6MWT) with both the cardiac and respiratory function assessment in at risk population.

Methods:
We studied 575 patients aged ≥ 45 recruited after admission to a tertiary hospital. All had one or more cardiovascular risk factors or IHD but no previous diagnosis of heart failure (HF). Patients exhibiting clinical symptoms of HF were excluded from the analysis. Functional status was assessed with 6MWT. Cardiac function was assessed by transthoracic echocardiography including measures of Tissue Doppler (e'), LVEF, left atrial volume (LA), LV filling Deceleration Time (DT), Diastolic mitral inflow E/A, and LV filling pressure (E/e'). Respiratory function was assessed with vital capacity (FVC) and FEV1.

Results:
Predominantly male population 72%, with a mean age 66±11years and mean BMI 28±6. Echo measures of DT, LA, E/e' and e' were correlated well with age ($p < 0.0001$). Distance covered was significantly correlated with e', E/e', DT, and LVEF when controlled for FVC and FEV1 (Table). The multivariate regression model of different myocardial parameters with clinical characteristics showed significant relationship of age and HbA1c with diastolic parameters while E/e' was independently correlated with the distance travelled on 6MWT ($\beta = -0.12; p < 0.05$).

Conclusion:
Myocardial function, in particular LV diastolic function was a major determinant of functional capacity in our studied population who has CV risk factors or IHD without diagnosis of heart failure. While LV diastolic function consistently declines with age, measuring LV filling pressure with echocardiogram can be useful in detecting preclinical heart failure especially HFNEF.

	DT	E/e'	e'	LVEF
6MWT	r =-0.12	r=-0.17	r=0.17	r=0.15
	p<0.05	p<0.005	p<0.005	p<0.005

WED 15

R Rayoo [1], **D Patrick** [2], **S Lovibond** [1], **J Grewal** [1], **Lu K Lu** [1,3], **P Srivastava** [1,3], **P Calafiore** [1]

Predictive Value of Dynamic Left Ventricular Outflow Tract Obstruction During Dobutamine Stress Echocardiography in Patients Undergoing Liver Transplantation

1. Department of Cardiology, Austin Health
2. Department of Gastroenterology, Austin Health
3. University of Melbourne

Introduction:
Left ventricular outflow tract obstruction (LVOTO) on Dobutamine stress echo (DSE) has led to the denial of transplantation at certain centers as these patients have previously been thought to have a poor response to haemodynamic stress associated with liver transplantation. The assessment of LVOTO during DSE is an important component of preoperative assessment of patients undergoing Liver transplant at our center.

Aims and Objectives:
This study examined all liver transplant recipients from December 2009 to March 2012, with a view to look at intraoperative and postoperative hypotension, fluid and inotropic requirements, ICU length of stay and postoperative Major adverse cardiac events (MACE).

Materials and Methods:
The collected data was analysed using SPSS software for any statistically significant differences in outcomes in two different groups of patients with or without LVOTO.

Results:
A total of 103 patients underwent Liver transplant during the study period. Of these 54(52%) underwent a DSE for preoperative cardiovascular risk assessment of which 10(18.5%) had evidence of dynamic LVOTO. There was no stastically significant difference in mean intraoperative fluid, inotropic dose, ICU length of stay or MACE. There was a trend towards increased use of postoperative fluid use within first 48 hrs (7.1 +/- 6.2 L vs 11.3 +/- 7.8 L), but this was not statistically significant.

Conclusion:
Dynamic LVOTO during DSE does not predict to significant differences in intraoperative or postoperative haemodynamic response or MACE in patients undergoing liver transplant surgery.

WED 16
This abstract has not been included at the request of the author

WED 17

Ryan J Spencer [1]**, Hari Sugumar** [2]**, Tina Lin** [3]**, Darragh Flannery** [3]**, Paula Rae** [3]**, David O'Donnell** [1]

Non Uniform Ventricular Remodelling Following CRT – Insights from Quadrapolar Leads

1. Cardiology department, University of Melbourne, Austin Health
2. Cardiology department, Box Hill Hospital
3. Cardiology department, Austin Health

Introduction
Structural remodelling has been reported following Cardiac resynchronization therapy (CRT). Electrical remodelling has been less well evaluated. This study evaluated intracardiac electrograms (EGM) from multipolar leads to determine the degree and uniformity of electrical remodelling following CRT.
Methods
58 consecutive patients in sinus rhythm undergoing CRT for recognised indications were included. EGM and echocardiographic measures were performed at implant, 24 hours and at 3, 6 and 12 months post implant. EGM's were recorded from each of the 4 electrodes of a quadrapolar lead during intrinsic rhythm, (Int RV-LV) during RV pacing (RVp-LV) and during LV pacing (LVp-RV). Response to CRT was defined as an improvement of EF > 10% and a reduction in LVEDD by >15%.
Results
55 patients completed follow up with a response rate of 78%. Overall there was a reduction in Int RV-LV delay (15+-10ms), LVp-RV (27+-12ms) and the RVp-LV (16+-21ms). The reduction in Int RV-LV was greater in responders 31+-11ms compared with non-responders 8+-6ms (p<0.01). In individual patients there were significant differences in EGM variation at different electrode sites. The mean maximal difference in LVp-RV in individual patients improved from 35+-13ms to 21+-12ms in the responders and from 33+-11ms to 31+-12ms in the non-responders. (p<0.01)
Conclusions
Electrical remodelling, measured by intracardiac EGMs, correlates with response to CRT and structural remodelling. The electrical remodelling is not uniform with significant regional variation seen across the 4 electrodes of a quadrapolar LV lead.

WED 18

Ryan J. Spencer, Jay Ramchand, Dharsh Fernando, David Clark

Achieving Door to Balloon Times (DTBT) <90 minutes Reduces Long Term Mortality in Lower risk ST Elevation MI (STEMI)

Cardiology Department, Austin Health

Background:
We hypothesized that reperfusion with primary PCI may not be as time critical amongst Lower-risk STEMI patients (LR-STEMI), defined as those without haemodynamic disturbance. The aim of this study was to determine the long-term mortality benefit of achieving a DTBT<90min in LR-STEMI.
Methods:
Of 2539 consecutive STEMI patients treated with primary PCI from the Melbourne Interventional Group (MIG) registry, 2144 patients (84.6%) were classified as LR-STEMI (defined as STEMI without Killip class ¤2, cardiogenic shock or out-of-hospital cardiac arrest). Through linkage with the National Death Index, we compared long term mortality in LR-STEMI between patients who achieved DTBT <90 minutes with those who did not, using Cox proportional hazards modelling.
Results :
In 55% of LR-STEMI, DTBT was <90min. In hospital mortality was 0.77 % in patients with DTBT<90 min and 2.26% in those with 90 min (p=0.004). After adjustment for other factors, a DTBT<90min remained an independent predictor of survival.
Conclusion:
Attaining a DTBT < 90 minutes significantly reduces long term mortality risk in LR STEMI. This underscores the time critical nature of all patients with STEMI.

WED 19

Ryan Spencer [1], **Tina Lin** [1], **Hariharan Sugumar** [2], **Paula Rae** [1], **David O'Donnell** [1]

Implant Electrical Characteristics Predict Response to Cardiac Resynchronisation Therapy

1. Department of Cardiology, Austin Health
2. Department of Cardiology, Box Hill Hospital

Background:
The optimal site for left ventricular (LV) lead placement with cardiac resynchronisation therapy (CRT) is still uncertain. Intra-procedural measures for predicting response to CRT have shown mixed results. This study analysed intracardiac electrogram (EGM) characteristics at implant and assessed patients' response rates (RR) to CRT.
Methods and Results:
Forty-one consecutive patients undergoing CRT were enrolled. Medically optimized patients in sinus rhythm, with an ejection fraction (EF) <35%, and abnormal dyssynchrony index (DI) were included. The right ventricular (RV) lead was positioned in the mid septum, and the LV lead was targeted to the latest mechanical activation identified by transthoracic echocardiography. Intracardiac EGMs were measured assessing intrinsic RV to LV delay (Int RV-LV), RV-paced delay (RVp-LV), and LV-paced delay (LVp-RV). The difference between LVp-RV and RVp-LV was recorded as the delta LV. Response was defined as an improvement of EF >10%, a reduction in LVEDD >15% and a symptomatic improvement of 1 New York Heart Association (NYHA) class.
Overall RR was 79%. The LV lead was placed in the target location in 91%. The Int RV-LV was 101+/-14ms in responders and 78+/-11ms in non-responders ($p<0.05$). An Int RV-LV >100 had a RR of 87% and an Int RV-LV <100 had a RR of 68%. The LVp-RV and RVp-LV did not differ significantly between responders and non-responders. A delta LV >70ms had a RR 56%; compared with a delta LV <70ms RR 85%. There was no significant correlation between lead position, DI, QRS duration or EF and IEGM measurements.
Conclusion:
Intracardiac EGM measures at implant are easily obtained. Significant intrinsic electrical delay and shorter delta LV both predict response. These assessments of electrical dyssynchrony may be used to determine optimal lead positions and response to CRT.

WED 20
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WED 21
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WED 22
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WED 23

Susan G. Singh [1], Gerard Smith [1], Leighton Kearney [1], Emma K. Hornsey [1], Michael Galea [1], Brenden McColl [1], Jennifer Shoobridge [1], Rinku Rayoo [1], Jasmin Grewal [1], Jian Xu [2], Melanie Rayner [1], George Matalanais [1], Ruth P. Lim [1]

ECG-Gated Contrast Enhanced CTA of the thoracic aorta versus Non-Contrast Thoracic MRA: A valid alternative?

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Introduction:
ECG-gated contrast enhanced CT angiography (eCTA), offers accurate evaluation of the thoracic aorta, but utilises nephrotoxic contrast, of concern in patients with renal impairment. It also imparts ionising radiation, with doses ranging between 1.9 - 9.5 mSv. We evaluate a breath hold non-enhanced MRA (NEMRA) sequence, as a contrast and radiation free alternative, with eCTA as the reference standard.
Methods:
10 patients were imaged with both NEMRA and eCTA. Images were reviewed by an experienced reader for aortic pathology, diagnostic confidence, vascular contrast and image quality. Aortic dimensions were compared in 7 defined segments. Diagnostic confidence and image quality scores were scored on a 5-point Likert scale (1=worst, 5=best).
Results:
At eCTA, aortic aneurysm (n=6), dissection (n=1 each of Type A and B), Sinus of Valsalva aneurysm (n=1) and 1 normal study were diagnosed, all identified with NEMRA with high diagnostic confidence (4.5±1.4 vs. eCTA 5±0, p=0.18). 1 false positive diagnosis of left subclavian stenosis was made, and 1 small graft dissection flap was missed with NEMRA. Mean vascular contrast (3.8±1.3) and image quality (3.5±1.3) were diagnostic for NEMRA, however, these parameters were significantly superior with CTA (4.8±0.4 and 4.6±0.7 respectively, p<0.001 for both comparisons). There was no significant difference in aortic dimensions.
Conclusion:
In our preliminary experience, NEMRA identified all major aortic pathology with high diagnostic confidence, and high concordance of aortic dimensions. Although image quality and vascular contrast remain inferior to CTA, NEMRA is a promising alternative technique, free of both ionising radiation and exogenous contrast.

WED 24

Angela J. Mountain [1]**, Tracy Fuhrmeister** [2]**, Lewis Lee** [1]**, Nina J. Paleracio** [1]**, Mehrdad Nikfarjam** [2, 4]**, Christopher Christophi** [2, 4]**, Amber Johns** [3]**, Andrew Biankin** [3]**, Carmel Murone** [1]

Victorian Pancreatic Cancer Patients Support Genomic Research

1. Austin Health Tissue Bank, Department of Anatomical Pathology, Austin Health
2. Hepatopancreatobiliary Unit, Austin Health
3. The Australian Pancreatic Cancer Genome Initiative, Garvan Institute of Medical Research
4. Department of Surgery, University of Melbourne, Austin Health

Aim
The Austin Health Tissue Bank is a member of The Victorian Cancer Biobank (Biobank); a tissue banking facility which provides high-quality biospecimens with clinico-pathological data to researchers. The Biobank at the Austin Hospital is one of 11 collaborators and the only Victorian site aiming to provide 500 specimens for the Australian Pancreatic Cancer Genome Initiative (APGI) research project.

Method
Since December 2011, through the support of Hepatopancreatobiliary Surgical Unit, 20 patients from Austin Hospital and 5 from Warringal Private Hospital, have given consent to provide surgical biospecimens and clinical data to the Biobank and the APGI.

Results
All 25 patients supplied information for a questionnaire through interview and medical notes and included demographics, clinical presentation, risk factors, co-morbidities, family history and current medications. Fresh tissue was snap frozen from 15 surgical patients undergoing a Whipples Procedure or a Pancreatectomy and stored at -80°C for 1 month prior to shipment.

Conclusions
Specimens including pancreas adenocarcinoma tumour, uninvolved pancreas and normal duodenum were provided 80% were frozen within 120 minutes after surgery. Auditing of biospecimens by the Garvan Institute showed that an average RNA Integrity Number (RIN) of 8.36 out of 10 was achieved by the 11 sites providing high quality material for analysis.

WED 25

Lewis Lee [1], James Lynam [2], Angela J. Mountain [1], Nina J. Paleracio [1], Pavel Sluka [2], Ian Davis [2] and Carmel Murone [1]

Biobanking Provides Prostate Tissue for Research

1. Austin Health Tissue Bank, Department of Anatomical Pathology, Austin Health
2. Uro-oncology, Ludwig Institute for Cancer Research, Olivia Newton-John Cancer and Wellness Centre, Austin Health

Aim:
The Victorian Cancer Biobank (Biobank) is a tissue banking facility which provides high-quality cancer biospecimens with clinical data to researchers in the academic and commercial sectors. The Biobank was established as a Consortium funded by the Victorian State Government and is built on the expertise of four founding member tissue banks, located at Austin Health, Melbourne Health, Southern Health and Peter MacCallum Cancer Centre.
Method:
Tissue from Austin Health patients scheduled for prostate surgery to remove cancer and consented to biobanking was collected. Based on the donor's previous TRUS biopsy report, a pathologist extracted a 6mm punch tumour core from an area which would not affect the diagnostic process. This core was provided fresh to the laboratory in culture medium for research. Review of the stained histological diagnostic section was used to confirm the quality of the specimen provided.
Results:
During 2010-2013 the Biobank has provided 177 cores of fresh prostate tissue for culture and development of assays. Quality control has shown that Pathologist's typically obtain a 63% rate of sampling positive tumour cores. An Aperio ScanScope XT image analysizer was used to scan sections at high magnification and confirm the type and density of tumour cells in the region of tissue provided.
Conclusion:
 Aperio Image Analysis provides high capacity, whole-slide digital images of prostate biospecimens for viewing. The Biobank was able to extrapolate the number and type of tumour cells with cell culture yield obtained by the researcher in order to add value and improve and refine experimental data.

WED 26

This abstract has not been included at the request of the author.

WED 27

Elif I Ekinci [1,2,7,*], **Wei-Ling Chiu** [8,*], **Zhong X. Lu** [3,4], **Ken Sikaris** [3], **Intissar Bittar** [5], **Que Lam** [5], **Nick Crinis** [5], **Christine A. Houlihan** [1,6]

A LONGITUDINAL STUDY OF THYROID AUTOANTIBODIES IN PREGNANCY

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7. Menzies School of Health Research, Darwin
8. Department of Medicine, Eastern Health
* Equal first authors

BACKGROUND/AIM:
Thyroid-peroxidase (TPOAb) and thyroglobulin (TGAb) antibodies are frequently measured to investigate thyroid dysfunction in pregnancy. Despite the recognised fall of these autoantibodies during pregnancy, there is limited guidance on the timing of such testing. We aimed to assess the optimal timing on testing, if required, of TPOAb and TGAb in pregnancy.
METHODS:
Healthy women were recruited from Mercy Hospital for Women, a tertiary obstetric hospital in Melbourne between May 2006 and February 2011. Serum TPOAb, TGAb, TSH and free T4 were measured at 9-13 weeks, 22-26 weeks, and 35-39 weeks gestation to represent Trimester-1 (T1), Trimester-2 (T2) and Trimester-3 (T3), and 8-12 weeks post-partum (PP).
RESULTS:
Samples from140 women at T1 (11.8±0.2) (mean±SE weeks gestation); 95 at T2 (24.4±0.3), 79 at T3 (35.9±0.3) and 83 at PP (13±0.4) were available. At T1, 13 (9%) and 15 (11%) women had positive TPOAb and TGAb, respectively. Of those with positive TPOAb at T1, 56% (5/9) and 43% (3/7) remained positive, at T2 and T3, respectively, and 100% (9/9) were positive again at PP ($\chi2$, p=0.003). Similarly, of those with positive TGAb at T1, 36% (4/11) and 33% (3/9) remained positive at T2 and T3, respectively, and 92% (11/12) were positive again at PP ($\chi2$, p<0.001).
CONCLUSIONS:
A significant proportion of pregnant women lose their TPOAbTGAb positivity between 12-24 weeks gestation. Testing for these antibodies, if not performed pre-pregnancy, should occur at T1 or after 12 weeks post-partum, as a negative result during T2 or T3 does not exclude autoimmune thyroid disease, and is of limited value.

WED 28

Elif I Ekinci [1,2,7,*], Wei-Ling Chiu [8,*], Zhong X. Lu [3,4], Ken Sikaris [3], Intissar Bittar [5], Que Lam [5], Nick Crinis [5], Christine A. Houlihan [1,6]

A LONGITUDINAL STUDY OF TSH-RECEPTOR AUTOANTIBODY IN NORMAL PREGNANCIES

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2. Department of Medicine, University of Melbourne
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6. Mercy Hospital for Women
7. Menzies School of Health Research, Darwin
8. Department of Medicine, Eastern Health
* Equal first authors

BACKGROUND/AIM:
Graves' disease has a high prevalence in young women, with frequent onset after pregnancy, and fetal microchimerism is a proposed trigger. Maternal physiological immunosuppression is thought responsible for the amelioration of Graves' disease that is commonly experienced in pregnancy. The potential multiple influences on thyroid auto-immunity in pregnancy led us to study the changes in TSH-receptor antibody (TSHRAb) in healthy women throughout gestation and post-partum.

METHODS:
Healthy women were recruited as part of a longitudinal study of thyroid function in pregnancy. Serum TSHRAb, TSH and free T4 were measured at trimester-1 (T1), trimester-2 (T2), trimester-3 (T3) and post-partum (PP) using Roche assays. The cut-off value used was TSHRAb <1.75 IU/L.

RESULTS:
At T1, 8% (11/133) women had positive TSHRAb. Of these women, 22% (2/9) and 13% (1/8) remained positive at T2 and T3, respectively, and 50% (3/6) were positive again at PP (χ2, p<0.001). Of the women who had negative TSHRAb at T1 (1.0±0.02 IU/L), 30% (21/71) had a transient positive result at T3 (3.1±0.1 IU/L). At baseline, there was a significant difference in fT4 (16.5±1.0 versus 15.0±0.3 pmol/L, p=0.03) between TSHRAb positive and negative groups, without differences in TSH. There were no differences in thyroid function at any other time-points.

CONCLUSION:
The transient trimester-3 rise in TSHRAb is a novel finding of this study and was not associated with altered thyroid function. This finding requires further investigation, and if confirmed may represent an important variation of normal immunologic expression of TSHRAb in the third trimester of pregnancy.

WED 29

Renata Libianto 2, George Jerums [1], Scott Baker [1], Richard MacIsaac Elif I Ekinci [3]

Relationship between 24h urinary sodium-to-potassium ratio with blood pressure and renin angiotensin aldosterone activity in people with diabetes

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3. Menzies School of Public Health, University of Melbourne, Austin Health

Background:
Previous cross sectional studies have been inconsistent in demonstrating a relationship between 24h urinary sodium (24hUNa), 24h urinary potassium (24hUK) and 24h urinary sodium-to-potassium (24hUNa/K) ratio with systolic blood pressure. There are no such previous studies in patients with diabetes and none assessing the relationship between 24hUNa/K ratio and renin angiotensin aldosterone system activity. In this study, we examined the relationship between 24hUNa/K ratio with blood pressure and RAAS activity in patients with diabetes mellitus.
Methods:
In a cross-sectional study, clinical characteristics, 24hUNa, and 24h urinary potasium (24hUK) were recorded in 328 consecutive patients with diabetes attending diabetes clinics at a tertiary referral hospital in Melbourne. Plasma renin activity (PRA) and serum aldosterone were measured in 222 patients.
Results:
The mean age was 64±15 years, 60% were males and 77% had type 2 diabetes. The mean 24hUNa, mean 24hUK and mean 24hNa/K ratio was 164±72 mmol/24h, 71±26 mmol/24h and 2.5±1.2, respectively. These levels compared to 155±63 mmol/24h for 24hUNa, 82±28 mmol/24h for 24hUK, and 2±0.8 for 24hUNa/K ratio in a group of similar aged community participants from previous study[1] . There was no relationship between 24hUNa, 24hUK and 24hUNa/K ratio with systolic, diastolic or mean arterial blood pressure in the entire cohort. There was no relationship between 24hU/K ratio with PRA. However, serum aldosterone level negatively correlated with 24hUNa/K ratio (r= -0.22, p=0.001).
Conclusions:
Although the 24hUNa/K ratio in patients with diabetes was higher than in the general population, there was no relationship between Na/K ratio and blood pressure in this group of patients. Higher 24hUNa/K ratio was associated with lower serum aldosterone levels in people with diabetes.
References: 1. Huggins CE et al. Med J Aust 2011 195(3):128-32

WED 30
This abstract has not been included at the request of the author

WED 31
This abstract has not been included at the request of the author

WED 32

Nick. H. Hewitt [1,2]**, Karen. F. Urbancic** [1,2]**, Andrew. P. Grigg** [1,2]**, M. Lindsay. Grayson** [1,2]

Detailed Antifungal Stewardship (AFS) is Key to Achieving Excellent Plasma Levels During Oral Posaconazole (PCZ) Prophylaxis in High Risk Hematology Patients

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Background:
Oral PCZ is effective antifungal prophylaxis in high risk neutropenic patients. However, achieving adequate plasma PCZ levels can be problematic due to variable absorption with the current formulation. The role of AFS and therapeutic drug monitoring (TDM) for PCZ prophylaxis remains controversial.
Methods:
Since August, 2011, all high risk hematology patients receiving PCZ prophylaxis were prospectively managed within a detailed AFS program to ensure PCZ compliance and TDM, and to optimize absorption. All patients who received =7 days PCZ prophylaxis and had =1 PCZ level (via HPLC assay) were reviewed. Demographics, known factors associated with poor PCZ absorption (age, diarrhea, mucositis, and proton pump inhibitor [PPI] administration) and rates of proven or probable invasive fungal infection (IFI) as per EORTC/MSG criteria were studied.
Results:
Of 61 patients, 53 (46 AML/MDS; 3 ALL; 4 other) had a total of 93 PCZ prophylaxis courses, with 111 PCZ levels measured. Mean trough PCZ levels were 0.83 ± 0.43mg/L (median 0.75; range <0.1-2.15), with 7/93 (8%) <0.3mg/L, 17/93 (18%) <0.5mg/L and 41/93 (44%) <0.7mg/L. Factors associated with low (<0.3mg/L) PCZ levels included: PPI administration ($p=0.03$), diarrhea ($p=0.004$), collective gastrointestinal intolerance (nausea, vomiting, diarrhea, poor oral intake, and/or mucositis) ($p=0.02$) and age =60 years ($p=0.01$). Among the 7 patients with PCZ levels <0.3mg/L, AFS resulted in improved levels or change in prophylaxis regimen in 71%. IFI was identified in only 2 cases (proven) - both of whom had levels >0.5mg/L. Implementation of the AFS required 0.3 EFT specialist pharmacist, but saved approx. twice this salary cost in improved antifungal use.
Conclusions:
AFS is highly effective in ensuring generally excellent levels with PCZ prophylaxis. We identified similar risk factors to others for low PCZ levels, but found that these can be effectively managed to achieve good outcomes. Although some have questioned the role of TDM for PCZ prophylaxis, we found it a useful component of effective AFS for high risk hematology patients.

