NHMRC Clinical Trials Centre

COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

The achievement of better health outcomes for patients and those affected by brain tumours through clinical trials research

www.cogno.org.au

email: cogno@cogno.org.au | tel: 02 9562 5000

8th COGNO ANNUAL SCIENTIFIC MEETING

'Where the Future Lies'

FRIDAY 23rd — SATURDAY 24th OCTOBER 2015

STAMFORD PLAZA BRISBANE, AUSTRALIA

CONFERENCE BOOKLET

COGNO

COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

CONTENTS

2015 ASM ORGANISING COMMITTEE

Dr Cecelia Gzell, Convenor	Radiation Oncologist, Genesis Cancer Care
Dr Bryan Day	Translational Scientist, Queensland Institute of Medical Research
Ms Marcia Fleet	Care Coordinator, Melbourne Health
A/Prof Matthew Foote	Radiation Oncologist, Princess Alexandra Hospital
A/Prof Hui Gan	Medical Oncologist, Austin Hospital
Dr Ben Jonker	Neurosurgeon, Royal Prince Alfred Hospital
Ms Jenny Chow	Executive Officer, COGNO
Ms Yi Feng	Administrative Assistant, COGNO

INTERNET

Complimentary wireless internet is available for all delegates in the COGNO ASM meeting rooms.

Wireless Status: Wireless@Stamford
Login to: Conference
Password: HMZNE2Z9

COGNO
COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

COOPERATIVE TRIALS **G**ROUP FOR **N**EURO-**O**NCOLOGY
The achievement of better health outcomes for patients and those affected by brain tumours through clinical trials research

Dear Colleague

On behalf of the Organising Committee, welcome to the 8th COGNO Annual Scientific Meeting! The theme of this year's meeting is *'Where the Future Lies'*.

We are delighted at COGNO to announce that this year we will be sponsoring a foreign delegate to assist with expenses to attend the ASM. This year's successful applicant is Dr Haresh Kunhiparambath. Please make him feel welcome! ASM delegates still have the opportunity to help sponsor a delegate from a low-income country, to attend a future COGNO meeting. We are also delighted to introduce for the first time a new award. The Young Investigator Award is aimed at encouraging clinicians and scientists early in their career to submit their research for presentation and review.

We are excited to host four renowned international guest speakers:

- Professor Martin J van den Bent, MD, PhD
- Professor Kenneth D Aldape, MD
- Professor Vinay K Puduvalli, MD
- Professor Amy B Heimberger, MD

Highlights of our program include:

- Grade II & III Glioma: the present and the future
- Immunogenetics in Practice in Australia and Internationally: an interactive panel discussion
- Management approaches to recurrent High Grade Glioma
- "Can We See It": technological advances in neurosurgical technique and imaging
- Personalising the treatment of brain metastases
- Emerging targets in High Grade Glioma
- Unforgettable tumours Part II

Our appreciation goes to all our sponsors: Cancer Australia, Cure Brain Cancer Foundation, Roche, MSD Oncology, Bristol-Myers Squibb, AbbVie, Genesis Cancer Care, Brainlab, Cancer Institute NSW and Bridge 2 Bridge.

We hope you enjoy the ASM!

Kind regards

Dr Cecelia Gzell
Convenor
COGNO ASM 2015

Professor Mark Rosenthal
Chair
COGNO

The COGNO Scientific Program has been developed independent of sponsor involvement.

Australian Government
Cancer Australia

Cure Brain Cancer FOUNDATION

Platinum Sponsor

Roche

MSD ONCOLOGY

Bronze Sponsors

Bristol-Myers Squibb

Young Investigator Award Sponsor

abbvie

Coffee Cart Sponsor

Genesis Cancer Care New South Wales

BRAINLAB

Morning Tea Sponsors

NSW GOVERNMENT cancer institute NSW

BRIDGE2BRIDGE

Travel Grant Sponsors

PROGRAM OF EVENTS

Thursday 22 October: Pre-ASM Meetings (Raffles room)		
TIME	**MEETING**	**CHAIR**
2:00 - 5:15pm	**COGNO Scientific Advisory Committee Meeting** (open to COGNO members only)	Dr Liz Hovey
5:30 - 6:30pm	**COGNO Management Committee Meeting** (closed meeting)	Prof Mark Rosenthal