WED 33
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WED 34
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WED 35

Miranda Siemienowicz, Anthony Schelleman

Quality Assurance in CT Pulmonary Angiography: Phase 2 and Completed Audit Cycle

Radiology

Introduction:
Computed tomography pulmonary angiography (CTPA) is a common and clinically critical investigation in suspected pulmonary embolus, requiring high quality scans with adequate intravenous contrast enhancement of the pulmonary trunk (PT). This poster presents a completed audit cycle assessing factors associated with suboptimal enhancement of the PT in CTPA.
Method:
Phase I comprised restrospective review of 100 CTPAs. Late scan acquisition relative to contrast injection was a major factor in suboptimal quality. Both machine and operator factors were implicated. To address this, hardware factors were optimised and a re-education package developed. A further 100 studies were then retrospectively reviewed and data again collected on technique and scan quality.
Results:
Phase II showed the proportion of late scans decreased from 81% to 8%. Operator performance improved, with the rate of as-per-protocol operator-defined factors increasing from 55% to 87%. The suboptimal quality scans in Phase II were analysed in further detail. Many were showed dilution of contrast bolus by unopacified venous return from the inferior vena cava (IVC). The literature indicates that IVC return is greatest during forceful inspiration. This group likely represents patients who have taken a forceful inspiration in response to the breath-hold instructions. Excluding these, the rate of suboptimal CTPA improved from 22.5% to 13.5%.
Conclusion:
Staff re-education and hardware optimisation significantly improved the quality of CTPA at Austin Health. A further target for future intervention, patient breath-hold coaching, has been identified. This represents an opportunity for future improvement.

WED 36

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Clinical outcomes with early and late arteriovenous fistula creation in chronic kidney disease

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Aim:
Optimal timing of arteriovenous fistula (AVF) surgery in pre-dialysis patients with chronic kidney disease (CKD) is uncertain. This study aims to determine optimal timing and outcomes for AVF creation in CKD patients.
Method:
A single centre retrospective study was conducted of all pre-dialysis patients who had a first AVF creation between 01/01/2007-31/12/2009 with follow-up until 31/12/2011. Survival analysis was performed for the primary outcome of time from AVF creation to first haemodialysis (HD) need.
Results:
100 patients had a first AVF created with a median estimated glomerular filtration rate (eGFR) at the time of AVF surgery of 15 ml/min/1.73m^2. Patients were classified as having had an early AVF if eGFR was >15 ml/min/1.73m^2 (n=46) or a late AVF if eGFR was =15 ml/min/1.73m^2 (n=54). In the late AVF group 81% (44/54) of patients required HD, compared with 63% (29/46) of the early AVF patients (P=0.04). At 12 months post AVF creation, 56% of late AVF patients required HD compared to 26% of early AVF patients. A dialysis catheter was required at HD commencement in 11% (5/44) from the late AVF group and 24% (7/29) from the early AVF group (P=0.20). Additional interventions prior to HD were required for 35% of late AVF and 39% of early AVF patients.
Conclusion:
A higher risk of AVF non-use was observed in patients having AVF surgery with an eGFR >15 ml/min/1.73m^2, whilst the rate of catheter use at HD start remained low in patients having AVF surgery with an eGFR =15 ml/min/1.73m^2.

WED 37

Saad A. Khan [1,2], Patrick W. Carney [1,3], John S. Archer [1,3,4]

Asymmetric Tonic Seizures and Diffuse Low Voltage Fast Activity are Characteristic in Mesial Parietal Seizures

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4. University of Melbourne

Background:
Seizures originating from the parietal lobe are said to have variable semiologic and electroclinical features. Our aim was to describe the electroclinical features of seizures originating from the mesial parietal lobe.
Method:
We compared the electroclinical phenotype of four patients, identified through the Comprehensive Epilepsy Program of Austin Health, who had strong evidence of a mesial parietal source for their epilepsy. All four patients had a mesial parietal structural lesion: dysplasia (2), AVM with gliosis (1), post-meningitis gliosis (1). Three have had lesionectomies and are seizure free, whilst one had previous subtotal lesionectomy and temporary seizure freedom, confirming seizures were being driven from the mesial parietal lobe.
Results:
Patients had very frequent brief seizures despite anticonvulsants, typically with five or more attacks per day, each lasting 10-30 seconds, and with rapid return of awareness post-event. Clinically attacks were bland, or showed asymmetric tonic posturing, often with partially preserved awareness (claimed recall, mumbling speech). Ictal EEG showed diffuse low voltage fast activity. Interictal EEG showed recurrent midline-central (Cz) sharp waves.
Conclusion:
Epilepsy arising from the precuneus of the mesial parietal lobe appears to be characterised by frequent brief asymmetric tonic seizures and diffuse low voltage fast activity on ictal EEG. This brain region is a key component of the default mode network (DMN), important for internal reflective thinking. Although the clinical and EEG features might be considered 'non-localising', the striking similarity across patients suggests this is a recognisable electroclinical phenotype.

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WED 39

John A. Damiano [1], Saul A. Mullen [1, 2], Henrik H., Dahl [1], Kate Lawrence [1], Todor Arsov [1], Susannah Bellows [1], Michael S. Hildebrand [1], Ingrid E Scheffer [1, 2] and Samuel F. Berkovic [1, 2]

Microdeletion and missense mutation at 15q13.3 in a family with genetic generalised epilepsy and neuropsychiatric disorder.

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2. *Florey Neuroscience Institutes and Department of Paediatrics, University of Melbourne, Royal Children's Hospital*

Introduction
There is evidence that the 15q13.3 region harbors a susceptibility allele for epilepsy, intellectual disability and neuropsychiatric disorders. Deficiency of candidate genes at this locus such as the acetylcholine receptor CHRNA7 and its partial duplication CHRFAM7A may underlie these phenotypes. The aim of this study was to screen CHRNA7, CHRFAM7A and the 15q13.3 region for mutation in a cohort of patients with neuropsychiatric comorbidities.
Methods
We report screening of 188 genetic generalized epilepsy families with or without intellectual disability or psychosis using DHLPC, direct sequencing or array comparative genomic hybridization.
Results We identified two novel and one reported missense change by DHPLC or direct sequencing of CHRNA7 and CHRFAM7A, and a 15q13.3 microdeletion by array comparative genomic hybridization. In one kindred we identified the first example of co-segregation of copy number variations at the 15q13.3 locus and a missense variant in the CHRNA7 gene. The clinical features of this family include genetic generalized epilepsy and schizophrenia, both phenotypes previously associated with microdeletion of the 15q13.3 locus.
Discussion Discovery of a missense mutation in CHRNA7, in concert with microdeletions at the 15q13.3 locus, for the first time directly links variation in this gene to genetic generalized epilepsy and schizophrenia. Our data suggests that there is a cumulative effect of deleterious variation at this locus increasing the likelihood of multiple neurologic and neuropsychiatric morbidities.

WED 40

Paul A. Yates [1,2], Christopher C. Rowe [1,2], Victor L. Villemagne [1,2], Patricia M. Desmond [2,3], Colin L. Masters [2,5], David Ames [2,4], Lorraine Dennerstein [2], Philippe Lehert [2], Kathryn A. Ellis [2,5], Cassandra E. Szoeke [2]

Midlife Vascular Risk and Late-life Amyloid Burden: Data from the Women's Healthy Ageing Project (WHAP)

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4. National Ageing Research Institute, Parkville
5. Florey Institute of Neuroscience and Mental Health, Parkville

Introduction.
Midlife vascular risk factors are associated with increased risk for later-life dementia. However it is unclear whether this is mediated through increased Alzheimer's disease (AD) pathology, or concomitant cerebrovascular disease. We used ß-amyloid imaging (18F-Florbetaben Positron Emission Tomography, FBB-PET) in participants of the Women's Healthy Ageing Project, a longitudinal study of Australian women, commenced in 1991, to determine if vascular risk measures taken in mid-life were associated with AD-pathology in later life, and whether presence of ApoE4 influenced this finding.
Methods.
78 participants (age 71.1±1.3 years) underwent FBB-PET. FBB retention (SUVR) was normalized to cerebellar cortex. Composite cardiovascular risk was estimated for 1992 data using Framingham 10-year Coronary Risk (FCRP) and PROCAM Scores. Nonparametric tests and linear regression were used to compare the distribution of FBB SUVR between tertiles of FCRP and PROCAM, overall, and stratified by ApoE4 (+/-).
Results.
FBB SUVR distribution differed significantly according to PROCAM tertile (p=0.03), in all participants, and in ApoE4+ (p=0.02), but not ApoE4-. There was no significant difference in age between PROCAM tertiles. Trend-level significance was observed using FCRP.
Conclusion.
To our knowledge this is the first study to find link a composite vascular risk measure taken in mid-life and, and in vivo Aß burden later in life, suggesting that ApoE4 and vascular risk factors may interact to increase risk for AD. Incorporation of biomarkers such as Aß burden (FBB-PET) into a cohort established in mid-life can shed new light on risk factors for AD across the life-course.

Richard A.J. Masterton [1,2], **Graeme D. Jackson** [1,2,3], **David F Abbott** [1,2]

Group analysis of EEG-fMRI using event-related independent components analysis (eICA)

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Background and Aim:
Simultaneous EEG-fMRI (electroencephalography and functional magnetic resonance imaging) studies of patients with epilepsy utilise scalp EEG to determine the timing of cortical interictal epileptiform discharges (IEDs). The fMRI is then analysed together with the event timings to determine where in the brain the abnormal activity is occurring. However conventional event-related fMRI analysis can fail to identify much relevant brain activity because the fMRI response to IED's does not always have a typical response timecourse [1]. We aimed to develop an analysis approach that avoids typical model-based limitations.
Methods:
We first use deconvolution to estimate an event-related time-course for each voxel in the brain, and then use spatial independent component analysis (ICA, a data-driven blind-source separation algorithm) to estimate the underlying sources of these timecourses. We call this approach event-related ICA (eICA). For group analysis, the ICA decomposition is performed upon temporally-concatenated data. We validate the approach with an analysis of 14 patients with rolandic epilepsy – with stereotypical IEDs arising from a focus in the rolandic fissure [1].
Results:
A single event-related component was detected in the group eICA, concordant with the known source location.
Conclusions:
The eICA method combines the benefits of non-canonical modelling and independent components analysis to objectively identify sources of event-related BOLD signal changes associated with events of interest. Our validation demonstrates the effectiveness of the method in one of the most challenging applications: EEG-fMRI studies of internally generated brain events.
References:
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WED 42

Paul A. Yates 1,3, Patricia M. Desmond 2,3 Pramit M. Phal 2, Cassandra E. Szoeke 3,4, Victor L. Villemagne 1,3, Christopher Steward 3 , Olivier Salvado 6, Ralph N. Martins 7, Colin L. Masters 3,5, David Ames 3,4, Kathryn A. Ellis 3,5, and Christopher C. Rowe.1,3

Cerebral Microbleeds and Cognitive Trajectories: Results from AIBL

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7. Edith Cowan University, Joondalup, WA

Introduction.
Cerebral microbleeds (MB) are commonly observed with SWI MRI in individuals with stroke, Alzheimer's disease (AD) and in cognitively-normal elderly. It is postulated that they may be associated with worse cognitive outcomes in AD.
Methods.
134 participants (97 cognitively-normal, 37 with mild cognitive impairment) from the Australian Imaging, Biomarkers and Lifestyle Study of Ageing, assessed at with 3T-SWI and 11C-PiB PET, and followed up for 3 years. MB and cerebrovascular disease (CVD) was identified by two blinded readers. PiB retention (Aß-burden) was dichotomized (PiB+/-) threshold SUVR=1.5. Clinical outcomes were assessed by expert panel review, blind to neuroimaging. Individuals were stratified by baseline PiB, MB+/-, CVD+/-. Logistic regression with interaction terms was used to determine whether cognitive decline was associated with PiB+, MB+ or CVD+ status.
Results.
37.3% were PiB+, 20.1% MB+ and 22.4% CVD+. Over three years, 71.6% were cognitively stable, 13.5% declined, 11.9% withdrew, and 3.7% died. The proportion of decliners was similar between PiB+MB+ (30%) vs PiB+MB- (30.8%) and PiB+CVD+ (37.5%) vs PiB+CVD- (28.6%, p>0.05), but significantly less in PiB-MB- (6%) and PiB-CVD- (4.9%, p2, >5) did not alter these findings.
Conclusion.
Individuals with high Aß-burden were more likely to experience cognitive decline over 3 years, but presence of MB or CVD did not influence this association. Analyses incorporating specific cognitive domains may provide additional insights into these relationships.

WED 43

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10-year MRI changes and FBB PET: Results from the Women's Healthy Ageing Project (WHAP)

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Introduction.
In normal aging and Alzheimer's disease, there are divergent trajectories of brain structure and function, proposed from post-mortem studies, longitudinal Magnetic Resonance Imaging (MRI) and ß-amyloid imaging cohorts. However, there are no studies combining ß-amyloid and MRI over extended follow-up. The Women's Healthy Ageing Project (WHAP) is a longitudinal study of Australian women, first enrolled in 1991. In 2002 and 2012, participants underwent 3T-MRI, and in 2012 had ß-amyloid imaging with 18-F Florbetaben Positron Emission Tomography (FBB-PET). We compared 10-year brain atrophy according to late-life ß-amyloid.
Methods.
FBB-PET Standardized Uptake Value Ratio (SUVR), was stratified as low, intermediate and high ß-amyloid, and Freesurfer V5.1 used to compare total grey matter and hippocampal volumes between MRI performed in 2002 and 2012.
Results.
The mean age of participants at 2012 scan was 69.1±2.6 years. Brain volumes in midlife did not differ according to later-life FBB status. Later-life hippocampal volume was significantly lower in those with high FBB. Stratified by FBB SUVR, participants with high FBB had greatest 10-year decrements in hippocampal and total grey matter volume (trend-level only, p=0.1). Individuals with an intermediate FBB SUVR had 10-year declines in hippocampal volume midway between high- and low- SUVR.
Conclusion.
Presence of brain ß-amyloid in later-life in cognitively-normal women was associated with greater declines in hippocampal and grey matter volume over the preceding ten years. Second, the findings suggest that intermediate FBB SUVR may also represent an "at-risk" group, and further study of this is warranted.

WED 44

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THK523 selectively binds to neurofibrillary tangles and neuropils in Alzheimer's disease subjects

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4. Department of Anatomical Pathology, The Alfred Hospital, Monash University
5. Innovation of New Biomedical Engineering Center, Tohoku University, Sendai, Japan.

Objectives:
Cortical Aß and tau deposition are the hallmarks of Alzheimer's disease (AD). Human PET studies have shown significantly higher retention of 18F-THK523 in AD grey matter when compared with age-matched controls (HC). The purpose of this study was to further characterize in vivo and in vitro THK523 binding to other non-AD tauopathies, such as Corticobasal degeneration (CBD), Progressive supranuclear palsy (PSP), Pick's disease (PiD) and Parkinson's disease (PD).
Methods:
Serial sections from AD (n=3), CBD (n=2), PSP (n=1), PiD (n=2) and PD (n=2) brains were analysed by immunohistochemistry and fluorescence microscopy. Noteworthy, the PSP subject analysed in this study had undergone an 18F-THK523 PET scan, five months earlier.
Results:
While THK523 stained tau-containing lesions such as neurofibrillary tangles and neuropils in the hippocampus and frontal regions of AD brains, it failed to stain/bind tau-containing lesions in non-AD tauopathies. Furthermore, no binding of THK523 to a-synuclein containing Lewy bodies was observed in PD.
Conclusions:
18F-THK523 selectively binds to PHF-tau in AD brains, but does not bind to tau lesions in non-AD tauopathies, nor to a-synuclein in PD brains.

WED 45

Lin Hung [1,] **Andrew Watt** [2], **Rachel S. Mulligan** [3], **Shozo Furumoto** [4], **Michelle T. Fodero-Tavoletti** [1], **Jacky Chan** [1], **Kazuhiko Yanai** [4], **Colin L. Masters** [1], **Yukitsuka Kudo** [5], **Christopher C. Rowe** [3,6], **Kevin J. Barnham** [4], **Nobuyuki Okamura** [4], **Victor L. Villemagne** [1,3,6]

Detectable levels of white matter PHF-tau in Alzheimer's disease

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Background:
Cortical paired helical filaments (PHF)-tau deposition in the form of neurofibrillary tangles is one of the hallmarks of Alzheimer's disease (AD). Utilizing a novel and selective PHF-tau imaging ligand 18F-THK523, preliminary human PET studies have shown significantly higher retention of 18F-THK523 not only in grey matter, but also in white matter of AD patients, when compared with age-matched controls (AC).
The purpose of this study was to ascertain the presence of PHF-tau aggregates in brain homogenates of grey and white matter of AD patients and AC, to further enhance 18F-THK523-PET analysis of AD and non-AD tauopathies.
Methods:
Western blot (WB) assessment of hyperphosphorylated tau (p404 and p396) in AD and AC grey and white matter brain homogenates (insoluble fraction of the frontal cortex only) was conducted. In vitro binding of 18F-THK523 using the same AD and AC brain homogenate preparations, was also determined.
Results:
WB studies showed significantly higher ($p<0.05$) expression of hyperphosphorylated and aggregated tau in grey and white matter of AD brains compared to AC. These results correlated with in vitro binding studies that demonstrated that 18F-THK523 binding was significantly higher in AD preparations of both grey and white matter, compared to their respective AC brain homogenates.
Conclusions:
Both WB and in vitro binding studies are consistent with previous reports of higher PHF-tau concentration in the white matter of AD patients. Therefore, higher 18F-THK523-PET retention observed in the white matter of AD patients can be attributed to 18F-THK523 specific binding to tau aggregates.

WED 46

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Graph analysis of resting-state ASL data reveals nonlinear correlations among CBF and network metrics

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Introduction:
Measures of network metrics are of great importance for understanding the pathogenesis and treatment of brain disorders at network level. As a novel MRI technique, arterial spin labeling (ASL) can not only measure CBF directly but may also map functional connectome. In this study, we investigate the connectome using ASL, which allows us for the first time to measure the network metrics of human brain during resting state based on direct blood measurements, as well as to investigate the relationship between CBF and certain network metrics.
Methods:
Ten subjects were scanned on a 3T Siemens scanner with a whole-brain 3D-GRASE pCASL sequence. A sigmoid function was employed to estimate the relationships between network metrics, such as degrees (K_i), characteristic path length (L_{pi}), vulnerability (V_i) and eigencentrality (EC_i), and region-wise mean CBF estimates by nonlinear fitting.
Results:
Our results demonstrate that the 4 network metrics vs. CBF estimates show consistent nonlinear patterns across 10 normal subjects. More specifically, while L_{pi} shows negative nonlinear pattern, the others show positive patterns.
Conclusion:
In this study, investigations on complex network properties of ASL perfusion data have been conducted. To our knowledge, this is the first study that unravels the intrinsic relationships between specific network metrics and CBF estimates. This should provide useful information to further our understanding of the metabolic energy consumptions with which the brain can maintain constrained cognition with the lowest cost.

WED 47

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WED 48

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An automated method for identifying artifact in Independent Component Analysis of resting-state fMRI

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Background and Aim:
To assist with interpretation of data-driven independent component analysis (ICA) of resting-state functional magnetic resonance imaging (fMRI) we aimed to develop and validate an automatic method for identification of artifact-related components.
Methods:
We designed and implemented an algorithm we call Spatially Organised Component Klassifikator (SOCK) which assesses each independent component (IC) for features likely to indicate motion, physiological noise, or machine or undetermined noise. With assistance of k-means clustering, ICs dominated by one or more of these artifacts are identified and can be removed from further analysis. We assessed SOCK's classification performance in resting-state fMRI of 50 healthy control subjects consisting of 30 subjects that had participated in studies at our institute and a further 20 subjects obtained from the 1000 Functional Connectomes Project website. MELODIC ICA [1] was applied after pre-processing using SPM8 [2] with the aid of iBrain™ [3,4]. For validation purposes, expert manual classification was performed blind to the SOCK classification, by visual inspection of IC spatial maps, time courses and power spectra.
Results:
A total of 2722 components (average of 54 components per subject) were obtained. SOCK classified between 26% and 72% of each subject's components as artifact (mean 55%). Only seven components (0.3%) identified as artifact by SOCK were discordant with the manual classification; retrospective examination suggested SOCK had correctly identified these as artifact.
Conclusions:
SOCK is effective in separating noise from signal by identifying a high proportion of artifact-related ICs without removing biologically plausible components. SOCK is freely available at www.brain.org.au/software

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See also www.brain.org.au/software

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WED 50
This abstract has not been included at the request of the author

WED 51

Susannah T. Bellows [1]**, Michael S. Hildebrand** [1]**, John A. Damiano** [1]**, Saul A. Mullen** [1,2]**, Ian Luk** [3]**, Karen L. Oliver** [1]**, Hans-Henrik M. Dahl** [1]**, Ingrid E. Scheffer** [1,2,4]**, Samuel F. Berkovic** [1]

GLUT1 Mutations are the Only Significant Cause of Generalised Epilepsy Amongst the Major Brain Glucose Metabolism Transporter Genes

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4. Department of Paediatrics, University of Melbourne, Royal Children's Hospital, Parkville

Introduction: Glucose is an essential energy source for normal brain metabolism and functioning. Transportation of glucose across the blood-brain barrier is regulated by specific brain transporters GLUT1 and GLUT3. Other transporters regulate transportation of lactate, the glycolytic product of glucose, across the blood-brain barrier. Mutations in the gene SLC2A1 encoding GLUT1 are an important known cause of a characteristic early-onset encephalopathy, genetic generalised epilepsy and paroxysmal exercise-induced dyskinesia. SLC2A1 mutations account for 5% of cases of epilepsy with myoclonic-astatic seizures (MAE) and 10% of early onset absence epilepsy (EOAE) cases.

We investigated whether mutations in the specific brain glucose metabolism transporters other than GLUT1 are important in generalised epilepsies. Epilepsy caused by GLUT1 mutations are known to respond to the ketogenic diet, therefore mutations in other energy transporters are likely to have treatment implications for patients.

Method: Eighty MAE and 39 EOAE patients with nucleotide and copy number variations in SLC2A1 excluded were Sanger sequenced for nucleotide variants in five candidate genes of the SLC glucose and lactate transporter family: SLC2A3, SLC16A1, SLC16A7, SLC16A8 and SLC16A3.

Results: Eight heterozygous coding substitutions were identified. Seven variants are reported polymorphisms, and a novel missense change in SLC2A3 p.Ile14Leu is likely benign as it involves functionally equivalent amino acids. No pathogenic mutations were identified.

Conclusion: Mutations in glucose transporter gene SLC2A3 and lactate transporter genes SLC16A1, SLC16A7, SLC16A8 and SLC16A3 are not associated with MAE and EOAE, indicating that of the major energy transporters in the brain, only GLUT1 is a significant cause of generalised epilepsy.

WED 52

Michael Hildebrand

Unravelling the genetics of the common epilepsies using discordant monozygotic twins

Department of Medicine, University of Melbourne, Austin Health

Introduction:
Elucidation of genetic generalised epilepsies and other common epilepsy syndromes is challenging. To unravel the complex genetics we are using discordant monozygous twins to exploit new sequencing technologies and identify somatic mutations that explain the discordance.
In a previous study we identified a somatic mutation causing Dravet syndrome in one pair of discordant monozygous twins, demonstrating proof-of-principle.
Methods:
We sequenced lymphoctye DNA from twin pairs at a high depth of coverage to detect somatic mutations that may occur at low abundance during the first few cleavages but not at later stages of development. For the analysis we focussed on coding variants covered by at least ten sequence reads and with minor allele frequencies less than one percent.
Results:
Using these criteria we identified thirty-one potential discordant variants (approximately four per pair) that we then validated by conventional Sanger sequencing. Of these variants, four were real but present in both twins, and the remaining twenty-seven were false positive, most likely due to sequencing errors.
Conclusions:
This study highlights the challenges of identifying discordant mutations in identical twins on a genome wide basis: (1) they may be present at low abundance and (2) they may show variable expression due to tissue mosaicism. To address these issues we will increase sequence coverage and source DNA from neural tissue.
Although we have established a framework for tracking down such mutations, the limitations of current sequencing technology mean we will have to investigate many candidate mutations to find truly discordant ones.

WED 53

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GRIN2A mutations cause epilepsy-aphasia spectrum disorders

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Introduction

GRIN2A encodes NR2A, alpha subunit of the NMDA glutamate receptor. The NMDA receptor is a glutamate receptor and glutamate is a key excitatory neurotransmitter in the brain. Rare pathogenic deletions encompassing GRIN2A have been implicated in neurodevelopmental disorders.

We sought to delineate the role of GRIN2A by performing targeted re-sequencing in probands with various epileptic encephalopathies, including cases with epilepsy-aphasia syndromes (EAS). EAS is a group of rare epilepsy and speech and language disorders. The syndromes form a spectrum of varying severity, including epileptic encephalopathies Landau-Kleffner Syndrome (LKS) and Epileptic Encephalopathy with Continuous Spike and Wave in Sleep (EECSWS). These are characterised by developmental regression, particularly affecting language, and have a distinctive EEG pattern. The cause of EAS is unknown although an immune basis has been postulated given their response to steroids.

Method

We performed high-throughput sequence analysis of GRIN2A in 519 probands with a range of epileptic encephalopathies. We re-sequenced all exons and flanking 5 base pairs using molecular inversion probes (MIPS), highly multiplex PCR and next generation sequencing. On average, 98% coverage was achieved for all probands.

Results

We identified GRIN2A mutations in four probands. Strikingly, all presented with EAS, accounting for 4/44 (9%) of epilepsy-aphasia cases in the cohort. We did not detect pathogenic variants in any other epileptic encephalopathy group (n=475).

Conclusion We report the first cause for EAS. GRIN2A mutations have important ramifications for diagnostic testing, and provide novel insights into the pathogenesis of this debilitating group of conditions.

WED 54

Karen L. Oliver [1,2]**, Vesna Lukic** [1]**, Natalie P. Thorne** [1]**, Samuel F. Berkovic** [2]**, Ingrid E. Scheffer** [2,3]**, Melanie Bahlo** [1,4]

Harnessing gene expression networks to prioritize candidate epileptic encephalopathy genes

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Introduction:
Epileptic Encephalopathies are a group of rare devastating childhood epilepsies where the genetic basis for many patients remains unknown. Recently, large cohort studies have identified a considerable number of candidate genes that require more supportive evidence.
Using expression data specifically from brain, we wanted to explore whether we could develop an approach for candidate gene prioritization that would further implicate candidates based on their co-expression with known Epileptic Encephalopathy genes.
Method:
Expression data for 20,782 genes was downloaded from the Allen Human Brain Atlas (AHBA). Known (n=29) and candidate (n=178) Epileptic Encephalopathy genes were chosen. Pairwise Pearson's correlation coefficients (r) were calculated for each Epileptic Encephalopathy gene pair of interest (n=5,568). Correlation values between known Epileptic Encephalopathy genes were compared to 1,000 random gene pairs (n=499,500), representing the null distribution. Significant associations were determined by an empirical 95th percentile cut-off. Candidates were ranked based on the sum of their significant |r| associations with known Epileptic Encephalopathy genes.
Results:
Known Epileptic Encephalopathy genes were highly correlated. 120 candidate genes had at least one significant correlation with a known gene in the AHBA. The highest-ranking candidate genes included KCNB1, GRIN2B, DAO, PLXNA1, ACOT4 and MYO5A each with 14 significant correlations.
Conclusion:
We have shown that known Epileptic Encephalopathy genes are significantly co-expressed in brain. This enabled a disease-specific prioritization approach to be developed whereby those candidates with similar co-expression patterns ranked highest further implicating them as true Epileptic Encephalopathy genes. These genes can now be prioritized for follow-up studies enhancing future gene discovery efforts.

WED 55

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Targeted resequencing in epileptic encephalopathies reveals marked genetic heterogeneity and novel genes including CHD2 and SYNGAP1

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Introduction:

Epileptic encephalopathies are a devastating group of epilepsies with a poor prognosis, of which the majority are of unknown aetiology. De novo mutations in several genes (SCN1A, STXBP1, PCDH19, CDKL5, ARX) are responsible for some epileptic encephalopathies. In addition, rare, de novo copy number variants account for up to 8% of cases.

Method:

We performed targeted massively parallel resequencing of 19 known and 46 candidate genes for epileptic encephalopathy in 500 individuals with an epileptic encephalopathy.

Results:

We identified pathogenic mutations in 52/500 (10%) of our cohort, including 10/19 known epileptic encephalopathy genes and 6/46 candidate genes. We show that de novo CHD2 and SYNGAP1 mutations are new causes of epileptic encephalopathies, accounting for 1.2% and 1% of cases, respectively and investigate the phenotypes of these patients. We also further expand the phenotypic spectra explained by SCN1A, SCN2A, and SCN8A mutations.

Conclusion:

This is the largest cohort of patients with epileptic encephalopathies to undergo targeted resequencing and this study shows that this is a rapid and cost-effective method for diagnosis. Understanding the molecular aetiologies of these disorders enables a definitive aetiological diagnosis, prognostic and genetic counselling and is the first step to targeted therapies.

WED 56

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Changes in acute hospital costs for stroke after clinical facilitators employed to improve stroke care: an Australian case study

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Introduction:
Understanding trends in resource use within hospitals is important since the most expensive costs related to stroke in the first year are from hospitalisation. In 2007, the Victorian Government in Australia selected eight hospitals to employ clinical facilitators for three years to establish stroke units and protocols to improve stroke care. It is unclear if inpatient costs changed over this period. We aimed to describe the costs of acute care before and after the implementation of stroke care initiatives.
Methods:
Pre (financial year [FY] 2006-07) and post (FY 2010-11) cohort design of all admitted episodes of stroke or Transient Ischemic Attack (TIA) using ICD-10 discharge codes (I61, I63, G45). Patient-level clinical costing data was provided by the Victorian Department of Health. Generalised linear regression models were used to compare FYs.
Results:
Data on 4827 episodes, 2125 pre (age >75 years 52%) and 2702 post (age >75 years 50%) showed a 27% increase in episodes managed at the selected hospitals; half explained by more TIA admissions (39% increase since 2006-07). Overall, average length of stay (LOS) reduced by 20% (mean 8.3 days pre to 6.6 days post). Six hospitals provided cost data with AUD10.4 million spent in the care of stroke patients in 2006-7, and AUD13.7 million in 2010-11, a 32.4% increase in the setting of 8% health cost inflation. After adjusting for patient age, gender, stroke subtype, and hospital there was a 1.1% increase in mean per-episode costs between 2006 and 2010 (AUD7303 pre; AUD7386 post, p=0.70). When LOS was additionally adjusted for, these costs increased by 21% reflecting a change in the mean cost per day.
Conclusion:
Cost containment for the mean cost per acute inpatient episode was observed after the implementation of stroke care initiatives despite increasing numbers of episodes and shorter lengths of stay. Future research should assess costs across the whole chain of recovery to better inform health policy.

WED 57

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A Clinical and Electrophysiological Study of the Effects of Fampridine on Upper Limb Impairment in Multiple Sclerosis

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Background:
Multiple Sclerosis (MS) is a common and disabling demyelinating disorder of the central nervous system. Despite recent advances in disease-modifying immunotherapies, options for symptomatic treatment of MS-related motor disability are limited. Modified-release 4-aminopyridine (fampridine) recently received TGA approval for treatment of MS-related walking disability but its precise mode of action and potential use for functions other than ambulation remain unknown. Furthermore, only around 40% of patients are defined as clinical responders to fampridine.
Aims:
In this study we propose to examine whether fampridine can improve upper limb impairment in MS and whether objective electrophysiological measures of central conduction differ between responders and non-responders and between patients on and off drug.
Methods:
This is a randomised, placebo-controlled, double-blind study including 40 patients with MS and upper limb impairment and 20 healthy controls. Patients will be randomised to fampridine 10mg bd or placebo for a period of 8 weeks. The following clinical measures will be made at several timepoints on and off treatment: 9-hole peg test (9HPT), upper extremity manual muscle strength, sensory discrimination capacity, visual acuity, contrast sensitivity, fatigue impact scale. The following electrophysiological measures will be made: upper limb motor threshold, motor evoked potential recruitment curves, paired pulse transcranial magnetic stimulation (TMS) and central motor conduction time; upper limb somatosensory evoked potentials; peripheral nerve conduction studies; visual evoked potentials.
Results and Analysis:
The primary outcome is clinical response to fampridine based on performance on 9HPT. Secondary outcomes are: correlation between clinical and electrophysiological measures in responders as compared with non-responders, healthy controls and the placebo group; changes in upper limb strength, visual function, sensory discrimination capacity and fatigue. We hypothesize that clinical responders will show reduced latency and increased amplitude of evoked potential responses and increased motor pathway recruitment and excitability with TMS measures.

WED 58

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Neonatal epilepsy and KCNQ2 mutations: Frequency and patterns of later seizures

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Introduction:

Benign familial neonatal epilepsy (BFNE) is characterized by neonatal onset of seizures, typically on the second or third day of life, which resolve by 6 months of age. BFNE is caused by mutations in potassium channel genes KCNQ2 and KCNQ3, with KCNQ2 mutations being the responsible gene in the majority of families. Seizures later in life have been reported in approximately 15% of individuals from BFNE families, however this is from single families or studies performed prior to the availability of genetic testing.

Methods:

Detailed clinical data from 27 BFNE families with KCNQ2 mutations were collected and the seizure course and occurrence of seizures later in life were analyzed.

Results:

Febrile or afebrile seizures after the neonatal and infantile period were reported in 31% of individuals (40/130) with KCNQ2 mutations. Three patterns of later seizures were observed: simple febrile seizures, childhood seizures and sporadic single seizures or clusters of seizures predominantly in adolescence or adulthood. Individuals with a larger number of neonatal seizures had a greater likelihood of experiencing later seizures ($p<0.005$, OR=8). Afebrile seizures in childhood and adult life were typically infrequent, but occasionally the epilepsy was more active and harder to control.

Conclusion:

Seizures later in life are more common in BFNE than previously reported and are associated with a greater number of seizures in the neonatal period. Although essentially a neonatal syndrome, child and adult neurologists need to be aware that BFNE with KCNQ2 mutations can be associated with recurrent seizures at any time throughout life.

WED 59

Dexter Yak Seng Chan, Barend Mees, Domenic Robinson, Franklin Pond

Endovascular repair of popliteal artery pseudoaneurysm with covered stent following total knee joint replacement

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Introduction:
Vascular complications following total knee joint replacement (TKJR) are uncommon and include haemorrhage, arterial occlusion, dissection, pseudoaneurysm and arteriovenous fistula formation. Popliteal artery pseudoaneurysm is rare with a reported incidence of 0.15% of all TKJR. Traditional open surgical repair of this condition may lead to further morbidity including worsening oedema and limb loss. The use of covered stents is a minimally invasive and safe alternative to surgery. Concerns raised pertain to stent kinking and fracture from deployment across the knee joint. The authors report a case of percutaneous covered stent repair of popliteal pseudoaneurysm complicating TKJR.
Method:
The index case and operative technique of covered stent deployment are described with associated imaging.
Results:
Using percutaneous femoral artery access, the covered stent was successfully deployed under angiographic guidance with demonstration that the popliteal artery flexion point is proximal to the knee joint line. Complete exclusion of the popliteal artery pseudoaneurysm was immediately achieved, and stent patency confirmed at 12 months.
Conclusions:
Covered stent repair of popliteal pseudoaneurysm is an alternative to open repair. With modern stent technology and anatomical knowledge that the knee joint flexion point is proximal to the joint line, durability and patency are not compromised.

WED 60

Sharon F. Kramer [1,2,] **Toby Cumming** [1]**, Leonid Churilov** [1]**, Julie Bernhardt** [1,2]

Measuring activity levels at an acute stroke ward: Comparing observations to a device

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2. School of Physiotherapy, La Trobe University

Aim:
To establish whether a device containing a dual-axis accelerometer provides similar information to behavioural mapping on physical activity patterns early after stroke.
Background:
If a simple system of instrumented monitoring were possible early after stroke, therapists may be able to more readily gather information about activity and monitor progress over time.
Methods:
Twenty participants with recent stroke = 2 weeks and aged > 18 years were recruited and monitored at an acute stroke ward. The monitoring device (and behavioural mapping (observation) were simultaneously applied from 8 a.m. to 5 p.m. The device was attached to the participant's unaffected leg. Behavioural mapping was performed by a trained observer who recorded the activity of the participant every 10 minutes. Both methods recorded the time participants spent lying, sitting and upright.
Results:
The median percentage and interquartile range (IQR) of time spent lying, sitting and upright recorded by the device was 36% (15 - 68), 51% (28 - 72) and 2% (1 - 5) respectively. Agreement between the methods was good; Intra Class Correlation Coefficient (95% CI): lying 0.74 (0.46 - 0.89), sitting 0.68 (0.36 - 0.86) and upright 0.72 (0.43 - 0.88).
Conclusion:
Patients are inactive in an acute stroke setting. In acute stroke, estimates of time spent lying, sitting and upright measured by a device are valid.

WED 61

E. L. Roberts, D. A. F. Cossigny and G. M. Y. Quan

THE VEGF AND TNF-αPATHWAYS IN PROSTATE CANCER METASTASES TO THE BONY SKELETON

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Background:
Despite the clinical implication and the high incidence of spinal metastasis from prostate cancer there is little known about the mechanisms that promote these actions. Two factors that have been linked to this are VEGF-A and TNF-α. Previous studies have shown these factors to be involved in angiogenesis while aiding in colonisation of the tumour cells in the bone. With this in mind, our laboratory developed a mouse model of human spinal cancer in order to analyse the molecular interaction between the tumour and the bone microenvironment.
Aims:
To confirm that growth factors VEGF-A and TNF-α are expressed in human prostate cancer cell lines PC-3 and Du145 in vitro and in our in vivo animal model of human spinal cancer.
Methods:
Human prostate cancer PC-3 and Du145 cell lines were cultured in RPMI whereby RNA was extracted to test mRNA levels through RT-PCR and Real-Time PCR and cell lysates were prepared to detect protein levels through Western Blot analysis and FACS. Using spines from our mouse model of human spinal cancer, sections were taken at 5-10µm and stained for the VEGF-A and TNF-α antibody markers.
Results:
Using Real-Time PCR, high mRNA levels of VEGF-A and TNF-α were detected in the PC-3 and Du145 cell lines. Furthermore, both these cell lines highly expressed VEGF-A and TNF-α on Western Blot and FACS. Sections taken from our mouse model of human spinal cancer also showed high levels of these markers in comparison to our control.
Conclusion and Future Directions:
We observed high levels of VEGF-A and TNF-α protein and mRNA in these aggressive human prostate cancer cell lines. This confirms a key role for VEGF-A and TNF-α in prostate cancer metastasis to bone. Future directions involve targeting the VEGF-A and TNF-α pathways in these cell lines

WED 62

S. Dushyanthen, D.A.F. Cossigny, G.M.Y. Quan

OSTEOBLASTIC AND OSTEOCLASTIC INTERACTIONS IN SPINAL METASTASIS OF HUMAN PROSTATE CANCER

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Prostate cancer is one of the leading cancers arising in men and has a high propensity for bone metastasis, particularly to the spine. At this stage it often causes severe morbidity due to pathological fracture and/or metastatic epidural spinal cord compression, which if untreated inevitably leads to intractable pain, neurological deficit and paralysis.

Aim:
To investigate the underlying molecular mechanisms and factors involved in driving the tumour-bone interactions in spinal metastasis.
1. To identify and confirm the presence of specific bone and tumour markers which are involved in prostate cancer (PC-3) metastasis of the spine, in order to characterise the in vivo animal model.
2. To quantify protein and gene expression levels of these markers in vitro and in vivo.

Methods:
A clinically relevant novel in vivo mouse model of spinal cancer was established, mimicking the human condition of paraplegia. A grading scale was developed to score the degree of paralysis and Immunohistochemical analysis was undertaken on these sections. The PC-3 cell line was used to analyse gene and protein expression of various factors through RT-PCR, FACS and Western Blotting.

Results:
In vivo, high expression levels were observed for RANKL, MMP-9, IL-6, PTHrP and OPG through Immunohistochemistry. In vitro, positive results were obtained for these markers via RT-PCR, FACS and Western Blot.

Conclusion:
It is evident that the tumour-bone microenvironment interaction is essential for cancer progression in spinal metastasis. Future directions will include investigating the bone-tumour interactions in vitro using co-culture as well as exploration into inhibitory drug effects through proliferation, migration and invasion assays. By investigating these interactions and characterising the various factors implicated in this process, potential therapeutic targets can be identified for tumour regression in spinal metastasis.

WED 63

Kenny Rao [1]**, Mildred Yim** [2]**, Damien Bolton** [1,2]**, Arthur Shulkes** [2]**, Graham Baldwin** [2]**, Oneel Patel** [2]

Zinc preconditioning protects the rat kidney against ischemic injury

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Introduction:
Approximately 2000 new cases of kidney cancer are diagnosed in Australia each year. Nephron sparing partial nephrectomies are being increasingly performed to preserve renal function but are associated with a risk of acute renal failure due to ischemic injury, particularly in patients with underlying renal disease. Zinc preconditioning has been shown to protect brain, heart and liver tissue against ischemic injury possibly through up-regulation of Hypoxia Inducible Factor (HIF) and/or metallothionein.
Aim:
To investigate the protective effects of Zinc against renal ischemic injury.
Methods:
25 Sprague Dawley rats were assigned to control (5); Cobalt 30mg/kg (5); Zinc 5mg/kg (5), Zinc 10mg/kg (5), and Zinc 30mg/kg (5) groups. All rats underwent a right nephrectomy and were allowed to recover for 7 days, before occlusion (60min duration) of the left renal pedicle. Rats in interventional groups were preconditioned with subcutaneous Zinc or Cobalt injections 24hr and 4hr prior to occlusion. Serial serum urea and creatinine measurements were used to assess renal function. Rats were monitored using animal health scores.
Results:
The mean creatinine was lower in the Zinc 10mg/kg group than in the control group (Day 1: 207vs390; Day 3: 79vs403; Day 5 67vs234; Day 7 53vs104) ($p<0.05$). Preconditioning with Cobalt 30mg/kg or Zinc 30mg/kg also resulted in lower creatinine values but the differences were not statistically significant.
Conclusion:
Zinc appears to protect the kidneys against ischemic injury in a dose dependant manner with 10mg/kg providing the optimum protection. Further studies should be undertaken to assess the feasibility of potential clinical trials.

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Reliability of the 6-minute walk test in idiopathic pulmonary fibrosis

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4. Austin Health
5. University of Melbourne

Background:
The 6-minute walk distance (6MWD) is commonly used to measure exercise capacity and treatment effects in idiopathic pulmonary fibrosis (IPF), but the magnitude of the learning effect for 6MWD has not been well defined. Little is known about the reliability of oxyhaemoglobin saturation (SpO2) and heart rate (HR) measures obtained during the 6-minute walk test, although there is increasing interest in their use as markers of prognosis.

Methods
Participants completed two 6-minute walk tests on a straight 30 meter track with standardised encouragement. The second test was conducted on the same day after 30 minutes rest. Measures of SpO2 and heart rate were collected with pulse oximetry. No oxygen was administered during the tests. Variation between the two tests for 6MWD, nadir SpO2 and maximum heart rate was assessed using the Bland and Altman method. Reliability was assessed using the intra-class correlation coefficient (ICC) and coefficient of variation.

Results
Fifty-three participants with mean age 71(SD 9) years, TLCO 46(18) %predicted and 6MWD 398(133) meters took part. The mean improvement in 6MWD on the second test was 23 meters with limits of agreement (LOA) -41 to 87 meters. The ICC for 6MWD was 0.97 with a CV of 0.09. The mean difference for nadir SpO2 was -0.5%, with LOA -4.4 to +3.4%. The corresponding ICC and CV were 0.95 and 0.02. There was a mean difference in maximum HR between tests of 4bpm with LOA -12 to +20bpm. The ICC and CV for maximum heart rate were 0.92 and 0.08.

Conclusions:
The 6MWD is a reliable measure in IPF, however there is a substantial learning effect which may be clinically important when evaluating change over time. Nadir SpO2 and maximum HR during the 6-minute walk test show acceptable measurement variation, although limits of agreement for HR are wide. A single 6-minute walk test may be sufficient to obtain reproducible measures of SpO2 in IPF, however two tests should be considered if the 6MWD is being used to evaluate treatment effects.

THURS 03

Danny J. Brazzale [1,2], Graham L. Hall [3,4] and Jeffrey J. Pretto [2,5,6]

The effect of adopting the new GLI reference equations on the interpretation of spirometry.