Friday 23 October: Day 1 (Ballroom)		
TIME	**MEETING**	**CHAIR**
8:30am	On arrival tea/coffee	
9:00 - 9:10am	**Welcome and Day 1 program overview**	Dr Cecelia Gzell
9:10 - 10:30am	**Session 1: *COGNO Trials Update***	Ms Marcia Fleet
	Prof Martin van den Bent: CATNON	
	Dr Liz Hovey: CABARET	
	Dr Mustafa Khasraw: ACED	
	Dr Mustafa Khasraw: VERTU	
	Prof Martin van den Bent: Neuropathology, molecular genetics and glioma: a change has come	
10:30 - 11:00am	Morning tea	
11:00 - 12:15pm	**Session 2: *Grade II & III Glioma: The Present and the Future***	Prof John Simes
	Prof Martin van den Bent: Grade II glioma beyond RTOG 9802	
	Dr Liz Hovey: Targeted agents: challenges in neuro-oncology trials	
	Oral abstract/proferred paper – Dr Alison Salkeld: Impact of a combined neurosurgery / neuro-radiation oncology clinic for patients with brain metastases: a pilot study	
	Invitation to Lunch / Poster Walkaround / Welcome Reception	Dr Cecelia Gzell
12:15 - 1:45pm	Lunch / Poster Walkaround / Welcome Reception	
1:45 - 3:15pm	**Session 3: *Immunogenetics in Practice in Australia and Internationally: An Interactive Panel Discussion***	**Moderator:** Dr Tom Robertson
	Integration of immunogenetics into clinical practice in Australia	
	Panel: • Dr Michael Rodriguez • A/Prof Kerrie McDonald • Prof Martin van den Bent • Prof Vinay Puduvalli	
3:15 - 3:45pm	Afternoon tea	
3:45 - 5:30pm	**Session 4: *Management Approaches to Recurrent High Grade Glioma***	A/Prof Matthew Foote
	A/Prof Hui Gan: Clinical trials for progressive high grade glioma	
	Dr Mark Pinkham: Salvage options for high grade glioma (reRT & Avastin)	
	Dr Zarnie Lwin: Lost in Translation	
	Oral abstract/proferred paper – Dr Adrian Lee: Palliative treatment with Bevacizumab for recurrent high grade glioma	
	Oral abstract/proferred paper – A/Prof Michael Back: Patients with Favourable Anaplastic Glioma who relapse after definitive intensity modulated radiation therapy have a pattern of relapse involving distant brain sites and ventricular	
7:00pm	**COGNO Conference Dinner (Alchemy)**	

W: www.cogno.org.au
E: cogno@cogno.org.au

PROGRAM OF EVENTS

Saturday 24 October: Day 2 (Ballroom)		
TIME	**MEETING**	**CHAIR**
8:00am	On arrival tea/coffee	
8:40 - 8:45am	**Welcome and Day 2 program overview**	Dr Cecelia Gzell
8:45 - 9:35am	**Session 5: *"Can We See It": Technological Advances in Neurosurgical Technique and Imaging***	Dr Sarah Olson
	Dr Ben Jonker: Advances in neurosurgical techniques for tumour resection	
	Dr Geoff Schembri: Functional imaging and theranostics in the management of brain tumours	
9:35 - 10:05am	Morning tea	
10:05 - 11:45am	**Session 6: *Personalising the Treatment of Brain Metastases***	Dr Ben Jonker
	Dr Jodi Saunus: Breast cancer brain metastasis	
	Dr Mustafa Khasraw: Targeted agents for brain metastasis & histology based evidence	
	A/Prof Matthew Foote: WBRT versus SRS	
	A/Prof Tamara Ownsworth: Considerations for neuro-cognitive assessment and psychosocial management of people with brain metastases	
11:45 - 12:30pm	Lunch	
12:30 - 2:20pm	**Session 7: *Emerging Targets in High Grade Glioma***	Dr Bryan Day
	Prof Stephen Rose: Developing EphA2 based theranostic and imaging targets for glioma	
	Dr Sameer Greenall: Simultaneous targeting of the cell cycle and gene transcription as an effective therapy for high grade glioma	
	Dr Anchit Khanna: Therapeutic targeting of Cancerous Inhibitor of Protein Phosphatase 2A (CIP2A) in Glioblastoma	
	Prof Amy Heimberger: Immunotherapy for GBM	
	Prof Vinay Puduvalli: Overcoming resistance in glioblastoma	
2:20 - 2:50pm	Afternoon tea	
2:50 - 3:40pm	**Session 8: *Unforgettable Tumours Part II***	A/Prof Hui Gan
	Prof Martin van den Bent: Treatment options for medulloblastoma in young adults	
	Prof Vinay Puduvalli: Primary spinal cord tumours overview & Leptomeningeal disease	
3:40 - 3:45pm	**ASM Summary**	Dr Cecelia Gzell
3:45 - 4:00pm	**ASM Awards and Close**	Prof Mark Rosenthal
4:15 - 4:45pm	**COGNO Annual General Meeting** (open to COGNO members only) **(Raffles room)**	Prof Mark Rosenthal