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Aim:
The new spirometry reference equations from the Global Lung Initiative (GLI) provide an opportunity for adoption of a globally applicable set of reference equations. The aim of this study was to document the likely effects on interpretation of test results of changing from commonly used current reference equations to the 2012 GLI equations.
Method:
2400 sets of spirometry results from Caucasians with equal gender representation and evenly divided over the age range of 5-85 years from clinical pulmonary function laboratories at three Australian public hospitals were analysed. The frequency of obstruction and spirometric restriction was assessed using commonly used reference equations.
Results:
GLI mean predicted values were on average very similar to all except ECSC values (which were 150mls and 280mls lower for FEV1 and FVC respectively). The limits of normality were different resulting in altered rates of obstruction (FEV1/FVC < LLN) and spirometric restriction (FVC < LLN):

Reference Valuesquations	FEV1/FVC < LLN	FVC < LLN
NHANESIII (1999)	28.5%	25.8%
ECSC (1993)	24.4%	14.2%
Stanojevic (2009)	20.0%	24.8%
GLI (2012)	26.3%	20.5%

Conclusion:
This analysis of a consecutive clinical dataset shows that changing to GLI spirometry reference data will result in some changes in rates of obstructive and spirometric restrictive interpretation. The level of agreement with GLI is worst when comparing with ECSC equations and best with NHANES equations.
This analysis should facilitate implementation of the 2012 GLI reference values into clinical practice.

THURS 04

Rebecca L. Smith, Yet H. Khor, Christine McDonald

Suboptimal Management of UFH compared with LMWH in the management of Pulmonary Embolism.

Department of Respiratory Medicine, Austin Health

Aim:
Both LMWH and UFH have been shown to be equivalent in efficacy and safety profiles for management of PE. However, UFH management is complex requiring regular monitoring and titration. This audit was performed to assess real world anticoagulation management for PE.
Methods:
An audit of patients with a new diagnosis of PE from March 2011 to March 2012 was performed. Data collected included patient characteristics, anticoagulant, complication, mortality, time to first administration, frequency of monitoring and dose adjustment for UFH, time to therapeutic range for UFH (based on activated partial thromboplastin time (APTT)), length of hospital stay.
Results:
Of the 211 patients who were included, 139 were admitted via the emergency department and 45 were managed with UFH. Average length of hospital stay was 8 days (range 0-40). There was no significant difference in time to initial dose between those treated with LMWH and UFH (192 vs 98 minutes, p=0.16). For UFH, average time to therapeutic range was 594 minutes (range 87-2257 minutes). During the course of UFH therapy, only 22% of APTT were within therapeutic range, while 44% were above and 33% were below therapeutic range. Average number of UFH dose adjustment was 5. Increasing weight significantly delayed time to therapeutic range for patients on UFH (p=0.02). Up to 18 months following PE, overall mortality rate was 28% with no significant difference between LMWH and UFH.
Conclusions:
PE was predominantly managed with LWMH. UFH was suboptimally managed when used, although there was no impact on mortality rate.

THURS 05

Sue Rochford [1,2]**, Peter Rochford** [1,2]**, Michael Sutherland** [1,2]

DOES CHANGE IN SYMPTOM SCORE REFLECT CHANGE IN LUNG FUNCTION FOLLOWING 6 MONTHS OF OMALIZUMAB TREATMENT?

1 Dept of Respiratory and Sleep Medicine, Austin Health
2 Institute for Breathing and Sleep, Austin Health

Background:
Omalizumab treatment aims to improve lung function, asthma control and quality of life in patients with severe, poorly controlled, IgE mediated asthma. Predicting an individual patient's response to Omalizumab remains difficult and current recommendations suggest that monitoring response to treatment should include measurements of both symptom control and lung function.
We sought to examine the relationship between these outcome measures in clinical practice and whether symptom control was generally reflected by improvements in lung function.
Methods:
Baseline and 6 month follow-up data was collected in 12 consecutive patients referred to the Allergy Service at the Austin Hospital and who were prescribed Omalizumab. Follow-up measures included spirometry and Asthma Control Questionnaire (ACQ).
Results:
The patients showed moderate to severe obstruction pre-treatment. After 6 months of Omalizumab, modest improvement in spirometry and substantial improvement in ACQ were observed. There appeared to be no consistent relationship between change in ACQ and change in FEV1 with the majority of patients having substantial improvement in asthma control symptoms with little change in spirometry results.
Conclusion:
In this small group of patients, symptom and spirometry improvements after six months of Omalizumab were poorly correlated. The explanation for this observation is yet to be determined.

Marnie Graco [1]; Rachel Schembri [1]; Douglas J Brown [2]; Jeanette Alexander [2]; Melinda Millard [2] & David J Berlowitz [1]

HOW RECRUITING TO MORE THAN ONE ACUTE CLINICAL TRIAL IN SPINAL CORD INJURY AFFECTS RECRUITMENT, WITHDRAWAL AND OTHER TRIAL PROCESSES: THE COSAQ EXPERIENCE.

1. Institute for Breathing and Sleep, Austin Health
2. Spinal Research Institute, Austin Health

Introduction
Spinal Cord Injury (SCI) is a relatively rare event and multicentre trials are commonly required to achieve clinically relevant and sufficiently powered sample sizes. Anecdotally, concerns are expressed for participants, units and the integrity of the research around the potential consequences of multiple trials "competing" for the same participants. However, there is little literature which examines this in SCI. This paper will use process data from the multicentre COSAQ (Continuous Positive Airway Pressure for Obstructive Sleep Apnoea in Quadriplegia) study to determine whether recruiting to more than one clinical trial has adverse consequences on recruitment rates, patient withdrawal and trial timeframes.

Methods
The number of concurrent clinical trials that recruited patients with acute, traumatic, quadriplegia since COSAQ commenced was determined for each of the 11 sites and data was dichotomised for sites recruiting to one versus two or more trials. Comparisons were made examining the proportion of eligible patients recruited, the proportion of patient-initiated withdrawals and the mean number of days from consent to randomisation.

Results
1026 patients have been screened for COSAQ, 200 consented and 85 randomised across Australia, the UK, Canada and New Zealand. Five sites recruited to COSAQ only, two recruited to an average of two trials, two recruited to three, and two recruited to four studies concurrently. No significant difference in recruitment rates (62% vs 54%, p=0.14) or patient-initiated withdrawals (16% vs 8%, p=0.06) was observed in the sites recruiting to one versus more than one studies. Closer inspection of the data revealed that 7 of the 11 patient initiated withdrawals in the COSAQ only group were from one site, and 3 of these withdrawals were directly attributable to external factors outside the site's control. When these withdrawals were removed the difference was reduced to 12% vs 8% (p=0.28). Sites recruiting to COSAQ only took 7.5 days longer to randomise participants following consent. This difference approached significance (27.5 vs 20 days, p=0.06).

Conclusion
Using the COSAQ trial as an example, recruiting to more than one clinical trial in acute SCI does not appear to impact significantly on recruitment or participant withdrawal rates. Sites recruiting to more than one trial may be more efficient at completing baseline assessments and tasks associated with the trial. While this needs to be explored in more detail, we hypothesise that this may be because these sites are more experienced in conducting clinical trials and have more efficient systems in place.

THURS 07

Al Matroodi, S.A. [1,2,3], McDonald, C.F. [2], Collins, A.L. [2], Darby, I.A. [1], Pouniotis, D.S. [1,2]

Blood Monocyte Phenotype Is Not Altered In Primary Lung Cancer

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2. Institute for Breathing and Sleep, Austin Health
3. Laboratory Medicine Department, Applied Medical Sciences Collage, Qassim University, Buraida, Saudi Arabia

Monocytes play a vital role in the immune response against tumour cells. The expressions of M1 (classical activated macrophage) and M2 (alternative activated macrophage) markers have been detected in circulating peripheral blood mononuclear cells (PBMC). These studies have demonstrated conflicting results regarding monocyte phenotype and function in different cancer microenvironments.
Aim:
To evaluate the influence of NSCLC on phenotype of PBMC and to examine if NSCLC cause monocyte phenotype to skewing from M1 to M2 phenotypes.
Methods:
PBMC samples were obtained from patients with lung cancer (NSCLC) (n = 20) (stage I = 2, II = 3, III = 6 and IV = 9) and from control subjects (n = 20). Monocytes were obtained using the using the Ficoll-Paque technique and flow cytometry was performed to investigate their phenotype using specific markers. Cytokine production in the plasma looked at Th1/Th2 (TNF-a, IL-10 and IFN-?) cytokines using cytometric bead arrays (CBA).
Results:
There were no significant differences in the percentage surface expressions (SE %) and the mean fluorescence intensity (MFI) of M1 marker (HLA-DR), M2 markers (CD163 and CD36) and/or (CD11c and CD44) in patients with NSCLC compared to controls. Expressions of myeloid marker CD11b and transferrin receptor CD71 were also shown to be similar in patients with NSCLC compared controls. Cytokine analysis revealed no significant difference in secretion of TNF-a, IL-10 and IFN-? in comparison between controls and NSCLC patients.
Discussion:
This study shows that the phenotype of PBMC in patients with NSCLC is not altered and does not show skewing from M1 to M2 phenotypes. This study gives a better understanding of the effect of primary lung tumours on the local versus systemic microenvironment.

Meaklim, H.J. [1], Berlowitz, D.J [1]; Jackson, G. [2], Brown, D.J. [3], Connelly, A. [2], Farquharson, S. [2], Bilston, L.E. [4], Hatt, A. [4], Cistulli, P.A. [5,6], Sutherland, K. [5,6], Skordilis, C. [1], and O'Donoghue, F. [1]

TO 3T-MRI OR NOT TO 3T-MRI? ISSUES WITH THE USE OF 3T-MRI IN PATIENTS WITH QUADRIPLEGIA AND OBSTRUCTIVE SLEEP APNOEA

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2. The Florey Institute of Neuroscience and Mental Health, Melbourne Brain Centre, Heidelberg, VIC, 3084, Australia
3. Spinal Research Institute, Austin Health, Heidelberg, VIC, 3084, Australia
4. Neuroscience Research Australia, Randwick, NSW, 2031, Australia
5. NHMRC Centre for Integrated Research and Understanding of Sleep (CIRUS), The University of Sydney, NSW, 2050, Australia
6. Centre for Sleep Health and Research, Department of Respiratory Medicine, Royal North Shore Hospital, St Leonards, NSW

INTRODUCTION:
3-Tesla (3T) Magnetic Resonance Imaging (MRI) produces images with superior soft tissue resolution to 1.5 Tesla (1.5T) MRI, and was chosen to investigate the soft tissue structure of the upper airway in participants with quadriplegia and obstructive sleep apnoea (OSA). However, detailed 3T MRI safety information of metallic spinal instrumentation is not readily available. This paper examines the effect of our choice of MRI (3T versus 1.5T) on participant recruitment.
METHOD:
Participants with quadriplegia who received treatment from the Victorian Spinal Cord Service had their medical records screened against the inclusion criteria and whether they had 3T MRI compatible spinal instrumentation. Those who met criteria were given the opportunity to participate and underwent further 3T MRI safety screening if they consented. Participants that were deemed safe were scanned at the Melbourne Brain Centre.
RESULTS:
Of the 1094 participant records screened, 987 participants did not meet the studies inclusion criteria. Seventy-one participants were excluded because their spinal instrumentation was not 3T MRI compatible. Of the 36 people who were contacted to participate, 8 were not deemed safe upon further screening. Only 3 participants with quadriplegia and OSA have been successfully scanned.
CONCLUSIONS:
Whilst 3-Tesla MRI is an imaging technique that produces images with superior soft tissue resolution to 1.5 Tesla MRI, recruitment of participants with quadriplegia is very difficult for 3T MRI safety reasons. Careful consideration of the practicalities of recruiting an adequate sample size with 3T MRI is critical prior to choosing this newer technology over existing 1.5T MRI.

THURS 09

This abstract has not been included at the request of the author

THURS 10

Justine Westlake [1], Gerard Kennedy [2], Paul Emerson [1], Philip Swann [3], Mark Howard [1]

Do shift workers fare as badly as obstructive sleep apnoea patients: investigating sleepiness, mood and performance.

1. Institute for Breathing and Sleep, Austin Health
2. School of Psychology, Victoria University
3. VicRoads

Introduction:
This study compared objective sleepiness, mood and performance on vigilance and neuropsychological tasks of obstructive sleep apnoea (OSA) patients, shift workers and controls.
Methods:
Untreated OSA patients (n=41), shift workers (n=41) and control participants (n=40) completed a 30-minute driving simulation, the Psychomotor Vigilance Task (PVT) and two Oxford Sleep Latency Resistance Tasks (Osler). Optalert™ objectively determined sleepiness by measuring eyelid movements. Three mood questionnaires were completed: Beck Depression Inventory, State-Trait Anxiety Scale and Profile of Mood States (POMS), and four neuropsychological tasks: Logical Memory, Trails, Digit Span and Stroop. Testing occurred in the afternoon, allowing >24 hours recovery for shift workers after their shift schedule ended.
Results:
Across all tasks, OSA patients performed worse than shift workers and controls, with increased speed deviation and more crashes on the drive, and more missed responses on the PVT and Osler ($p < 0.05$). Maximum Optalert drowsiness scores reached critical levels on the Osler tasks for OSA patients and shift workers but not controls ($p < 0.01$), however no differences were seen during the drive and PVT. Neuropsychological performance was worse for the OSA group, with the shift workers' performance comparable to controls. Whilst OSA patients had the highest mood disturbances across all measures but one (POMS anger subscale), shift workers had greater mood disturbances than controls and highest POMS anger scores.
Conclusion:
People with OSA have increased sleepiness, and impaired mood, neuropsychological and psychomotor performance compared to controls and shift workers. Shift workers have persistent mood and sleepiness impairments despite a night of recovery sleep.

THURS 10A

Mark E. Howard [1,2,3], **Michael L. Lee** [1,2], **William J. Horrey** [4], **Yulan Liang** [4], **Claire Anderson** [1,2,5], **Michael S. Shreeve** [1], **Connor O'Brien** [1], **Charles A. Czeisler** [1,2]

Driver awareness of drowsiness and prediction of falling asleep prior to critical driving events during actual motor vehicle driving after actual night shift work

1. Division of Sleep Medicine, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston MA
2. Division of Sleep Medicine, Harvard Medical School, Boston MA.
3. Institute for Breathing & Sleep, Department of Respiratory & Sleep Medicine, Austin Health
4. Liberty Mutual Research Institute of Safety, Hopkinton MA
5. Monash University

Introduction:
We assessed the relationship between self-reported drowsiness indicators and critical driving events during an instrumented vehicle drive in night shift workers.
Methods:
Sixteen night shift workers (age 18-65) completed two 2-hour drives in an instrumented vehicle on a closed-loop driving track. One drive after >7 hours' sleep the previous night, the other after night shift. Self-reported indices of drowsiness were collected every 15 minutes: the Karolinska Sleepiness Scale (KSS); frequency of specific Symptoms of Sleepiness (scale 1-7); and self-rated likelihood of falling asleep (scale 1-5). Self-reported indices were correlated with critical driving events, in the subsequent 15 minutes of driving, and when participants lost control of the vehicle and the investigator applied the brakes.
Results:
Subjective sleepiness (KSS) was related to the occurrence of critical driving events in the subsequent 15 minutes (OR 1.60, 95%-CI 1.28-2.00). Drivers were "sleepy" to "extremely sleepy" prior to 82% of events. Specific sleepiness symptoms also predicted driving events. All events occurred after drivers had noticed "difficulty keeping eyes open" at least occasionally (OR 1.75, 95%-CI 1.36-2.15). "Head dropping" was not a sensitive predictor, as 45% of events occurred without prior reporting of this symptom. Drivers' self-rated likelihood of falling asleep was related to driving events (OR 1.97, 95%-CI 1.64-2.37); however drivers only believed they were likely to fall asleep prior to 45% of events.
Conclusion:
Night shift workers were aware of sleepiness and/or other drowsiness indicators prior to critical/near-crash events; but did not always comprehend they were likely to fall asleep

THURS 11

Jessica L. Raubenheimer [1,2]**, Tom J. Churchward** [1,2]**, Warren .R Ruehland** [1,2]**, Fergal O'Donoghue** [1,2]**, Julie Tolson** [1,2] **and Peter D Rochford** [1,2]

Investigation Into Periodic Limb Movements (PLM) Muscle Activation Patterns and the Impact of Sensor Type on PLM Detection.

1. Department of Respiratory and Sleep Medicine, Austin Health
2. Institute for Breathing and Sleep, Austin Health

Introduction:
Published evidence supporting currently employed PLM detection methods is limited. Sensor types used are predominantly EMG or movement sensors. Recommended sensor site assumes highly stereotyped PLM movements. This study aims to: 1) identify the type of sensor and sensor placement that most reliably detects PLMs
2) characterise PLMs in terms of leg muscle group involvement and determine the degree of stereotypicality within and between PLM patients.
Methods:
Overnight PSG was performed on four patients previously diagnosed with PLMD. In addition to standard PSG on one leg, EMG signals for six leg muscles were recorded (Tensor Fascia Latae(E1), Quadriceps (E2), Biceps Femoris (E3), Tibialis Anterior (E4), Soleus(E5) and Extensor Digitorum Brevis (E6)). Three movement signals using piezoelectric sensors were recorded from the thigh (P1), lower leg (P2) and foot (P3). For each subject, 100 consecutive PLMs were measured from nine signals. The proportion of movements captured by each signal, and muscle activation patterns of PLMS were assessed.
Results:
The table shows the percentage of PLMs detected across all participants for signal type and site. The highest detection rates of PLMs for the EMG and movement sensors were 69% (E4) and 91% (P3) respectively.

	E1	E2	E3	E4	E5	E6	P1	P2	P3
Median	33	41	51	69	56	52	52	88	91
Range	14 - 79	17 - 79	15 - 80	52 - 81	14 - 81	22 - 70	26 - 90	79 - 95	86 - 96

The most frequent patterns of muscle activation observed were the whole leg (35, 10-87% median, range) and the lower leg (13, 0-58%), but with large inter-subject variation.
Discussion:
In this sample, we conclude that: 1) movement sensors on either the foot or the lower leg were highly sensitive for PLM detection, 2) Of six leg muscles examined, Tibialis Anterior was best for PLM detection, but with significant under detection rate; 3) EMG data suggests that the muscle activation pattern of leg muscles is not highly stereotyped.

THURS 12

Y.H. Khor, J. Tolson, T. Churchward, P. Rochford, C.J. Worsnop

Comparison of estimated and measured sleep latency during home polysomnography among patients with suspected obstructive sleep apnoea

Department of Respiratory and Sleep Medicine, Austin Health

Introduction

Home polysomnography (PSG) is an alternative method for the diagnosis of obstructive sleep apnoea (OSA). Types 3 and 4 home PSG do not monitor sleep and so rely on the patient's estimated sleep latency (SL) in the calculation of total sleep time, used to calculate the apnoea-hypopnoea index (AHI).

The aim of this analysis was to compare patients' estimated SL with objective measures in patients who underwent type 2 home PSG for diagnosis of OSA.

Methods

The subjects were 536 consecutive patients of one of the authors between November 2006 and January 2013. A standard questionnaire was completed by the patients the morning after the home PSG to record patients' estimation. Estimated SL was derived from these two values. Measured SL on home PSG was scored based on the guidelines of the American Academy of Sleep Medicine.

Results

Only 530 patients were included in the analysis due to incomplete data in 6 patients. Median estimated SL was 20 minutes compared to 10 minutes for measured SL (p < 0.0001). Bland-Altman analysis showed mean difference of 13 minutes with wide limits of agreement (95% limits of agreement: -89 and 116 minutes). There were no significant correlations between estimated SL and age, Epworth Sleepiness Scale score, body mass index, AHI and sleep efficiency.

Conclusion

The overall estimated SL in the patients was significantly longer than measured, although there was significant individual variability. There were no identified factors that influence SL estimation. Subjective estimation of SL should be interpreted with caution.

THURS 13

Kyle G. Smart [1,3], **Fergal J. O'Donoghue** [1,2,3], **Christopher J. Worsnop**[1,2,3], **Allison L Collins**[1], **Maree Barnes** [1,2,3]

Short term outcomes for obstructive sleep apnoea patients treated with hypoglossal nerve stimulation

1. Institute for Breathing and Sleep, Austin Health
2. University of Melbourne
3. Austin Health

Novel modes of treatment for OSA are sought by patients and clinicians for whom CPAP tolerance may be problematic. We report the findings of a randomised controlled trial of hypoglossal nerve stimulation (HGNS). This trial was conducted in 22 centres worldwide and was prematurely closed by the company (Apnex Medical) in January 2013 following a negative interim analysis. We report here the 6 month results from our centre.

Methods

Participants with an apnoea hypopnoea index (AHI) of 20-80 and had failed usual treatment options were enrolled. Recruitment, surgical procedure, device activation and titration have been previously described (ASA 2012). Participants were randomly allocated on a 2:1 basis to have the device activated 1 month or 7 months post-implantation. Outcome assessment at 6 months post randomisation included sleep measures and behavioural outcomes as below. Responders were a priori defined as achieving an AHI < 20 with at least 50% reduction from baseline.

Results

All data are mean (SEM). The device was implanted in 4 females, 17 males, mean age 54.3 (1.7) years. There was a significant improvement in AHI, arousal index and depression (BDI) in the active group, but the only inter-group difference at 6 months was in the Beck Depression Index (BDI). Using logistic regression, responder status was predicted by ODI4%, not group, and there was an association with obesity (BMI).

Measure	Baseline		6 months	
	Active (n=14)	Control (n=7)	Active (n=14)	Control (n=7)
AHI	34.1 (3.5)	40.9 (6.5)	22.1 (5.2) †	29.7 (6.2)
4% ODI*	10.8 (2.5)	22.2 (4.3)	11.4 (4.1)	19.5 (5.2)
Arousal Index	37.2 (3.2)	33.2 (6.9)	25.0 (2.4) †	30.9 (5.5)
ESS	11.1 (1.6)	13.6 (2.0)	9.8 (1.0)	14.1 (2.5)
BDI#	14.0 (2.7)	13.6 (3.4)	9.8 (1.7) †	14.1 (2.5)
Responders (%)			7 (50)	2 (28.6)

P<0.05:
* Active vs Control, baseline; † change from baseline;
# Active vs Control, 6 mths
Conclusion: Further research is warranted into this potentially promising therapy.

Ali Ghasem-Zadeh [1], Roger Zebaze [1], Åshild Bjørnerem [2], Xiaofang Wang [1], Yohann Bala [1], Ego Seeman [1]

Assessing Age, Sex, and Racial Differences in Cortical Porosity Requires Adjustment for Site-Specific Variation in the Selected Region of Interest

1. Endocrine Centre, Austin Health, University of Melbourne
2. Department of Clinical Medicine, University of Tromsø, Norway

High-resolution peripheral quantitative computed tomography (HR-pQCT) measures micro-architecture in a region of interest (ROI) at the distal radius and tibia. Bone width and micro-architecture vary slice by slice along the length of a bone so differences in micro-architecture by age, pubertal stage, sex and racial group may be the result of differences in the placement of the ROI rather than the characteristics of the subjects.