RANZCR CPD POINTS AVAILABLE: 11.75 RANZCR CPD points can be claimed for attendance at the 8th COGNO Annual Scientific Meeting.

RACS CPD POINTS AVAILABLE: This educational activity has been approved in the College's CPD Program. Fellows who participate can claim one point per hour (maximum 12 points) in Maintenance of Knowledge & Skills. ASM delegates who wish to claim RACS CPD points and have not yet advised COGNO must email the COGNO ASM secretariat (cognoasm@ctc.usyd.edu.au) by **Monday 26 October 2015** with their full name and RACS Member ID (also known as Fellowship ID).

ORAL ABSTRACT LISTING

Session 1 **Impact of a combined neurosurgery / neuro-radiation oncology clinic for patients with brain metastases: a pilot study**
Alison Salkeld, Najmun Nahar, Wei Wang, Gemma Olsson

Session 4 **Palliative treatment with Bevacizumab for recurrent high grade glioma**
Adrian Lee, Marina Kastelan, Michael Back, Helen Wheeler

Session 4 **Patients with Favourable Anaplastic Glioma who relapse after definitive intensity modulated radiation therapy have a pattern of relapse involving distant brain sites and ventricular**
Michael Back, Dasantha Jayamanne, David Brazier, Marina Kastelan, Lesley Guo, Helen Wheeler

POSTER ABSTRACT LISTING

P1 **Endoscopic transsphenoidal pituitary surgery – a single surgeon consecutive series of 154 cases**
Anson Chan, Sarah Olson, Ben Wallwork

P2 **Patterns of Care and survival of patients diagnosed with glioblastoma in a regional cancer centre**
Glaucia Fylyk, James Chen, Zaid Househ, Kyaw Linnhtun, Elias Nasser, Phillip Clingan, Morteza Aghmesheh

P3 **Whole Brain Radiotherapy: Preserving Neurocognitive Function through Hippocampal Avoidance**
Carly Albiez, Yurissa Ikeda, Kelli Mason, Minjae Lah

P4 **Predicting patterns of failure in temporal lobe GBMs: possible implications on radiotherapy treatment portals**
Dasantha Jayamanne, Helen Wheeler, David Brazier, Alison Newey, Marina Kastelan, Lesley Guo, Michael Back

P5 **Evolving management of Low Grade Glioma: No consensus amongst treating clinicians**
Kathryn Field, Mark Rosenthal, Mustafa Khasraw, Kate Sawkins, Anna Nowak

P6 **Trends of second surgery in GBM patients**
Alysson Wann, Patrick Tully, Craig Love, Zarnie Lwin, Lindy Jeffree, Liz Barnes, Kate Drummond, Hui Gan, Mustafa Khasraw

P7 **Anaplastic oligodendroglioma treated with adjuvant radiation and concurrent and maintenance Temozolomide**
Haresh KP, Subhash Gupta, Supriya Mallick, Ajeet Gandhi, Nikhil Joshi, Dayanand Sharma, Pramod Kumar Julka, Goura Kishor Rath

P8 **Craniopharyngioma – Demography and treatment outcomes – a single institution experience**
Subhash Gupta, Haresh K P, Prashanth Giridhar, Umesh Velu, Dayanand Sharma, P K Julka