To assess the slice-by-slice variation in cortical porosity we used images of the distal tibia, fibula and radius acquired by HR-pQCT and assessed cortical porosity using Strax 1.0 software in 69 women aged 40 to 61 years.

The mean (SD) cortical porosity at the distal tibia, fibula and radius were 57.6% (5.4), 38.1% (7.3) and 46.9% (6.2).

Each 1 mm (12 slices) more distal ROI increased porosity as shown:

	Tibia Mean ±SE	Fibula Mean ±SE	Radius Mean ±SE
Total	1.22%±0.06	0.89% ±0.06	2.43%±0.09
Compact cortex	1.27%±0.06	0.68%±0.09	2.01%±0.08
Outer transitional zone	0.67%±0.11	0.51%±0.12	1.25%±0.08
Inner transitional zone	0.16%±0.05	0.58% ±0.10	0.34%±0.05

We infer that a more distal ROI has a significant effect on cortical porosity which may result in erroneous age, sex and racial differences being reported. This variation needs to be considered when interpreting data in persons who differ in bone length.

THURS 15

David Story

The University of Melbourne and research in Anaesthesia, Perioperative and Pain Medicine

Department, Anaesthesia, Perioperative and Pain Medicine Unit, Melbourne Medical School, University of Melbourne, Austin Health

Australia and New Zealand are world leaders in research in Anaesthesia, Perioperative and Pain Medicine; per capita we are THE leaders. Hospitals affiliated with the University of Melbourne play an important role in this research which in 15 years has led Anaesthesia from being unrecognised at the NHMRC to having the highest ranked NHMRC project grant in 2012. The key to this success has been collaboration.

To further enhance multicentre research (and teaching) the University of Melbourne has appointed a foundation Professor and Chair of Anaesthesia. This position uses a new model where the Chair is based on campus at the Melbourne Medical School in Parkville. The Chair has no single hospital affiliation but instead works with all 14 hospitals affiliated with the University of Melbourne. This innovative model of a Chair with a University affiliation but without specific hospital affiliation provides a platform for research collaboration across hospitals with both clinical and geographic diversity.

The foundation Chair of Anaesthesia is Professor David Story, formally a full time staff Anaesthetist at the Austin. He has ongoing clinical interest in perioperative management of critically ill adults including liver transplantation.

The role of Anaesthesia at the University and affiliated hospitals has been further enhanced with formation of the Anaesthesia, Perioperative and Pain Medicine Unit within the Melbourne Medical School.

As well as participating in major national and international trials, the Department of Anaesthesia at the Austin, in conjunction with the University, is playing important role in an evolving program of collaborative research including the areas of particular expertise at the Austin: post operative care, intravenous fluid management, perioperative haemodynamic monitoring, and clinical chemistry.

THURS 16

Philip Peyton, Christine Wu

Nitrous oxide induced postoperative nausea and vomiting is related to duration of exposure

Dept of Anaesthesia, Austin Health

Background:
Nitrous oxide (N2O) has been identified as a cause of postoperative nausea or vomiting (PONV) in many previous studies and meta-analyses. However, there is significant heterogeneity in the findings among these studies. A possible unexplored cause of this is the influence of duration of exposure to N2O on the incidence of PONV.
Methods:
We examined data from all available randomized controlled studies that were included in the most recent meta-analysis of the effect of N2O on PONV. All studies that reported the rate of PONV within the first 24 postoperative hours and the duration of anaesthesia or surgery were included. A random effects meta-regression relationship was derived and confidence limits for this best fit were calculated.
Results:
32 studies in 30 papers met the inclusion criteria, randomizing 10,706 patients. There was a significant relationship between ln RR PONV and duration, ($r2 = 0.76$, $p = 0.01$) equivalent to an increase in RR PONV of 1.16 per hour of exposure to N2O. The RR for the overall effect of N2O on PONV was 1.21, $p = 0.03$. The number needed to treat (NNT) was 25, 23, and 10 where duration of anesthesia was less than 1 hour, 1-2 hours, and over 2 hours, respectively.
Conclusion:
Possible mechanisms for a duration related effect, including disturbance of methionine and folate metabolism, are discussed. No clinically significant effect of N2O on the risk of PONV is present with less than 40-60 minutes exposure. N2O related PONV should not be seen as an impediment to its use in minor or ambulatory surgery.

THURS 17

Philip Peyton, Christine Wu

POOR CORRELATION BETWEEN META-ANALYSES AND SUSEQUENT LARGE RANDOMISED CONTROLLED TRIALS IN ANAESTHETIC LITERATURE

Dept of Anaesthesia, Austin Health

AIMS:
To compare findings of meta-analyses with findings of subsequent large randomized controlled trials (RCTs), with the premise that the large RCT is considered the gold standard for answering a clinical question.
METHODS:
Using Medline, large RCTs in anaesthetic literature (>500 subjects, published since 2000) were compared with previous meta-analyses on the same topic, with particular focus as to whether each study found a significant or non-significant result (at the conventional level of statistical significance, $p<0.05$) to the given clinical question.
RESULTS:
15 large RCTs and 17 meta-analyses addressing the same clinical questions were identified, encompassing many important clinical topics in anaesthesia. For a total of 40 primary and secondary outcomes, 24 of 40 outcomes (60%) were predicted correctly by the meta-analysis, with agreement between the meta-analyses and RCTs being only "poor" (kappa=0.200; -0.017–0.417) (McNemar's test p value = 0.0012). The positive predictive value of meta-analyses was 25%; the negative predictive value was 95%.
CONCLUSIONS:
The outcomes of the 15 large RCTs were predicted correctly on 60% of occasions by the preceding meta-analysis. There was a strong tendency towards positive findings in meta-analyses which were not substantiated by subsequent large RCTs, which may in part be influenced by publication bias in the literature. This finding might influence the weighting of meta-analyses in clinical decision making.

THURS 18
This abstract has not been included at the request of the author

THURS 19

David Gray [1]**, Elizabeth Watt** [2]

Prioritising care for newly diagnosed men with prostate cancer: development of a supportive care needs risk factor assessment tool.

1. Olivia Newton John Cancer and Wellness Centre, Austin Health
2. Latrobe University, Austin Health

Aims:
The primary aim of this review is to identify specific risk factors that predict patient distress and poor health related quality of life (QoL) outcomes following the diagnosis of prostate cancer. The secondary aim is to develop a 'supportive care needs risk factor assessment tool' to prioritise contact with men attending Austin Health by a prostate cancer specialist nurse.
Methods:
Between 2006 and 2012 a literature search was performed using MEDLINE and Cumulative Index databases in Nursing and Allied Health (CINAHL) using the specific terms: prostate cancer; supportive care; psychosocial factors, and health related quality of life. The initial search revealed over 350 articles. After an exclusion criteria was applied a final 55 articles were included in the review.
Findings:
Several factors that contribute to poorer health related QoL outcomes and psychological distress in men newly diagnosed with prostate cancer were identified in the literature review. The most significant factors include: current relationship status (specifically being single); past physical and psychological health issues; employment status (unemployment); lower standard of education ; health issues of significant others; logistical issues related to ongoing healthcare (including transport; clinic accessibility); assistance required for activities of daily living and current perception of distress. Questions related to these factors in addition to a distress thermometer have been incorporated into the development of a 'supportive care needs risk factor assessment tool'.
Conclusions:
There are increasing numbers of men attending Austin Health with a new diagnosis of prostate cancer. While the prostate cancer nurse specialist aims to make contact with all of these patients, the use of a supportive care needs risk factor screening tool and distress thermometer may assist in identifying those men who have the greatest need for supportive care early after diagnosis.

THURS 20
This abstract has not been included at the request of the author

THURS 21
This abstract has not been included at the request of the author

THURS 22

Katherine Woods [1]**, Anupama Pasam** [1]**, Ashley Knights** [1]**, Jonathan Cebon** [1]**, Catherine Gerard** [2]**, Anne-Laure Puaux** [2]**, Sandra Morel** [2]**, Jamila Louahed** [2]

QS21 adjuvant enhances cross presentation of NY-ESO-1 antigen by Dendritic Cells in vitro.

1. Ludwig Institute for Cancer Research, Austin Health
2. GlaxoSmithKline Vaccines, Rixensart, Belgium

Introduction:
NY-ESO-1 is a prototypic cancer-testis antigen with frequent immunogenicity, which has been extensively characterized and studied as a candidate for immunotherapeutic cancer vaccine development. Dendritic cells take up and cross-present antigen to T cells, leading to their activation and stimulation of an immune response in vivo. Cross-presentation by antigen presenting cells is therefore an essential element of any immunotherapeutic treatment and several studies have attempted to enhance antigen cross-presentation by dendritic cells.
QS21 is a naturally occurring saponin molecule which is in current use as an immunostimulant either alone or in combination with other immunostimulants in several clinical trials. Some clinical studies have shown that in order to achieve strong and persistent immune responses protein antigen must be combined with an immunostimulant at the time of initial immunization.
Method:
We assessed the impact of QS21 on cross-presentation of 3 individual NY-ESO-1 epitopes by dendritic cells in vitro. NY-ESO-1 was delivered as a soluble recombinant protein, or as an immune complex, in the presence or absence of QS21. Cross-presentation of the HLA-A2 restricted 157-165, the HLA-B7 restricted 60-72, and the HLA-Cw3 restricted 92-100 NY-ESO-1 epitopes were assessed.
Results:
In all cases presence of QS21 at the time of antigen delivery resulted in significantly enhanced cross-presentation of each of the three epitopes. Strikingly, NY-ESO-1 antigen could be cross-presented when delivered as a soluble protein only in the presence of QS21.
Conclusion:
These results suggest an important role for QS21 as a component of a cancer immunotherapeutic vaccine.

THURS 23

Dylan King [1], Dahna Makris [1], Violeta Spirkoska [1], Rachael Canfield [1], Paul Ramsland [2], William Farrugia [2], Bruno Catimel [1], Andrew Scott [1] and Ingrid Burvenich [1]

Implications of Fc-engineering to a humanised anti-Lewis Y antibody on Fc gamma receptor binding

1. Ludwig Institute for Cancer Research, Austin Health
2. Centre for Immunology, Burnet Institute

The interaction between the immunoglobulin G (IgG) Fc region and Fc? receptors (Fc?Rs) is the primary mechanism linking antibody-mediated immune responses with cellular effector functions. Enhancement of this interaction through amino acid variation and glycoengineering of the Fc region has provided a way to improve immune effector functions. The majority of this research has been aimed at enhancement of interactions with Fc?RIIIa, which is the key mediator in natural killer (NK) cell antibody-dependent cell-mediated cytotoxicity (ADCC). But as NK cells are poor infiltrators of solid tumours, engineering for additional receptors and their linked effector functions is warranted. A previous study has shown that mutant antibodies with increased affinity for Fc?RIIa relative to Fc?RIIb have enhanced macrophage phagocytosis of antibody-coated tumour cells. This is mirrored by clinical data showing improved survival in patients possessing the R131 polymorphic Fc?RIIa variant, which has higher affinity for IgG class used in therapy. Here, we describe a set of novel hu3S193 Fc variants created through amino acid engineering with altered Fc?R binding affinities. These novel variants were first determined by in silico methods from crystal structures and then produced in a mammalian expression system for further analysis. Preliminary binding affinity data and ADCC activity for each of the variants is described.

THURS 24

Andrew J. Weickhardt, Teresa T. Nguyen, Diego D. Paskulin, Anh T. Le, Dara Aisner, Nathan Schulte, Fiona J.M. Chionh, John Mariadason, Niall C. Tebbutt, Robert C. Doebele, Marileila Varella-Garcia

ALK and ROS1 gene rearrangements detected in colorectal cancer (CRC) by fluorescence in situ hybridization (FISH).

Ludwig Institute for Cancer Research, Austin Health

Background:
Activation of ROS1 and ALK tyrosine kinases through gene fusions lead to unchecked cell proliferation and transformation. ROS1 and ALK gene fusions were found in about 5% and 2% of lung adenocarcinomas and are highly sensitive to specific tyrosine kinase inhibitors. This study aimed at identifying the presence of ROS1 and ALK rearrangements in CRC using FISH technology.
Methods:
Arrayed specimens of metastatic CRC (mCRC) patients were tested with a novel 4-target, 4-color break-apart FISH probe set (Abbott Molecular) designed to simultaneously evaluate the genomic status of ROS1 and ALK. Fused 3'/5' signals of each gene were considered negative for rearrangement; single 3'/single 5' (for ROS1) and split 3'-5' or single 3' (for ALK) were considered positive for rearrangement. The upper cut-off for positive FISH patterns in the negative specimens was <15% both for ROS1 and ALK.
Results:
Among 236 mCRC tested, two were positive for ROS1 rearrangements (single 3'ROS1 signals in 39% and 61% of cells) and one was positive for ALK rearrangement (single 3'ALK in 41% of tumor cells). Interestingly, the ALK+ patient displayed intra-tumoral heterogeneity, detected in the tissue cores and confirmed in two resection blocks. The fusion partner for ALK was identified as EML4 by PCR-based tests and sequencing. The fusion partner(s) for ROS1 remains to be identified. A small fraction of mCRC specimens presented duplicated or clustered copies of native ALK and ROS1.
Conclusions:
The novel FISH probe set was effective in identify the first cases of ROS1 rearrangements in mCRC and re-confirming the occurrence of ALK rearrangements. This supports further evaluation of mCRC cases for ROS1 and ALK gene fusions as these may represent new targets for evaluation in clinical trials. ROS1 fusion partners are under evaluation by independent technologies. Tumor heterogeneity in the ALK rearrangement must be addressed for screening tests
.

THURS 25

Anna Huynh, James Jackson, Maureen Rolfo, Nigel Anderson, Morikatsu Wada

Association of 18F-FDG Metabolic Tumour Volume and Dysphagia in Head and Neck IMRT as a Prophylactic Feeding Predictor

Radiation Oncology, Olivia Newton-John Cancer & Wellness Centre, Austin Health

Aim:
The extent of the gross tumour volume for primary head and neck cancer lesions (GTVp) may be a useful clinico-radiological predictor of acute dysphagia for IMRT patients. GTVp frequently lies in close proximity to midline swallowing anatomy and directs subsequent dose received. GTVp delineation is a time-intensive construct of multimodal imaging, clinical findings and clinician expertise. Metabolic tumour volume (MTV) is an automated volume derived from 18F-FDG PET scans, that may provide prompt, unbiased risk stratification for feeding tube requirements.
Method:
Eighty-three patients with evaluable primary tumours and pre-therapy FDG-PET scans performed at Austin PET Centre were identified. All received IMRT, including bilateral, elective nodal irradiation. MTV was quantified and recorded for the primary lesion (MTVp) using a minimum standardised-uptake-value (SUV) threshold of 2.0. A prospective nutritional database identified patients relying on enteral feeding (EF) for more than 75% of their dietary needs for more than 6, 12 and 26 weeks and associations were analysed.
Results:
GTVp was positively correlated with MTVp (r=0.77; p<0.0001). EF dependence at 6 weeks was significantly higher in patients with a GTVp larger than 17.0cc (73.2% vs 33.3%; p=0.0012) or MTVp larger than 12.0cc (71.1% vs 42.0%; p=0.0164). Increasing GTVp and MTVp were associated with EF dependence at 12 (p=0.0002, 0.0012) and 26 weeks (p=0.0002, 0.0232).
Conclusion:
MTVp is an automated, objective volume that may be useful in the prediction of problematic dysphagia requiring the insertion of a prophylactic EF tube. The preemptive quantification of MTVp could ensure early intervention, prior to multidisciplinary consultation.

Sujitra Detchokul [1]**, Melissa J. Davis** [2] **and Albert G. Frauman** [1]

Biomarkers of prostate cancer progression: Evolution of genetic changes and molecular drivers in castrate-resistant prostate cancer (CRPC)

1. Clinical Pharmacology and Therapeutics, Department of Medicine, University of Melbourne, Austin Health
2. Institute for Molecular Bioscience, University of Queensland

CRPC is a major limitation to the treatment of prostate cancer (PC).
We aim to understand intermediate and detailed time-course profiles of genetic changes during the evolution to androgen-resistance, using in vitro PC models.
Methods:
PC cells, LNCaP, expressing mutated AR1, 2, and LAPC-4, expressing wild-type AR3, are used in the development of in vitro CRPC models. Subline cells are established by prolonged cultures in media+10%CS-FBS, with/without the AR-antagonist, bicalutamide, to mimic the clinical course of PC. Cell proliferation, cell motility and invasion, morphology, AR and PSA expression are examined. RNA-sequencing is performed using RNA extracted from parental cells and consecutively generated subline cells. Gene expression network analysis using Cytoscape4, GeneGo5 and IPA6 will be conducted to identify genes and pathways associated with different stages of androgen-resistance progression in a time-course manner.
Results:
LNCaP cells initially showed poor growth after prolonged exposure to androgen-deprived (AI) or androgen-deprived bicalutamide-treated (1µM) (BR) conditions but later adapted and started to grow well in these conditions. Earlier loss of androgen-responsiveness was seen for LNCaP-AI compared to LNCaP-BR cells suggesting delayed onset of androgen non-responsiveness with bicalutamide. AR expression in both LNCaP-AI and LNCaP-BR decreased with time. These cells have increased proliferation, motility and invasion. RNAseq data has been generated for LNCaP and subline cells and bioinformatics analysis has commenced. The development of in vitro LAPC-4 subline cells is ongoing.
Conclusion:
Knowledge of the genetic profiles during transition to androgen resistance will improve our understanding of this common clinical scenario and lead to biomarker discovery and targeted drug development.

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THURS 27

Paul Ioannidis, John M. Mariadason, Anderly C. Chueh

The role of Protein Kinase C (PKC) in Histone Deacetylase inhibitor (HDACi) induced apoptosis in colon cancer cells.

Oncogenic Transcription Laboratory, Ludwig Institute for Cancer Research, Austin Health

Background/Aims:
HDACi are an emerging class of anti-cancer agents. Although they have limited activity in colon cancer, patient subsets that benefit have been identified. Gene expression changes induced by HDACi are similar to those induced by PKC activators. We therefore hypothesise HDACi may induce their effects through PKC.
Our aims were to: 1) determine whether HDACi induced apoptosis is dependent upon PKC,
2) identify the specific PKC isoform(s) involved and
3) determine if basal PKC isoform expression is predictive of HDACi response.
Methods:
Apoptosis was detected by measuring sub-G1 populations by PI/FACS analysis. Gene knockdown was achieved by transient transfection of siRNA in HCT116 cells. Gene expression of PKC isoforms in colon cancer cell lines was determined by microarray and confirmed with Q-RT-PCR.
Results:
Pre-treating HCT116 colon cancer cells with the PKC inhibitor, H-8, resulted in a dose-dependent inhibition of HDACi-induced apoptosis. RNAi-mediated knockdown of PKC isoforms prior to HDACi treatment revealed that depletion of PRKCB attenuated HDACi-induced apoptosis (18% decrease cf. control, P

THURS 28

Anne-Sophie Hatat, Angelo Perani, Fiona E. Scott and Andrew M. Scott

Determination by Flow Cytometry of ErbB receptor number on Cancer Cell Lines

Ludwig Institute for Cancer Research, Austin Health

The overexpression of ErbB receptors is a common feature in variety of cancer types. Cancer cell lines that are representative of these cancer types also show the same abnormal ErbB receptor expression in their cell surface. Determination of the ErbB receptors number is therefore an important tool to analyse the receptor dynamics in those cell lines and also to select the appropriate ErbB expressing cell lines that can be analysed with specific monoclonal antibodies. The reference method to determine receptor number is the Scatchard analysis using isotope labelled antibodies however it is laborious and time consuming. Here we present a flow cytometry based method to estimate receptor number in various cancer cell lines.

THURS 29

Anne-Sophie Hatat, Angelo Perani, Bruno Catimel, Harjit Singh, Fiona E. Scott and Andrew M. Scott

Purification of ErbB receptors from Cancer Cell Lines

Ludwig Institute for Cancer Research, Austin Health

The characterisation of the ErbB receptors often overexpressed at the surface of many cancer cells is an important tool in cancer research. The number of receptors can vary from a range approximately between 100-100 millions of receptors, depending on the cell line. We describe here a technique to obtain sufficient quantities of receptors using cell culture and purification methods. To obtain large number of cells we used a Hyperflask that is a cell culture vessel that has the same external dimensions as a standard T175 cm2 flask with 10 times the cell yield. We evaluated two affinity based purification techniques using ErbB specific antibodies and we have analysed the product obtained by a variety of traditional analytical techniques such as SDS-Gel, SE-HPLC, Western-Blot.

THURS 30

This abstract is not included at the request of the author

THURS 31

Thomas John [1,2]**, Carmel Murone** [2]**, Khashayar Asadi** [1]**, Marzena Walkiewicz** [2]**, Adrienne Morey** [3]**, Simon Knight** [1]**, Paul Mitchell** [1]

MET expression, copy number and oncogenic mutations in early stage NSCLC

1. Austin Health
2. Ludwig Institute for Cancer Research, Austin Health
3. SydPath, St. Vincent's Hospital, Sydney

Aim
The MET receptor tyrosine kinase and its ligand are associated with the malignant phenotype. In non-small cell lung cancer (NSCLC), MET expression increases with disease stage and is involved in de novo and acquired resistance to tyrosine kinase inhibitors. We investigated a large cohort of patients treated with curative surgical resection to determine whether MET receptor or gene amplification was prognostic.
Methods
Tissue Microarrays (TMAs) were constructed using primary NSCLC tissues in triplicate. MET staining (SP44 clone) was performed and a H-score calculated based on % cells stained and intensity. MET gene amplification was detected using Ventana's MET DNP probe. DNA was isolated and mutationally profiled using Sequenom's LungCarta panel.
Results
Of 508 patients, 352 were (69%) male, 329 pathological node negative (pN0), 67 pN1, 104 pN2 and 8 with resected primaries and solitary brain metastases (M1). Median H-scores were significantly higher in adenocarcinoma compared to squamous cell carcinoma (140 vs 91.5, p<0.05). High MET expression (H-score >100) was seen in 227 (45%) patients. DNA was isolated in 443/508 (87%) of samples. The commonest mutations were in KRAS (21%), TP53 (10%), EGFR (5%), PIK3CA (4%) MET (3%) and NRF2 (3%). No mutation was found in 44% of samples. EGFR and KRAS mutations were associated with higher MET expression, conversely TP53 was associated with lower expression (p=0.0005). Increased MET copy number by SISH was observed in 6 samples. MET expression was not associated with cancer specific survival across all stages.
Conclusions
MET expression was not prognostic in early stage NSCLC.

THURS 32
This abstract has not been included at the request of the author

THURS 33

Peter J Wookey [1], **Sebastian G.B. Furness** [2], **Karly Sourris** [3], **Angela Kourakis** [1], **David L. Hare** [1]

Development of a unique antibody against human GLP-1 receptor

1. Department of Medicine, University of Melbourne, Austin Health
2. Monash Institute of Pharmaceutical Science, Monash University, Parkville
3. Baker IDI Heart and Diabetes Institute, Prahran

Aim:
Glucagon-like peptide 1 and its cognate receptor GLP-1 Receptor (GLP-1R) are important elements in the treatment of type 2 diabetes, heart disease and potentially important for novel treatments of hypertension. The aim is to develop an effective antibody that binds GLP-1R and to provide a reliable reagent to identify GLP-1R expression.
Method:
Based on the key structural features in the extracellular domain of the closely related GPCR, the calcitonin receptor (CTR), anti-human GLP-1R antibodies were raised in chickens (IgY). One chicken polyclonal IgY antibody was characterised using cell lines that express hGLP-1R compared to vector controls in immunoblots, immuno-fluorescence confocal microscopy and analysis with fluorescence-activated cell sorting. Confocal microscopy was used to investigate tissues from mice genetically modified such that the GLP-1R was non-functional, and compared to wild-type controls.
Results:
Immunoblots were developed with the chicken IgY antibody using membrane proteins extracted from cell lines that express GLP-1R and vector control. Three bands were identified with equivalent mobilities of 100kD, 70kD and 35kD, compared to pre-immune IgY controls. Confocal microscopy demonstrated that the anti-GLP-1 R IgY (compared to pre-immune control) identifies expression in capillaries of the mouse renal medulla and lung, and low level expression in cells of the pancreatic islets. These expression patterns were compared to similar tissues from the GLP-1R-/- gene modified mouse model.
Conclusion:
With the development of this unique antibody reagent, blood vessels that form the basis of blood pressure variations noted recently in the gene-modified GLP-1R mouse model, has been identified.

THURS 34

K.J. Lu [1,2], L.G. Kearney [1,2], M. Ord [2], E. Jones [2], L.M. Burrell [1,2], P.M. Srivastava [1,2]

Age adjusted Charlson Co-morbidity Index is an Independent Predictor of Mortality over long-term Follow-Up in Infective Endocarditis.

1. Department of Medicine, University of Melbourne, Austin Health
2. Department of Cardiology, Austin Health

Backgound:
Infective endocarditis (IE) is associated with high morbidity and mortality. The epidemiology of IE is changing, affecting more elderly patients with increased medical comorbidities. We aimed to assess the ability of the age adjusted Charlson Co-morbidity Index (ACCI) to predict early and late outcomes.
Methods:
Between 1998 and 2010, adult patients with definite IE according to the modified Duke criteria were identified. The primary outcome was in-hospital and all-cause mortality. The secondary outcome was predictors of the primary outcome incorporating ACCI.
Results:
148 patients with IE were followed up for a mean of 3.8±3 years. The mean age was 57±17 years and 66% were male. In-hospital mortality and all-cause mortality was 24 and 47% respectively. Comorbid conditions included diabetes mellitus (DM) (21%); ischaemic heart disease (16%); heart failure (HF) (14%); renal failure (eGFR <60ml/min/1.73m2) (19%); and anaemia (64%). The most common causative organism was staphylococcus aureus (53%). ACCI was >3 in 59% of patients. Cardiac surgery was performed in 45% of patients. On Cox regression analysis, ACCI>3 (HR 3.0 [1.5-6.0], p<0.002), new onset HF (HR 2.2 [1.3-3.6], p<0.003), anaemia (HR 1.8 [1.1-3.2], p=0.04) and age-per decade (HR 1.4 [1.1-1.7]. p=0.004) were independently associated with all-cause mortality. ACCI>3 was the strongest predictor of in-hospital mortality (OR 8.4 [2.8-24], p<0.001). Of the individual ACCI components, prior HF, DM with complications and metastatic disease were independent predictors of all-cause mortality.
Conclusion:
In-hospital and all-cause mortality of IE remain high. An ACCI >3 was a strong predictor of mortality, in addition to age, new HF and anaemia.

THURS 35

Y. Bala, S. Iuliano, A. Ghasem-Zadeh, X-F. Wang, E. Seeman, R. Zebaze

Distribution of voxel composition of the cortical bone discriminates patients with forearm fragility fractures

Endocrine Centre, Department of Medicine, University of Melbourne, Austin Health

Aim

High Resolution-peripheral Quantitative Computerised Tomography (HR-pQCT) quantifies microstructure in vivo using a fixed threshold to separate bone from background and bone into its compartments, failing to allocate voxels to the cortical compartment when they contain bone matrix and void. We hypothesise that considering the density of individual voxels as a continuum improves discrimination of patients with forearm fracture.

Method

33 women (57±9 years) with a wrist fragility fracture and 53 aged-matched controls had a DEXA scans of the lumbar spine (LS) and the femoral neck (FN) and HR-pQCT imaging of the non-fractured arm. Images were analysed using a new algorithm that automatically segments bone from background and cortex into its compact appearing cortex, outer and inner transitional zones. Attenuation of all voxels was compared to the one of fully mineralized bone and soft tissue. Voxels were classified according the mineralized bone matrix/void volume content. Sensitivity and specificity was evaluated with area under a receiver-operating curve (AUC).

Results

LS and FN aBMD did not discriminate cases from controls (AUC 0.58 and 0.53, respectively). Cortical and trabecular vBMD discriminated cases with AUCs of 0.69 and 0.63, respectively, $p<0.05$). The proportion of voxels containing 50-70%, 70-95% and >95% mineralized bone discriminated cases and controls (AUC from 0.63 to 0.87). The proportion of voxels containing 50-70% of mineralized bone in the outer transitional zone was the best discriminant (AUC 0.87 and $p<0.05$ vs. Ct.vBMD and Tb.vBMD). Having this proportion higher than the mean observed in controls was associated with an OR (95% CI) for fracture of 11.20 (2.77-52.65).

Conclusion

Fragility fractures are associated with subtle changes in cortical microstructure that are captured by analysing the composition of individual voxels.

THURS 36

Chee-Yuen Adrienne Lam, Richard Zwar, Brett Ayres

Retrospective audit of outpatient pre-operative chest x-rays and their contribution to pre-operative management in patients who meet and do not meet existing guidelines

Radiology

AIM:
This retrospective study on 200 outpatients who received pre-operative chest x-rays in May and June 2012 aims to determine if the clinical notes provided warranted the investigation, if the patients met existing guidelines for pre-operative chest x-rays (cardiopulmonary disease, suspected or confirmed malignancy, immunosuppression, significant smoking history, American Society of Anaesthesiologists score >2, acute clinical findings, age >70), and if the findings affected pre-operative management.
METHOD:
200 outpatients who received pre-operative chest x-rays in May and June 2012 were included. Data were collected from scanned medical records, picture archiving and communication system, and radiology information system. Categorical variables were summarised using frequency and percentage. Continuous variables were summarised using mean and standard error, and median and inter-quartile range.
RESULTS:
N=200; 15.5% of requests had relevant clinical notes, 23.5% had operation details only, and 60.5% had no relevant clinical notes or operation details. Of 154 patients who had recordable risk factors, 12.3% had no relevant risk factors, 9.7% had no risk factor or acute clinical findings. Of the 87 patients who were <70 years old, 12.6% had no risk factor or acute clinical findings. Results regarding the relationship between the chest x-ray findings and patients who met and did not meet existing guidelines will follow.
CONCLUSION:
The majority of patients who received pre-operative chest x-rays met existing guidelines, however, the clinical notes were often insufficient. It is our intention to develop Austin guidelines for pre-operative chest x-ray indications to ensure patients are appropriately investigated and not unnecessarily exposed to radiation.

THURS 37

Jan Heng [1], Stella Liong [2], Michael Permezel [2], Gregory Rice [3], Megan Di Quinzio [2], Harry Georgiou [2]

Cervicovaginal Fluid Biomarkers to Predict Term and Preterm Birth

1. Samuel Lunenfeld Research Institute, Toronto, ON, Canada
2. University of Melbourne
3. University of Queensland, Herston

Introduction:
Preterm birth (PTB) affects approximately 8-13% of all deliveries worldwide, and is a significant contributor of infant mortality and morbidity. Therefore, the discovery of biomarkers to predict PTB is warranted. During pregnancy, the physiological changes that occur in the cervix and overlying fetal membranes is reflected in the cervicovaginal fluid (CVF). Both term and preterm labour share a final common pathway of cervical ripening, myometrial activation and membrane rupture. Therefore, CVF biomarkers of term labour may also be useful in predicting PTB.

Method:
Proteomic analysis using 2D-PAGE was performed on two studies (n=9 women for each study) using CVF samples collected at term. ELISA validation of selected biomarkers was performed on an independent cohort of term women (n=300 samples from 70-120 women). 2D-DIGE and 2D-PAGE was also performed on CVF collected 6-23 days before preterm premature rupture of fetal membranes (PPROM) with subsequent PTB (n=5) and gestation-matched term controls (n=10).

Results:
IL1RN, CSTA, SOD1, TRX1, GSTP1-1, PRDX2, FABP5, ALBU, ANXA3, COL4A2, SERPINB1, SERPINB3 and SERPINB4 were significantly altered with term labour (p<0.05). Changes in IL1RN, CSTA, SOD1 and TRX1 were validated by ELISA (p<0.05). IL1RN, TRX1, FABP5, CSTA, GGCT, ANXA3, VDBP, SERPINB1 and SERPINB3 were also altered in the PPROM group.

Conclusion:
Common altered proteins were identified between normal term labour and PPROM. These proteins are involved in anti-inflammatory activity, protease inhibition and oxidative stress defence; highlighting the complex and diverse biochemical pathways involved in labour onset. The generation of a multi-biomarker test would improve the prediction of PTB.

THURS 38

Rachel Cooke, Stephen Valentine, Gerard Hale, Carole L Smith, Raymond Dauer

EVALUATION OF CD64 AS A MARKER OF EARLY SEPSIS AND PREDICTOR OF RECOVERY IN NEUTROPENIC PATIENTS POST MYELOABLATIVE CHEMOTHERAPY, AND ITS CORRELATION WITH LABORATORY MARKERS OF SEPSIS AND ABSOLUTE NEUTROPHIL COUNT.

Austin Pathology, Austin Health

Background and Aim

Sepsis invariably occurs in patients with prolonged, severe neutropenia (<0.5 x10^9/L) and, in patients receiving myeloablative chemotherapy, it is critical to commence broad spectrum antibiotics at the first sign of sepsis which may not be clinically obvious. CD64 (also known as FCγRI) is a high affinity receptor to IgG that is up-regulated on polymorphonuclear cells (PMN) in response to IFNγ and granulocyte-colony stimulating factor (G-CSF). Quantitative PMN CD64 expression by flow cytometry has been shown to be a sensitive and specific marker of sepsis in emergency and post-operative settings in adults and children. This study aims to show that PMN CD64 can be a valid and early marker of sepsis in patients with severe neutropenia.

Methods

Twenty patients accounting for 30 episodes were recruited from the haematology unit who were receiving myeloablative chemotherapy as treatment for various haematological malignancies. Daily PMN CD64 index measurements were correlated with clinical and laboratory evidence of sepsis. Patient receiving G-CSF were excluded from analysis.

Results

441 PMN CD64 measurements showed significant differences ($p<0.0001$) between patients who were not septic, were septic or were receiving G-CSF. PMN CD64 Index showed a sensitivity of 97% but low specificity (49%); strong negative predictive value(96%), but only 57% positive predictive value. PMN CD64 did not appear to normalise before CRP on resolution of sepsis.

Conclusion

Provided that there was a clearly definable population of neutrophils to gate on flow cytometry, PMN CD64 was a sensitive marker of sepsis when patients were severely neutropenic.

THURS 39

Chandran, S. [1], Parker, F. [2], Lontos, S. [1,3], Vaughan, R. [1,3], Efthymiou M [1]

Optical diagnosis of diminutive polyp histology with narrow band imaging: Accuracy without optical magnification and the financial impact on the health system.

1. Department of Gastroenterology, Austin Health.
2. Department of Anaesthetics, Austin Health
3. Department of Gastroenterology, Warringal Private Hospital, Heidelberg

Background:
The majority of colonic polyps are diminutive with benign histology, yet the cost of resection, histological analysis and outpatient follow-up is substantial. Objective: To validate non-magnified NBI assessment of meshed capillary (MC) pattern to determine underlying polyp histology and predict appropriate surveillance intervals.
Design:
Prospective cohort study Setting: Tertiary care center and a private hospital. Patients: 94 patients who underwent colonoscopy and polypectomy of diminutive (<5mm) polyps from October 2012 – July 2013 were recruited, yielding a total of 159 polyps.
Intervention:
Polyps were interrogated with NBI and classified according to their MC pattern (Sano-Emura classification). The endoscopic assessment of polyp histology was then used to predict appropriate surveillance intervals.
Main outcome measurement:
Accuracy of optical diagnosis of diminutive colonic polyps against the gold standard histological assessment.
Results:
Optical diagnosis was correct in 105/108 (97.2%) adenomas. This yielded a sensitivity, specificity, positive and negative predictive value (with 95%CI's) of 97.2% (92.1 - 99.4%), 78.4% (64.7 -88.7%), 90.5% (83.7 - 95.2%) and 93% (80.9 – 98.5%) respectively. Ninety-two (98%) patients were correctly triaged to their repeat surveillance colonoscopy. Therefore a cut and discard approach would have resulted in a saving of $504 per patient.
Limitations:
Endoscopic assessment of sessile serrated adenoma.
Conclusion:
Endoscopists of varying experience can accurately predict diminutive polyp histology using NBI to assess MC patterns and confer an appropriate surveillance interval immediately post procedure with an associated financial benefit to the healthcare system. The short learning curve and simplified classification system may lend this technique to be generalizable across our cohort.

THURS 40

Chandran, S. [1], Parker, F. [2], Vaughan, R. [1], Efthymiou, M. [1]

The current practice standard for colonoscopy in Australia

1. Department of Gastroenterology, Austin Health
2. Department of Anaesthetics, Austin Health

Background and study aims:
Despite having one of the highest rates per capita for colonoscopy worldwide, colorectal cancer remains the second most commonly diagnosed malignancy in Australia.
Our aim was to document colonoscopy/polypectomy practice nationwide and assess whether significant differences exist.
Methods:
An observational study via an online survey was conducted during 2012. Participants were medical practitioners registered with the Gastroenterological Society of Australia practising colonoscopy. End points include rates of polypectomy techniques for varying polyp sizes, post polypectomy bleeding prophylaxis techniques, and adenoma detection practices. Secondary end points were whether variations exist according to practice location, specialty, experience and comparison of practice to a previous American cohort.
Results:
Of the 846 members contacted, 244 (28.8%) responded. The cohort consisted primarily of consultant gastroenterologists (182/244, 74.6%). Cold snare technique was preferred (165/244, 67.6%) for polyps 3mm in size, however this reduced rapidly for increasing polyp size [5mm (120/244, 49.2%) and 7-9mm (18/244, 7.4%)]. Endoscopic mucosal resection was the preferred method of resection for polyps 7-9mm (148/244, 60.7%). Withdrawal technique predominantly consisted of double passing high-risk areas and rectal retroflexion (134/244, 54.9%). Significant differences across specialty, location, experience and between the American cohort included polypectomy method for diminutive polyps, the use of EMR and retroflexion.
Conclusion:
Whilst variations in colonoscopy and polypectomy practice exist, the majority of our cohort undertakes cold snare polypectomy for diminutive polyps and pass high risk poorly visualized areas twice on withdrawal. This is a significant shift in practice from the US cohort studied 10 years earlier.

THURS 41

S. Chandran [1], R. Vaughan [1], M. Efthymiou [1], J. Sia [1], C. Hamilton [2]

A pilot study of EUS guided fiducial insertion for the multidisciplinary management of gastric cancer

1. Department of Gastroenterology, Austin Health
2. Department of Radiation Oncology, Austin Health

Background:
Five year survival rates for gastric cancer remain poor despite evolving therapies. Fiducial insertion via EUS is novel within this setting with only two cases reported in the literature.
Objective:
To assess the feasibility of fiducial insertion for response assessment and anatomical localization in gastric cancer.
Design:
Prospective phase II feasibility study. Setting: Austin Health (Victoria, Australia) from February 2011 to November 2012.
Patients:
Consecutive adult patients with primary adenocarcinoma of the stomach with cancer stage (T1-3,N0-1,M0-1a), ECOG 0 or 1, medically suitable for gastrectomy and chemotherapy/chemo radiotherapy.
Interventions:
EUS guided insertion of gold fiducial markers into the margins of the gastric cancer primary.
Main outcome measurements:
Successful insertion of the fiducial without complications for response assessment and anatomical localization.
Results:
A total of 15 fiducials were successfully inserted into 7/8 (88%) patients. No immediate of delayed complications were noted. One patient proceeded to image guided radiotherapy through the use of the fiducials and is disease free at 12 months. Fiducials were used for treatment response in all patients who underwent CT imaging post insertion. Only 1/6 (16.7%) patients were found to have fiducial markers present in the gastrectomy specimen for anatomical localization.
Limitations:
Small cohort.
Conclusions:
Within the limitations of our small study cohort, EUS guided fiducial placement in gastric cancers was performed without complications and successful in the majority of our patients. Whilst potential benefits exist there remain substantial limitations to the generalization of this technique across our patient population.

THURS 42

Kathryn M. Marshall, Marie Laval, Mildred Yim, Arthur Shulkes, Oneel Patel, Graham S. Baldwin

Elevated gastrin levels protect against hypoxia-induced weight loss in mice

Department of Surgery, University of Melbourne, Austin Health

Hypoxia, or reduced oxygen, occurs in a variety of clinical, pathophysiological and environmental situations. Expression of amidated and non-amidated forms of gastrin are upregulated by hypoxia in gastrointestinal cell lines [1]. Oxygen availability is dependent on the blood concentration of the iron-containing oxygen carrier haemoglobin. This together with our data demonstrating an inter-relationship between gastrins and iron homeostasis [2] may establish a crucial link between iron status, hypoxia and gastrins.

Aim:

To investigate whether gastrin overexpression in mice enhances the adaptation to a hypoxic environment.

Methods:

Mice over-expressing human progastrin (hGAS) and wild type FVB/N mice were subjected to normoxia (21% oxygen) or hypoxia (10% oxygen) for 10 days using a hypoxia chamber. Mice were weighed daily and blood and tissues collected for further analyses.

Results:

hGAS mice lost significantly less weight (15%) exposed to hypoxia, compared to their normoxic counterparts. Hypoxic FVB/N mice had a decreased spleen weight and reduced number of platelets compared to normoxic FVB/N mice. No difference in spleen weight was observed in hGAS mice.

Conclusion:

Higher levels of gastrins decreased the amount of weight loss in animals exposed to hypoxia, providing evidence that gastrins may play a protective role in low oxygen conditions.

1. Xiao, L. et al. Induction of gastrin expression in gastrointestinal cells by hypoxia or cobalt is independent of hypoxia-inducible factor (HIF). Endocrinology 153, 3006-16 (2012).
2. Kovac, S. et al. Gastrin-deficient mice have disturbed hematopoiesis in response to iron deficiency. Endocrinology 152, 3062-73 (2011).

THURS 43
This abstract has not been included at the request of the author

THURS 44

David McD. Taylor [1], Paul Joffe [2], Simone E Taylor [3], Alicia Jones [4], John Cheek [5], Simon Craig [6], Andis Graudins [7], Reetika Dhir [1], Franz Babl [4], David Krieser [2]

Paediatric Emergency Department patients administered a high rate of off-label medicines

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Aim
To determine the prevalence, nature and safety of off-label medicine administration to paediatric emergency department (ED) patients.
Methods
We undertook a retrospective, observational study in six EDs (July 2011 to June 2012, inclusive). Patients, aged 0-17 years, who were administered a medicine in ED were included. At each site, 50 eligible patients were randomly selected each month of the study period. An explicit review of the medical records of each enrolled patient was undertaken. Medicines were classified as on/off-label according to categories of use approved by the Therapeutic Goods Administration. All adverse drug reactions were recorded.
Results
3343 patients were enrolled (56.5% male, mean age 7.2±5.2). Of the 6786 doses administered, 30.8% (95% CI 29.7-31.9%) were classified off-label. The off-label administrations were attributed to 653 (19.5%) patients. The mean number of off-label medicines per patient was 0.63 overall and 3.6 per patient, for those who had at least one off-label dose. In 1052 cases, the dose or frequency was greater than that approved, in 161 the medicine was not approved for the weight or age, in 743 there was an unapproved indication for treatment, in 188 the medicine was administered via an unapproved route and in 227 a non-TGA approved product was administered. Salbutamol, ondansetron, ipratropium, oxycodone and fentanyl were the medicines most-commonly prescribed off-label. No adverse reactions were identified.
Conclusion
The rate of off-label medicine administration to paediatric ED patients is high. This has implications for patient safety, drug licensing, medico-legal issues, best practice guidelines and future research.

THURS 45

Xiao-Fang Wang, Ali Ghasem-Zadeh, Qingju Wang, Jiawei Teo, Sandra Iuliano, Roger Zebaze, Yohann Bala and Ego Seeman

Differences in Cortical and Trabecular Microstructure in Chinese and Caucasian Females originate during Peripubertal Growth

Department Endocrinology and Medicine, University of Melbourne, Austin Health

Chinese women have fewer hip and forearm fracture rates despite having smaller and more slender bones. The aim of the study is to examine the underlying structural and biomechanical basis of the lower fracture risk in Chinese.

We studied distal radius images acquired using high-resolution pQCT (XTreme CT, Scanco) were quantified for 81 healthy Chinese and 103 Caucasian women aged 7 to 46 years using Strax 1.0, a non-threshold based image analysis algorithm that segments the mineralized matrix and void volumes of the compact-appearing cortex, the transitional and trabecular regions. The proportion of void (porosity) was quantified as the average of void spaces in each voxel. The 1st CT slice commenced at the 4% of the radius length in children (under 18 years old) to adjust for any effects of bone length on scan region.

There was no detectable structural difference between races before puberty. After menarche, Chinese had a similar cortical area but smaller medullary area relative to Caucasians (105.6 vs.124.4 mm2 $p<0.05$) and lower porosity of the compact-appearing cortex, outer and inner transitional zones (36.5 vs. 40.4%; 45.8 vs. 49.1%; 74.2 vs. 75.9% respectively, $p = 0.1$). Similarly, Chinese pre-menopausal women had a similar cortical area but a smaller medullary area (111.1 vs. 138.4 mm2, $p<0.001$), and lower porosity of the compact-appearing cortex, outer and inner transitional zone (21.0 vs. 23.1%; 31.3 vs. 33.0%; 67.8 vs. 69.3% respectively, all $p<0.01$).

Modelling and remodelling assemble a more robust skeleton in Chinese than Caucasian women. The smaller bone has a relatively thicker and less porous cortex perhaps attributed to excavation of a smaller medullary canal and fewer osteons. These morphological features may contribute to the lower fracture risk in Chinese women.