P9 **A new venture for the Hunter Cancer Biobank - Establishment of sequential blood collection for brain cancer research**
Pia Laegdsgaard, Sarah Nielsen, Amanda Koegelenberg, Susan Goode, Rick Thorne, Demi Lund, Craig Gedye, Fiona Day, Rodney Scott

P10 **Genomically unstable Glioblastoma (U-GBM) show exquisite sensitivity to Parp (poly[ADP-ribose] polymerase) inhibition**
Kerrie McDonald, Swapna Joshi, Toni Jue, Lisette Schroder, Julia Yin, Mustafa Khasraw

P11 **A lab-based hospital for personalising treatment for glioblastoma patients**
Kerrie McDonald, Sylvia Chung, Sheri Nixdorf, Wendy Ha, Swapna Joshi, Julia Yin, Martina Hochwartner, Manuri Gunawardena, Charlie Teo, Jacob Fairhall, Raj Reddy

P12 **CABARET Biomarker Study: Identifying biomarkers associated with longer overall survival in recurrent GBM after treatment with Bevacizumab**
Kerrie McDonald, Liz Barnes, John Simes, Sheri Nixdorf, Kathryn Field

P13 **Targeting CDK4 and 6 in the Classical Subtype of Glioblastoma**
Kerrie McDonald, Daniel Madani, Mustafa Khasraw

P14 **Crossing the great divide: aptamer engineering for targeted brain metastasis treatment**
Joanna Macdonald, Patrick Houghton, Wei Duan, Sarah Shigdar

P15 **Bevacizumab in Neurofibromatosis type 2 (NF2) related vestibular schwannomas: a UK nationally coordinated approach to delivery and prospective evaluation**
Katrina Morris, Martin McCabe, Shazia Afridi, Raj Jena, Claire Blesing, John Golding, Dorothy Halliday, Rosalie Ferner, D Gareth Evans, Patrick Axon, Pieter Pretorius, Allyson Parry

P16 **Behaviour of ependymomas in UK neurofibromatosis type 2 (NF2) patients on Bevacizumab**
Katrina Morris, Shazia Afridi, Dorothy Halliday, Anke Hensiek, John Ealing, Mark Kellet, Pieter Pretorius, D Gareth Evans, Allyson Parry

P17 **Risk adapted single or fractionated stereotactic radiotherapy using the Novalis system for management of Pituitary adenoma**
Raghav Murali-Ganesh, Daniel Ashrafi, Lani Attwood, Benjamin Jonker, Nitya Patanjali

P18 **Glioblastoma brain cancer invasion: how different subclasses move through the brain**
Thomas Grundy, Ellen De Leon, Brett Stringer, Bryan Day, Andrew Boyd, Justin Cooper-White, Geraldine O'Neill

P19 **Experience of Procarbazine, Lomustine and Vincristine (PCV) Chemotherapy in Low-Grade and High-Grade Glioma in the real-world setting**
Geoffrey Peters, Po-ling Inglis, Zarnie Lwin, Rosalind L Jeffree, Catherine Bettington, MIchael Colditz

P20 **Fluorescence in situ hybridisation (FISH) probe ratio independently predicts survival in 1p19q co-deleted gliomas**
Mark Pinkham, Tom Liptrot, Catherine McBain, Nick Telford, Fran O'Neill, Rao Gattamaneni, Anna Tran, Gillian Whitfield

P21 **Volumetric-Modulated Arc Therapy (VMAT) for adult craniospinal irradiation**
Esther Sim, Michael Buchanan, Minjae Lah, Marisa Xinis

P22 **Caesar Trial: Assessing effectiveness of Levetiracetam prophylaxis at reducing seizure incidence in patients undergoing craniotomy, with no previous seizure history**
Bhavneet Singh, Sarah Olson, Bruce Hall, Helen Brown, Caroline Airey, Aleksander Dionisio, Peter Pillans, Thomas Campbell

P23 **Determining a cut point for Ki-67 proliferation that predicts for poorer survival in high-grade glioma**
Eugene Ho-Lam Wong, Purnima Sundaresan, Najmun Nahar, Thomas Ng, Val Gebski, Winny Varikatt, Jayasingham Jayamohan

ORAL ABSTRACTS

Impact of a combined neurosurgery / neuro-radiation oncology clinic for patients with brain metastases: a pilot study

Alison Salkeld[1], Najmun Nahar[1], Wei Wang[1], Gemma Olsson[2]

1 Crown Princess Mary Cancer Centre Westmead Hospital, Sydney, Australia
2 Department of Neurosurgery, Westmead Hospital, Sydney, Australia

Introduction: Multidisciplinary models of care have been widely adopted in oncology units around the world. There is only limited outcome evidence that show a direct improvement in patient care with the use of multidisciplinary care, particularly in patients with brain metastases.