THURS 46

This abstract has not been included at the request of the author

THURS 47

Jwu Jin Khong [1,2]**, Rebecca F Goldstein** [1]**, Hans Schneider** [3,4]**, Jeffrey Pope** [3]**, Kerrie M Sanders** [1]**, Kathryn P Burdon** [5]**, Jamie E Craig** [5]**, Peter R Ebeling** [1]

Relative selenium deficiency in Graves' Orbitopathy

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4. Central Clinical School, Monash University
5. Department of Ophthalmology, Flinders University

Context: Selenium is effective in improving quality of life and reducing the progression of active Graves' orbitopathy, possibly by reducing oxidative stress. The effect of correcting relative selenium deficiency on improving Graves' orbitopathy is unknown, as baseline selenium levels have not previously been measured.
Objective:
To determine if serum selenium levels are reduced in patients with Graves' orbitopathy compared with patients without orbitopathy.
Design and Setting:
A prospective, case-control study performed between 2009 and 2012 at endocrine and ophthalmology clinics in Australia. A total of 200 patients with Graves' disease participated in the study: 101 with Graves' orbitopathy and 99 without Graves' orbitopathy.
Results:
Mean serum selenium levels were significantly lower in patients with Graves' orbitopathy (1.10+/-0.19µmol/L) compared with patients without orbitopathy (1.19+/-0.20µmol/L) (P=0.002). Serum selenium levels remained significantly lower in Grave's orbitopathy cases after adjusting for age, smoking status, thyroidectomy and radio-active iodine treatment.
Conclusion:
Serum selenium levels are lower in patients with Graves' orbitopathy compared with controls. Relative selenium deficiency may be an independent risk factor for orbitopathy in patients with Graves' disease.

THURS 48

Anna Ryan

Peer Engagement in Long Case Tutorials

Austin Clinical School, University of Melbourne, Austin Health

Introduction/Background: Typically, long case examination tutorials involve a format of one student presenting while the tutor and other students listen. Active participation from all students is often not required nor encouraged.
Purpose/Objectives: A 50 minute long case tutorial was designed, giving non-presenting students a structured examiner role. The tutorials were conducted in groups of eight, with each student given a card outlining their role during that tutorial.
These tutorials were provided for 2 groups of year 5 medical students (2010). They were introduced with a brief outline of the review of examiner mark sheets, and a discussion about the value of engagement in learning.
This poster presentation will outline the tutorial design, provide detail of the individual student "examiner" roles and present the results of the pilot study.
Results: Both groups of students rated the overall learning experience of the tutorials highly (9.5 & 10 out of 10 respectively) and results in final year long case assessments were encouraging with 75% of the long case tutorial students achieving a "Good" or "Excellent" result in their end of semester long case examination, compared to 60% of the 83 students who did not have these tutorials within the same clinical school environment.
Conclusion: This poster will present a model of long case tutorial design which may be helpful for tutors involved in medical education. This experience suggests that students value peer feedback and find it useful within a semi-structured long case tutorial environment.

This is a poster presentation and it has already been presented (in June this year) at the Australian & New Zealand Association of Health Professional Educators Conference in Melbourne. Due to the relevance of the topic to Medical staff at the hospital, it is being offered for presentation again during research week.

THURS 48A

Anna Ryan, Barbara Goss

The University of Melbourne MD

University of Melbourne, Austin Clinical School, Austin Health

Aim: The new MD program was introduced in 2011 with the first cohort of MD students arriving at Austin Health in 2012. Although this new program has run for nearly 2 years, there is still considerable confusion about how this course and its students, differ from the old MBBS program.

Methods: The proposed poster will provide an outline of the new 4 year Melbourne MD course. It will highlight the educational background of the new MD students and include pictorial representation of the overall course structure and each academic year of the new program along with brief description of the course and its unique features.

Conclusion: This poster will be of interests to all Austin Health staff who have involvement with medical students as it will provide a clear description of the new MD program and students.

THURS 49

K. Burton, F. Ciavarella, R. Griffiths

AUSTIN HEALTH STAFF ADHERENCE TO THE ORGANISATION WIDE POLICY OF USING 'THREE' PATIENT IDENTIFIERS: A PROSPECTIVE AUDIT

Quality, Safety and Risk Management, Austin Health

Aim: To evaluate Austin Health staff's compliance with the policy for the use of 'three' patient identifiers when providing care or prior to a therapeutic intervention.

Methods : In July 2013 a total of 592 observational audits were conducted in 40 areas across Austin Health were conducted. Local champions conducted each audit using a structured observation tool.

Results:

Audit findings revealed a 'three patient identifiers' compliance rate of 84%. Areas that were 100% compliant were 2West, Cath lab, Social work, Continence clinic, NECCS, Darley House, Non-emergency transport, Spinal rehabilitation centre, 3North, OVPP, PTRS, NEAMS, RT Psych Service, Nuclear Medicine and HITH. Areas with the lowest compliance rate were Pastoral Care (0%), Nutrition & Dietetics (40%), Emergency Department (50%), 7North (50%), Palliative Care (50%). Of the 592 audits undertaken 76% (499) patients were able to state their details, 37% (22) were identified using their ID band and 2% (13) were identified through a guardian/carer. Sixty six patients (11%) were identified using photographic ID or other document forms. The three most frequently used identifiers were: patient's name (83%), unit record (UR) number (for in-patients) (81%) and patient's date of birth (80%).

Conclusions: Austin Health staff are largely compliant with the use of three patient identifiers when providing care or prior to performing a therapeutic intervention. The most commonly used patient identifiers were: patient name, UR number and DOB. Repeat auditing, especially in high-risk areas, together with educational strategies to highlight the importance of using three patient identifiers every time should be continued.

THURS 50

K. Yeaman, K. Burton, F. Ciavarella

EVALUATION OF CLINICALCARE PROCESSES USING THE INTEGRATED BEDSIDE AUDIT TOOL (BAT)

Quality, Safety and Risk Management, Austin Health

Background:
With the introduction of the National Safety and Quality Health Service Standards (NSQHSS), there are significant audit requirements to ensure that care in high risk clinical areas is being provided to all patients in a systematic way. To reduce the number of audits needed and to improve audit consistency throughout Austin Health, the Quality, Safety and Risk Management Unit developed an integrated Bedside Audit Tool (BAT) based on the NSQHSS that covers multidisciplinary care processes. Designed to be completed on 10 patients per quarter, the BAT captures the whole patient journey with results reported back to participating wards, units and organisational governance committee's.

Aim:
To assess clinical ward compliance with the National Safety and Quality Health Service Standards and identify areas of clinical improvement across Austin Health.

Methods :
In June 2013, 245 patients were audited using the BAT tool from 24 wards across Austin Health. Local champions conducted each audit that included components of a structured observation tool, chart review and patient interview.

Results:
The findings of the 245 complete BAT audits addressed various aspects pertaining to Standards 2-10 of the NSQHSS. Areas of strength included use of patient identifiers; nursing care plan for documentation of nursing handover, falls and pressure injury; observation and response chart completion. Identified areas for improvement included: distribution of patient information brochures to patients; greater use of Cerner 'allergy' and 'VTE risk' documentation; promotion of the use of the nursing care plan to guide care interventions; and a need to outline documentation processes for Urgent Clinical Review (UCR).

Conclusions:
THE BAT has provided Austin Health ward areas with a single audit tool encompassing multiple NSQHSS Standards. Refinement and adoption of the BAT will provide long-term assessment of clinical care processes and benchmarking between wards and other external organisations.

THURS 51

Suet-Wan Choy [1,2,3]**, Scott A Fraser** [1]**, Matthew RP Davies** [1,2,3]**,Natasha Cook** [2]**, Marina Katerelos** [1]**, Peter F Mount** [1,2,3]**, Kurt Gleich**[1]**, Karen M Dwyer** [5]**, Kenneth R Hallows** [4]**, Bruce E Kemp** [6] **and David A Power** [1,2,3]**.**

A link between metabolism and renin: renin secretion in mice with mutations of the AMPK/ACC1 pathway

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6. St. Vincent's Institute, Fitzroy 3065, Victoria, Australia.

Introduction:
Salt reabsorption is the major energy-requiring process in the kidney and AMP-activated protein kinase (AMPK) is an important regulator of cellular metabolism. AMPK controls fatty acid metabolism by phosphorylation of acetyl-CoA carboxylase (ACC).

Methods and Results:
Mice with a targeted deletion of the b1 subunit of AMPK (AMPK b1-/- mice) had normal renin secretion. When placed on a salt-deficient diet, they were able to conserve urinary sodium but renin secretion increased 2.8-fold compared with controls.

To determine whether the increase in renin secretion was due to a change in regulation of fatty acid metabolism by AMPK, mice with a mutation of the inhibitory AMPK phosphosite in acetyl-CoA carboxylase 1 (ACC1-KIS79A mice) were examined.

When placed on a salt-deficient diet renin secretion increased significantly in the ACC1-KIS79A mice compared to controls. Biochemical studies showed that NKCC2, the major salt sensor for renin secretion in the kidney, co-localises with activated AMPK, and co-immunoprecipitates AMPK and ACC1 from the kidney.

Conclusion: This data demonstrates that renin synthesis and secretion are regulated by AMPK and coupled to metabolism by phosphorylation of ACC1. The complex of NKCC2, AMPK and ACC1 in the macula densa acts as a critical sensing node, linking energy metabolism with salt conservation.

THURS 52

Matthew R. P. Davies [1,2,3]**, Marina Katerelos** [1]**, Kurt Gleich** [1]**, Scott A. Fraser** [1]**, Peter F. Mount** [1] **and David A. Power** [1,2,3]

Enhanced Phosphorylation of NKCC2 by SPAK/OSR1 in a Murine Model of Diet Induced Obesity

1. Department of Nephrology, Austin Health
2. Institute of Breathing and Sleep, Austin Health
3. Department of Medicine, University of Melbourne, Austin Health

Aim:
To determine mechanisms of enhanced tubular sodium retention in obesity.
Methods:
C57Bl/6 mice were fed 40% (high fat, HFD) or 12% (control, CD) fat diets for 14 weeks. Abundance and phosphorylation of proteins were determined by western blotting. Surface expression was analysed with immunofluorescence. In vitro studies used murine embryonic fibroblasts (MEF's) from ß1-AMPK-/- and ß1-AMPK+/+ mice.
Results:
HFD mice gained weight and developed hyperinsulinaemia & hyperleptinaemia. Cortical expression of NKCC2 was reduced but activating phosphorylation (T96/T101) was increased. No change in expression or phosphorylation of NCC was found. Surface localisation of transporters was unchanged. SPAK/OSR1 is known to phosphorylate NKCC2 on T96/101. Phosphorylation of SPAK/OSR1 on S373/325 was increased, consistent with increased activity of the WNK/SPAK/OSR1 pathway. AMPK inhibition is involved in mediating obesity-related renal injury. Active AMPK (phosT172) was reduced in HFD mouse cortex. SPAK/OSR1 and AMPK were found to co-immunoprecipitate with NKCC2, indicating a possible kinase-kinase interaction. In vitro, activation of AMPK led to a reduction in S373/325-phos-SPAK/OSR1 in ß1-AMPK+/+ MEF's. No effect was seen in ß1-AMPK-/- MEF's, indicating a specific AMPK-mediated effect. Low Cl- solution invoked a significantly greater increase in S373/325-phos-SPAK/OSR-1 in ß1-/-AMPK MEF's than in ß1+/+AMPK MEF's, supporting an inhibitory role of AMPK in modulating the WNK/SPAK/OSR1 pathway.
Conclusions:
NKCC2 is the most important sodium co-transporter in this model of obesity-related hypertension. Enhanced phosphorylation of NKCC2 occurs due to activation of SPAK/OSR1, which itself may be secondary to AMPK inhibition. These data identify NKCC2, SPAK/OSR1 and AMPK as therapeutic targets in obesity-related hypertension.

THURS 53
This abstract has not been included at the request of the author

THURS 54

V. Dore [1], P. Bourgeat [1], L. Zhou [1], J. Fripp [1], R. Martins [2], L. Macaulay [1,3], K. A. Ellis [4,5], C. L. Masters [4,6], D. Ames [7,8], B. Brown [9], C. Rowe [10], O. Salvado [1], V. Villemagne [10] and the AIBL Research Group

MR-less cortical surface-projection of PET scans with 11C and 18F Labeled radiotracers

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9. Edith Cowan University, School of Medical Sciences, WA
10. Department of Nuclear Medicine and Centre for PET, and Department of Medicine, University of Melbourne, Austin Health

Background:
Clinical PET imaging in Alzheimer's disease relies in the visualisation of $A\beta$ deposition and glucose metabolism in the cortical gray matter. Due to the limited structural information in PET images, automatic tissue-specific assessment is usually performed with the aid of MR images, which may not always be available. We evaluated a novel MR-less method to locally estimate and project the cortical tracer retention on a common surface template.
Methods:
Several subjects were scanned with different radiotracers: 18F-Flutemetamol, 18F-Florbetapir, 18F-Florbetaben, 11C-PIB, 18F-NAV4694 and 18F-FDG. First, each individual PET image was normalised in the MNI space and SUVR scaled with a common cortical cerebellum mask. Radiotracer retention was then estimated within several GM prior atlases. On scans acquired on a PET/CT scanner, CT was used to estimate the GM priors. Atlas selection and Bayesian fusion were then used for generating estimated surface values, reflecting the pattern of higher ($A\beta$ ligands) or lower (FDG) tracer retention. Surface projections and native transaxial, sagittal and coronal PET images were visually graded by clinicians blinded to clinical diagnosis. Images were read separately and graded as normal, possible AD or probable AD. For sensitivity and specificity calculations, "possible" and "probable AD" were combined.
Results:
In the visual readouts, surface projection images provided higher inter-rater reliability and much greater reader confidence than native PET images. Visual assessment of surface projections were both very sensitive and specific for AD and performed better than visual readouts of native PET images.
Conclusions:
The proposed method demonstrated accurate estimations of radiotracer retention in the cortex for various 11C and 18F labeled radiotracers. Our approach provides a practical and efficient clinical inspection tool for PET.

THURS 55

Xiaoyun Liang [1,2], Alan Connelly [1], Fernando Calamante [1]

A novel efficient denoising method for ASL data: Assessment using voxel-wise network analysis

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2. Department of Medicine, University of Melbourne, Austin Health

Introduction:
Arterial spin labeling (ASL) is a technique to measure cerebral blood flow directly. However, given its intrinsic low SNR, the reliability of detecting networks, and thus that of measuring network metrics, is compromised. To enhance the reliability of measuring network metrics using ASL, we propose a method of combining non-local means (NLM）and dual-tree CWT (DT-CWT) to remove noise and preserve the true ASL signal more efficiently.
Methods:
Simulation: Simulated data were generated based on one of the acquired ASL images, with 8 different levels of (Rician) noise added. In vivo data: 2 healthy subjects were scanned on a 3T Siemens Trio scanner with a whole-brain 3D-GRASE pCASL sequence. The proposed denoising method was applied to both simulated and in vivo data.
Results:
Our results show increased sensitivity to detect connectivity and hub voxels by using the proposed method; this suggests that the loss of hubs caused by noise can be compensated by applying the proposed denoising method. The R2 values of degree distribution fitting demonstrate that the data, after denoising with the proposed method, can be better characterized by the exponentially truncated power law model than the original data.
Conclusion:
Simulations show that the proposed method was superior to DWT. The validity of the proposed method has been further confirmed by the more robust detection of functional connectivity from in vivo data. Overall, the proposed method can enhance the SNR of ASL data significantly and thus enable more reliable network detection.

Robert E. Smith [1]**, J-Donald Tournier** [1,2]**, Fernando Calamante** [1,2] **and Alan Connelly** [1,2]

The effects of SIFT on the reproducibility of the structural connectome

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2. Department of Medicine (AH/NH), The University of Melbourne, Austin Health

Introduction:
Characterisation of the brain connectome using diffusion MRI streamlines tractography is limited by the non-quantitative nature of the streamlines reconstruction process. The Spherical-deconvolution Informed Filtering of Tractograms (SIFT) method has been proposed for improving the correspondence between a whole-brain streamlines reconstruction and the underlying diffusion image data; and, by doing so, providing a quantitative measure of white matter connectivity. In this study, we investigated the effects of SIFT on the reproducibility of the structural connectome.
Method:
Image data were acquired from 8 healthy volunteers, with 8 repeated scans of one volunteer. Variables in connectome construction that were studied included: using either 10 million streamlines (denoted '10m'), or filtering 100 million streamlines to 10 million using SIFT ('SIFT'); initialising streamlines either throughout the white matter ('WM') or at the grey matter – white matter interface ('GMWMI').
Reproducibility of the connectome was assessed in four scenarios (N=8 for all):
•   Repeated reconstruction from a single scan ('Intra-scan')
•   Variation in streamline initialisation ('Inter-seeding')
•   Scan-rescan testing of a single volunteer ('Intra-subject')
•   Scanning of different subjects ('Inter-subject')
Variability of the connectome was summarised using a weighted mean of coefficients of variation of individual connections.
Results:

	Intra-scan		Inter-seeding	Intra-subject		Inter-subject	
Seeding	WM	GMWMI	Both	WM	GMWMI	WM	GMWMI
10m	0.0745	0.0874	0.4216	0.3074	0.3125	0.6048	0.5913
SIFT	0.0889	0.0956	0.2596	0.2780	0.2767	0.4998	0.4921

Conclusion: Inclusion of the SIFT method prior to connectome construction in fact improves its overall reproducibility. This result further motivates its use for structural connectome construction.

THURS 57

Robert E. Smith [1], **J-Donald Tournier** [1,2], **Fernando Calamante** [1,2] and **Alan Connelly** [1,2]

Evidence for the improved biological interpretability of white matter connectivity derived following tractogram filtering using SIFT

1. Imaging division, The Florey Institute of Neuroscience and Mental Health
2. Department of Medicine (AH/NH), The University of Melbourne, Austin Health

Introduction: Characterisation of the brain connectome requires a biologically relevant quantification of connectivity between grey matter areas. The Spherical-deconvolution Informed Filtering of Tractograms (SIFT) method has been proposed for improving the correspondence between a whole-brain streamlines reconstruction and the underlying diffusion image data; and, by doing so, providing a quantitative measure of white matter connectivity. In this study, we compared properties of the structural connectome estimated using streamlines tractography, with and without the application of SIFT, to estimates derived from post mortem human brain dissection.

Method: Image data were acquired from 8 healthy volunteers. Variables in connectome construction that were studied included: using either 10 million streamlines (denoted '10m'), or filtering 100 million streamlines to 10 million using SIFT ('SIFT'); initialising streamlines either throughout the white matter ('WM') or at the grey matter – white matter interface ('GMWMI'). The following connectome properties were compared to the corresponding dissection estimates:

•   Proportion of inter-hemispheric connections
•   Proportion of intra-hemispheric, long-range connections
•   Histograms of streamline length

Results:

	Inter-hemispheric	Intra-hemispheric long-range
Dissection	≈ 2%	≈ 2%
WM 10m	13.7 ± 1.6%	16.3 ± 1.8%
WM SIFT	2.8 ± 0.5%	5.9 ± 0.7%
GMWMI 10m	5.3 ± 0.7%	7.4 ± 1.0%
GMWMI SIFT	1.8 ± 0.3%	3.2 ± 0.4%

All assessed properties of streamlines reconstructions show improved correlation with dissection estimates if the SIFT method is applied, and if seeding is performed at the GMWMI.

Conclusion: SIFT is an important processing step to ensure that derived properties of the structural connectome are biologically relevant.

S. Farquharson [1,2,3], **J-D Tournier** [1,2], **F. Calamante** [1,2], **S. Mandelstam** [1,4], **M. Schneider-Kolsky** [3], **S.F. Berkovic** [5], **I.E. Scheffer** [1,5,6], **G. Jackson** [1,2], **A. Connelly** [1,2]

Whole Brain Tractography Mapping Reveals Abnormal Structural Connections in Neuronal Heterotopia

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Aim:
Individuals with neuronal migration disorders such as Periventricular Nodular Heterotopia (PVNH) often present with epilepsy, which is refractory to medical and surgical treatment[1]. Although heterotopias have been well described in the radiological literature[1], it has not been possible using in vivo imaging to investigate the internal architecture of heterotopic nodules. In this study, we apply novel diffusion MRI based whole-brain fibre tractography mapping to patients with PVNH to investigate the presence of abnormal structural fibres in regions of heterotopia.
Methods:
Fifteen patients with neuroimaging-confirmed diagnosis of heterotopia and a cohort of normal volunteers were recruited for this study. Axial DWI data were acquired on a 3T Siemens MRI system using 60 directions & b-value: 3000s/mm2. Each data set was analysed using the MRtrix package[3] to obtain whole-brain tractography images using Constrained Spherical Deconvolution (CSD)[2] and Track Density Imaging (TDI)[3].
Results:
Increased densities of oriented streamlines suggestive of abnormal fibre connections were observed emanating from at least one region of heterotopic grey matter in the majority of patients. These structures were not present in all nodules within individual patients, and were not present in the healthy control cohort.
Conclusion:
Whole brain tractography mapping revealed the presence of abnormal fibres emanating from heterotopic nodules in the majority of PVNH patients studied. The ability to visualise the presence of novel fibre bundles in disorders of neuronal migration is a significant radiological advance. It is an important step toward understanding cortical development malformations, in particular, which parts may interfere with normal brain functions.

THURS 59

Konstantine Sfrantzis, Jackie M.Y. How & Daniela M. Sartor

UNDERSTANDING THE MECHANISMS INVOLVED IN THE AETIOLOGY OF OBESITY-RELATED HYPERTENSION: IMPLICATIONS OF DIET MODIFICATION

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We have previously demonstrated that the gut hormone cholecystokinin (CCK) is involved in cardiovascular regulation via a sympathetic reflex. However, renal and splanchnic sympathoinhibitory and vasodilator responses to CCK are blunted in obese hypertensive rats fed a medium high fat diet (MHFD), possibly impacting on cardiovascular homeostatic mechanisms and contributing to the aetiology of obesity-related hypertension.

In the present study, we sought to determine whether swapping a MHFD for a low fat diet (LFD) would reverse the signs of hypertension and restore sympathoinhibitory reflexes in obese hypertensive rats. Male Sprague-Dawley rats were placed on a LFD (controls; n=8) or a MHFD (n=24) for 11 weeks; the latter animals exhibited either an obesity-prone (OP) or obesity-resistant (OR) phenotype as determined by weight gain falling into the upper or lower tertile, respectively. All animals were then placed on the LFD for a further 6 week period after which they were anesthetised with isoflurane and artificially ventilated for evaluation of resting arterial pressure (AP) and renal nerve responses to CCK (0.1-4 mg/kg).

Weight gain in OP animals remained higher than OR or controls following diet switch ($P < 0.05$ for all concentrations).

These results suggest that diet modification can impact the sympathetic nervous system and restore normotension without the need for weight reduction, further implicating sympathoinhibitory mechanisms in the aetiology of obesity hypertension.

THURS 60

Ana Antonic [2], Mirella Dottori [1], Jessie Leung [1], Geoffrey A. Donnan [2] and David W.Howells [2]

NXY-059 does not protect stem cell-derived human neurons: First use of a novel drug screening protocol

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2. Florey Institutes of Neuroscience and Mental Health

Introduction:
Recent failure of SAINT II clinical trial has prompt a re-evaluation of NXY-059's biochemistry and pharmacodynamics. Systematic review and meta-analysis of the preclinical data suggested that introduction of bias favoured an overoptimistic interpretation of NXY-059's potential but did not conclude that the drug was without effect. A gap in our understanding of NXY-059 is whether they in fact have activity in human tissue.
Aims:
To fill this gap we have derived neurons from human embryonic stem cells (hESCs) and subject them to models of ischemia and oxidative stress.
Methods:
hESCs were differentiated into neurons in the presence of the bone morphogenic inhibitor protein, Noggin and mature neurons we cultured for 11 days. Two injury models were used: Oxygen glucose deprivation (OGD) was induced by 2-deoxy-D-glucose in a hypoxic chamber; Oxidative stress was induced by either 100µM sodium nitroprusside (SNP) or 50µM or 90µM hydrogen peroxide (H2O2). The activity of NXY-059 and antioxidant control (AO) was assessed by measuring cell death (lactate dehydrogenase activity and Tunel Staining) and cell survival (MTT assay).
Results:
Following OGD, NXY-059 had no effect on cell survival at any concentration while the AO reduced the cell death of 55%. SNP and H2O2 induced cell death was also inhibited by the AO but not by NXY-059. Tunel staining indicated that NXY-059 had no effect on apoptosis in these preparations.
Conclusion:
This study demonstrates that NXY-059 has no effect on survival of human stem cell-derived neurons in the face of OGD or oxidative stress. This assay system can be used to provide a reproducible and high throughput screen of candidate drugs for human-specific activity in all relevant cell types and insults before progression to clinical trial.

THURS 61

Sharon F. Kramer [1], Leonid Churilov [1], Rosalie Kroeders [2], Marco Y.C. Pang [3], Julie Bernhardt [1,4]

Changes in activity levels in the first month after stroke

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4. School of Physiotherapy, La Trobe University

Aim
To quantify the activity levels of individuals in an acute stroke ward, and to determine if their activity levels change within the first month after stroke.
Method
In this pilot study, participant activity was monitored prospectively over a single day from 8 a.m. to 5 p.m. on two separate occasions. Individuals with confirmed stroke > 18 years of age and less than 15 days post-stroke at the time of recruitment were eligible for inclusion in this study. Activity was recorded using an electronic device. The first day was scheduled within 15 days and the second at four weeks post-stroke. We looked at the following activity categories: number of transitions, and the times spent lying, sitting and in dynamic activity.
Results
Sixteen individuals were included in this study with a median age of 79.5 years (interquartile range 62.5 to 85). Fifty-six % of the participants had mild, 31% had moderate and 13% had severe stroke, according to the NIHSS score. There were no significant changes in number of transitions, or times spent in dynamic activity and lying and sitting.
Conclusion
Activity levels were low at an acute stroke ward and did not significantly change within the first month.

THURS 62

R. Sheedy [1,2]**, N. Shields** [2]**, L. Churilov** [3]**, D.A. Cadilhac** [3,4]**, J. Bernhardt** [2,3]

Hospital admission for stroke encourages inactivity

1. Barwon Health Geelong
2. La Trobe University
3. The Florey Institute of Neuroscience and Mental Health, Austin Health
4. Translational Public Health Unit, Stroke and Ageing Research, Southern Clinical School, Monash University

Background:.
Early observational studies suggesting patients are 'inactive and alone' stimulated trials of early and frequent mobilisation. Higher resolution (instrumented) measurement may help us refine our practices.
Aim: To prospectively measure the physical activity patterns of patients with acute stroke during hospitalisation.
Method:
Cross-sectional study of consecutive patients admitted to an acute stroke unit and recruited within 48 hours of admission. Physical activity was recorded using an activPALTM accelerometer device over 14 days or the duration of admission (if shorter). Activity was categorised as: time spent inactive (lying or sitting), standing or stepping. Number of steps per day was also recorded.
Results:
Eighty patients were included: mean age 76 (SD 13) years; 48% female; 90% ischaemic stroke, average length of stay 7 days (SD 6). Initial mobilisation occurred within 24 hours of admission for 51% of patients. On average patients spent 96% [SD 3.6] of their admission inactive, 3.3% [SD 3.2] of their admission standing and 0.6% [SD 0.6] of their admission stepping. Patients who were independent on admission (modified Rankin Score <2, n = 17), were less likely to be inactive (Z = –3.205, $p < 0.05$) and more likely to spend time standing (Z = 3.364, $p < 0.05$) and stepping (Z = 1.993, $p < 0.05$). Daily average number of steps per patient was 372 (SD 555).
Conclusion:
Although half the patients were mobilised within 24 hours of admission, little physical activity occurred thereafter, highlighting the ongoing challenge of promoting activity in the acute stroke period.

THURS 63

J. Collier, S. Speare, L. Churilov, A. Thrift, R. Lindley, G. Donnan, H. Dewey, P. Langhorne, J. Bernhardt on behalf of the AVERT Trialist Collaboration

What are the main reasons for exclusion from an early rehabilitation trial (AVERT)?

The Florey Institute of Neuroscience and Mental Health, Austin Health

Aim:
To explore reasons for non-recruitment into A Very Early Rehabilitation Trial (AVERT) and whether rehabilitation commenced within 24 hours reduces death and disability.

Methods:
All patients admitted with stroke were screened. Trial exclusion criteria included: hospital attendance >24 hours after stroke, premorbid disability, early deterioration, admission to ICU and participation in other trials. We used binary logistic regression analyses to explore potential reasons for non recruitment.

Results:
Twenty thousand stroke patients were screened at 44 hospitals from July 2006 to December 2011, with 1158 recruited, 18,842 not recruited. Characteristics of patients not recruited: mean age (SD): 72.0 yrs (14.0); woman 47.3%; infarct 86.7%; stroke severity (NIHSS); mild 53.1%; mod 26.2%; severe 20.7%. In examining reasons for non recruitment (adjusted), patients with mild stroke had greater odds of admission >24 hours (OR 0.6 CI 95% 0.5–0.6) and women had greater odds of premorbid disability (OR 1.5 CI 95%1.3– 1.6). Increasing age (OR 1.1 CI 95% 1.1–1.1), haemorrhagic stroke (OR 2.9 CI 95% 2.5–3.3) and severe stroke (OR 10.4 CI 95% 9.2–11.6) were all associated with deterioration; and patients admitted to ICU had greater odds of having haemorrhagic stroke (OR 2.6 CI 95% 2.2–3.1) or severe stroke (OR 4.3 CI 95% 3.8–4.8). Patients with haemorrhagic stroke had lower odds of recruitment to other trials (OR 0.6 CI 95% 0.5–0.9).

Conclusion:
Exclusion criteria are selected to minimise harm and maximise the likelihood of study completion. Results support a typical clinical pattern for non recruited patients.

THURS 64

J. Bernhardt, of behalf of the AVERT Trialist's Collaboration

A Very Early Rehabilitation Trial (AVERT): Update

The Florey Institute of Neuroscience and Mental Health, Austin Health

Background:
Starting stroke rehabilitation within 24 hours with frequent out of bed activity may be an important component of effective stroke unit care. We hypothesize that early mobilisation will reduce death and disability and be cost effective, compared to standard care.
Aims include high data quality with outcome completion targets: primary ≥90%, secondary ≥90%, cognition and mood ≥80%.
Methods:
AVERT is a multi-centre, single blind randomised controlled trial. Randomization is concealed, with stratification by site and stroke severity. Included: Medically stable patients within 24 hours of stroke. Excluded: Patients with severe pre-morbid disability and co-morbidities. Early rehabilitation starts within 24 hours, for 14 days. Control group patients receive standard care.
Primary outcome: modified Rankin Scale at 3 months.
Secondary outcomes include Barthel Index and Assessment of Quality of Life. Cognitive and mood outcomes are Montreal Cognitive Assessment; and Irritability Depression Anxiety Questionnaire. Sample size is 2104 patients (n=1052 per group). Analyses are intention to treat.
Results:
54 hospitals from 5 countries are participating. At August 2013, 34,777 patients were screened with 1688 patients recruited. Recruited patients: mean(SD) age: 70.4(12.8) years; male: 62.3%; first stroke: 81.7%; infarct: 87.5%; mean(SD) NIHSS: 8.8(6.4); rtPA: 22.1%. 1584 patients have completed 3 month follow up, with 8 dropouts. Primary outcome completion: 99.5%. Secondary outcome completion: 98.2-99.6%, cognition 83.0% and mood 80.8%.
Conclusion:
Trial data quality is high and meeting data completion targets. The Data Monitoring Committee has met 9 times and no safety issues have been identified. We aim to complete recruitment in December 2014.

THURS 65
This abstract has not been included at the request of the author

THURS 66

The-Phung To [1]**, David A Story** [2]**, Jane Booth 1, Fiona Nielsen** [3]**, Joanne Sweeney** [4]**, Patricia Bruce** [5]**, Cathy D'Alterio** [5]**, Melodie Heland** [3]**, Andrew Hardidge** [6]

Improving the management of oral medications in patients who are fasting or nil by mouth.

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3. Surgical Clinical Service Unit, Austin Health
4. Speech Pathology Department, Austin Health
5. Consumer Representative, Austin Health
6. Orthopaedic Surgery, Austin Health

Background:
Medication administration errors have occurred when patients are fasting or nil by mouth and this has led to adverse patient outcomes. Aim: To develop strategies to improve oral medication adminstration in patients who are fasting or nil by mouth.
Methods:
Causes of oral medication administration errors in patients who were fasting or nil by mouth were investigated. Strategies were then developed with stakeholders (pharmacists, surgeons, anaesthetists, speech pathologists and nurses) to address the issues identified. A pilot study was conducted in a surgical ward to assess the effectiveness of the strategies.
Results:
Confusion and the use of 'fasting' and 'nil by mouth' interchangeably contributed to the medication administration errors. A policy was developed to distinguish 'fasting' from 'nil by mouth' with the mantra 'when fasting give oral meds; if nil by mouth use a different route instead'. The policy was supported by tools that were colour-coded to resemble the traffic lights, with green for 'go' if fasting and red for 'stop' if nil by mouth when giving oral medications. Pre-intervention 15.8% (171/1080) of patients missed at least one oral medication due to 'fasting' or 'nil by mouth' compared with 8.5% (56/660, to date) following policy rollout on the pilot ward. Feedback indicates the policy is applicable, practical and well received.
Conclusion:
A policy was developed to improve the administration of oral medications in patients who are fasting or nil by mouth. Piloting of this policy indicates there's a reduction in the number of patients who missed their oral medications.

THURS 67

The-Phung To [1]**, David A Story** [2]**, Jane Booth** [1]**, Fiona Nielsen** [3]**, Joanne Sweeney** [4]**, Patricia Bruce** [5]**, Cathy D'Alterio** [5]**, Melodie Heland** [3]**, Andrew Hardidge** [6]

Involving consumers as team members in research: The Fasting & Nil By Mouth Project.

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Background: The National Safety and Quality Health Service Standards and the National Health and Medical Research Council advocate the involvement of consumers in all aspects of healthcare, including research.

Aim: To illustrate a model of involving consumers as team members in research.

Methods: An expression of interest for involvement in the Fasting & Nil By Mouth research project was sent to consumers from the Austin Health volunteers pool. Consumers joined the research team once the following were established:

• The rationale of the project was discussed;

• The research project was of interest to the consumers;

• Clarity around the roles and responsibilities of the consumers as team members, including the agreement and signing of a position description document; and

• Ethics Committee requirements were met.

Results: Two consumers became members of the Fasting & Nil By Mouth project team. To-date their roles have included:

• Provision of a 'consumer voice' and/or non-hospital and non-medical viewpoints at project meetings and other aspects of the project;

• Development and piloting of a patient satisfaction survey;

• Development and piloting of a patient information brochure; and

• Collation of pilot data for the patient satisfaction survey and patient information brochure.

Conclusion: The Fasting & Nil By Mouth project adopted two consumers as members of its research team. These consumers have made valuable contributions to the project in many ways beyond the provision of a 'consumer voice'.

THURS 68

Dale Christiansen [1], **Effie Mouhtouris** [1], **Svjetlana Kireta** [2], **Paul Ramsland** [3], **Toby Coates** [2], **Frank Ierino** [4], **Mauro Sandrin** [1]

Production and Function of Soluble Marmoset ICOS-Ig

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3. Burnet Institute, Melbourne
4. Department of Nephrology, Austin Health

Aim.
Expression of soluble ICOS-Ig by cellular xenografts in mice significantly prolongs graft survival. Extend these studies to our established non-human primate model (Marmoset). Our rationale for using Marmosets is that they are New World primates, and unlike humans or Old World primates, express Gala(1,3)Gal thus eliminating any potential involvement of this xenoepitope. Consequently, this model will enable us to study non-Gal related pig-to-primate rejection processes in isolation.
Methods.
A BLASTN program search of the Trace Archive for Callithrix jacchus Whole Genome Shotgun database was performed using the mouse ICOS cDNA sequence. The DNA coding for the extracellular domains (transmembrane and cytoplamic tails were not included) was generated by PCR and splice overlap extension PCR added the human IgG1 Fc. Marmoset ICOS-Ig was subsequently subcloned into the pCDNA3 plasmid for sequencing, expression and functional studies.
Results.
Marmoset ICOS has 90% and 65% amino acid sequence identity compared with human and mouse respectively. Intracellular staining and Western blot analysis verified expression of soluble Marmoset ICOS-Ig. The soluble proteins completely inhibit proliferation in a mixed lymphocyte reaction. Homology modelling identified key interacting residues of Marmoset ICOS with Marmoset ICOSL.
Conclusions.
We have generated and expressed soluble Marmoset ICOS-Ig that functions in vitro, the efficacy of this protein will be further examined in vivo. Based on our findings in the mouse, we predict that Marmoset ICOS-Ig will significantly prolong xenograft survival and may ultimately have clinical application.

THURS 69

Fiona C. Brownfoot, Stephen Tong, Natalie Hannan, Laura Tuohey, Kenji Onda, Tu'uhevaha J Kaitu'u-Lino

Pravastatin quenches oxysterol-induced upregulation of soluble endoglin in primary endothelial cells: a potential therapeutic for preeclampsia

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Aim:
Preeclampsia is a serious pregnancy complication for which there are no cures besides delivery of the baby. Therefore, a therapeutic that quenches disease severity would be a major advance. One of the key anti-angiogenic factors central to the pathogenesis of preeclampsia is soluble endoglin (sEng). Recent evidence indicates that oxysterols can bind the liver X receptor (LXR) and activate MMP14 that leads to an increase in sENG release (1). Statins have vaso-protective properties (2) and can reduce both oxysterol production and inhibit LXR. The aim of this study was to characterize LXR expression in preeclamptic placenta and assess whether pravastatin can inhibit oxysterol induced sEng production in primary gestational tissues.
Methods and Results:
Immunohistochemistry revealed that LXR was localized to the syncytiotrophoblast and blood vessels of placenta, with staining increased in preeclamptic tissues (n=6). Furthermore LXR mRNA expression was significantly elevated in preeclampsia (n=27) compared to preterm controls (n=25; $p<0.05$). We next demonstrated a significant ($p<0.05$) dose dependent increase in soluble endoglin levels following oxysterol treatment of primary human umbilical vein endothelial cells (HUVEC). Excitingly, sEng was significantly decreased in a dose dependent manner following pravastatin treatment of primary HUVECs ($p<0.05$), likely resulting from a significant dose dependent ($p<0.05$) decrease in MMP-14, the final cleavage protease responsible for sEng production. Importantly, pravastatin treatment also induced a significant increase in TIMP-3, a naturally occurring MMP14 inhibitor.
Conclusion:
In conclusion, this work supports the therapeutic potential of pravastatin to treat preeclampsia, via its capacity to quench oxysterol induced sEng release.

THURS 70

Jodie Hahn [1], Cathy Cooper [1], Natasha van Zyl [2], Stephen Flood [2, 3], Michael Weymouth [2, 3],

Nerve transfers post Spinal Cord Injury: the therapist role in rehabilitation

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2. Dept of Plastic and Reconstructive Surgery, Austin Health
3. Victorian Spinal Cord Service, Austin Health

Background and aims:
Surgical reanimation of upper limb function post spinal cord injury (SCI) has traditionally occurred via tendon transfer methods. The introduction of nerve transfers as a reconstructive surgery option brings new hope for improved outcomes, but also raises many questions.

Nerve transfers are now a routine part of surgical management of brachial plexus injuries (BPI), however there is only a handful of published articles on its use for reconstruction of upper limb function post SCI (Tung 2011). These texts naturally concentrate on the specific surgical approach and none clearly describe the stages of rehabilitation and therapy techniques for the SCI population. Distinct differences in the donor and recipient nerves from BPI and the further deficits caused by SCI, makes adapting BPI protocols for SCI difficult.

In July 2012, the Victorian Spinal Cord Service Upper Limb Program increased the number of nerve reconstructions, resulting in the need for clearly specified rehabilitation protocols. This poster presents an overview of the protocols and discusses the resources used in their development.

Methods:
Development of the protocols arose from reviewing existing literature on rehabilitation post nerve transfer, discussions with multidisciplinary team and outcomes of clinical experience.

Results:
There are four stages in the rehabilitation of nerve transfers which need to considered. Stages include protecting the transfers, maintain the donor/recipient cortical representation and range of movement, strengthening the movements and separating and strengthening the recipient movements. Each stage requires different skills of the therapist.

Conclusion:
The current working protocol provides a platform for discussion and further development as our knowledge of rehabilitation post nerve transfer for SCI increases.

References:
Tung, T. H (2011)
Chapter 61: Nerve transfers. In Skirven, T et al. Rehabiliation of the hand hand upper extremity (6th Edition). Elsevier: Philadelphia
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THURS 71

Natasha van Zyl [1], **Stephen Flood** [1], **Michael Weymouth** [1], **Cathy Copper** [2], **Jodie Hahn** [2]

The Melbourne Triple Nerve Transfer - Upper limb reanimation in C6 tetraplegia

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2. Victorian Spinal Cord Service, Austin Health

Background of study
With the success of nerve transfers in peripheral nerve and brachial plexus injury attention has now turned to tetraplegic patients as the next group to benefit from these techniques. Nerve transfers allow direct reanimation of the paralysed muscle.
The authors' aim was to provide a nerve transfer solution for the reconstruction of elbow extension, grasp and release without using the nerves to muscles traditionally used for tendon transfers. If the nerve transfers were successful this would then leave these muscles intact and available for more distal reconstructions like intrinsicplasty and opponensplasty.
Materials and Methods
A 22 yo male sustained a C6 spinal cord (IFSSH group 4) injury following a diving accident. He had no triceps function on the left and a M3 triceps on the right. Six months after the injury he underwent teres minor to triceps, brachialis to median and supinator to posterior interosseous nerve transfers on the left upper limb. At nine months post injury he underwent only the latter two transfers on the right upper limb as his triceps function was adequate.
Interim
Results
Full and final results for the transfers will require a longer period of post operative recovery and rehabilitation time. The following results are interim results only. In the left upper limb (9 months 13 days post op) he has achieved M4 elbow extension, M3 finger flexion (index and middle fingers) and M3 thumb flexion and M4 thumb and digital extension. In the right upper limb (7 months 8 days post op) he has achieved M3 thumb and digital extension and M1 finger flexion (middle finger). There was no loss of function as a result of donor nerve harvest.
Conclusion
The utility of nerve transfers in the tetraplegic patient has yet to be determined but early results show promise. Adding successful nerve transfers to the reconstructive toolbox will expand the range of upper limb functions that can be restored using tendon transfers alone

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A Model for Facilitating Participant Recruitment in Spinal Clinical Trials in Victoria

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INTRODUCTION:
The Spinal Clinical Research Liaison Officer (SCRLO) role was established in response to receipt of three spinal cord injury (SCI) research program grants. It was recognised that these programs would run simultaneously, recruiting from the same small unique population, complicated by the complexities of SCI.
METHODS:
The SCRLO represents the research programs, but works independently of them to coordinate screening and recruitment of all acute spinal admissions and assists with recruitment to community trials, co-enrolling and co-ordinating assessments. Rarely is there a position that oversees and contributes to the coordination and collaboration of all studies within a speciality area. This is in contrast to the research co-ordinator model. Acute spinal research recruitment rates and process data collected by the COSAQ trial has been analysed. Enabling comparison of the SCRLO's performance to 9 other sites - days from admission to consent, consent to randomisation and proportion of eligible patients recruited.
RESULTS:
In Victoria, 200 acute SCI people were screened, 121 were eligible, 76% were recruited and 21% were enrolled in more than one study. 953 patients have been screened for COSAQ, 195 consented and 81 randomised. The Austin site took on average 23 days less to consent participants than the average of the other 9 sites ($p<0.01$), and 16 days less to randomise ($p<0.01$). There was no significant difference (χ^2, $p=0.8$) in recruitment rates between the Austin site (60%) and the 9 other sites (57%).
CONCLUSION:
Analysis of the COSAQ data indicates that a role like this may assist in increasing efficiency of trial processes and may facilitate participant recruitment when multiple trials are being conducted at a site.

THURS 73

S.N.S. Louis [1], J. Siviloglou [2], D. Debono [2], A. G. Frauman [1], K. Garrett [3], D. Liew [4]

Hospital costs of venous thromboembolism and their predictors

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Aim:
To determine the cost of venous thromboembolism (VTE) in the Austin Health and to identify the predictors of cost.
Methods:
Patients whose admission had primary diagnoses of deep vein thrombosis and/or pulmonary embolism over the period of 1 July 2005 and 30 June 2009 were included in the study. Cost data were provided by the Clinical Information Unit of Austin Health and was stratified into the following components for each patient: medical and nursing services, allied health services, medications, diagnostic services and theatre. Bottom-up costs were then estimated by aligning the relevant level of hospital spending with the number of services each patient received during his or her hospital stay to quantify the associations between total hospitalisation costs and the following variables: sex, age, type of VTE, use of the hospital-in-the-home program (HITH) and social disadvantage.
Results:
Between 1 July 2005 and 30 June 2009 there were 2157 admissions to Austin Health which included a primary diagnosis of VTE. The mean (SD) cost of a VTE admission was $19,159 ($31,030) with the bulk of the cost being attributable to healthcare staff. In addition, there was a large disparity between the median cost of Non-HITH and HITH admissions ($10,514 and $3542, respectively). Multivariate linear regression identified that the only significant, independent predictors of total hospital costs were age and whether or not the admission was part of the HITH program.
Conclusions:
This study represents the first bottom-up analysis of the cost of VTE to the Australian public health system. It highlights the burden of VTE and suggests that top-down approaches to costing and AR-DRG data may underestimate this burden.