Aim: To assess if review in a multidisciplinary neuro-oncology brain metastases clinic (MDT clinic) for patients with oligometastases decreases time to consultation and treatment with surgery or radiotherapy compared with historical controls.

Methods: A prospective pilot study was performed over 3 months with the establishment of a weekly MDT clinic for oligometastatic brain metastases patients with a good prognosis. Patients were reviewed by specialist neurosurgeons and neuroradiation oncologists with care facilitated by a nurse consultant (Figure 1). Time to consultation, surgery and radiotherapy were compared to historical controls who underwent treatment for brain metastases in the 12 months prior to the start of the MDT clinic.

Results: 29 new patients were seen over 3 months with patient details and treatment recommendations outlined in Table 1. Compared to historical controls (56 patients) the mean time to surgery from diagnosis was decreased from 18 to 13 days, for definitive radiosurgery (RS) 40 to 23 days (see Figure 2). For adjuvant radiotherapy (tumour bed RS or hippocampal avoidance whole brain radiotherapy), the time from diagnosis to treatment decreased from 51 to 39 days. The time from diagnosis to consultation for definitive or adjuvant radiotherapy was also decreased(Figure 2).

Conclusions: There was a dramatic improvement in the time from diagnosis to definitive (surgery and RS) and adjuvant treatment for patients with brain metastases. Given time from diagnosis to treatment is known to be important in local recurrence rates for the treatment of primary cancers(1–3), this pilot study has been expanded to a larger study and will report patient outcome data.

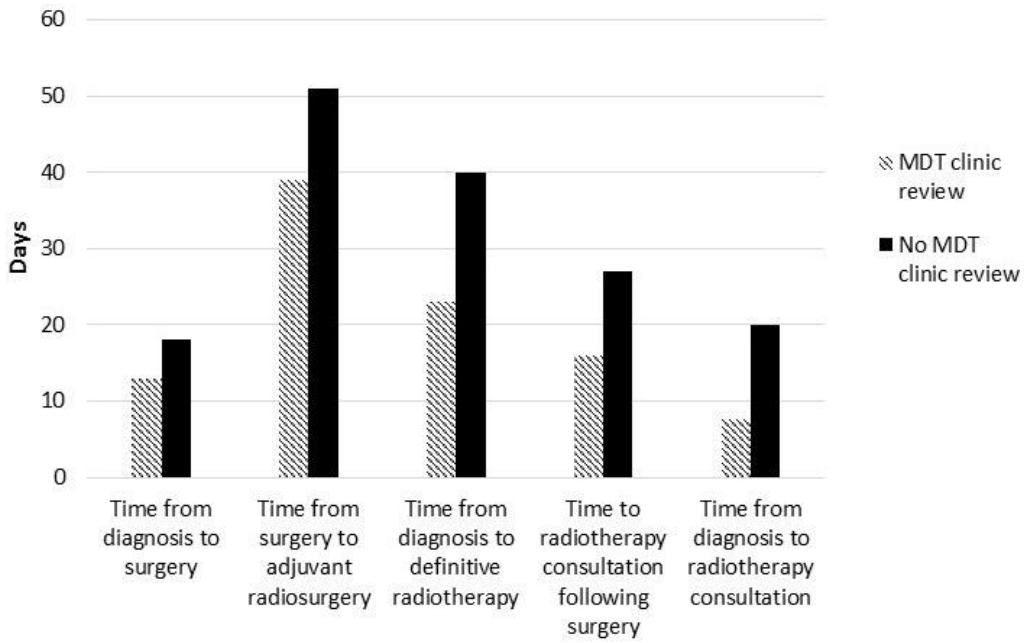
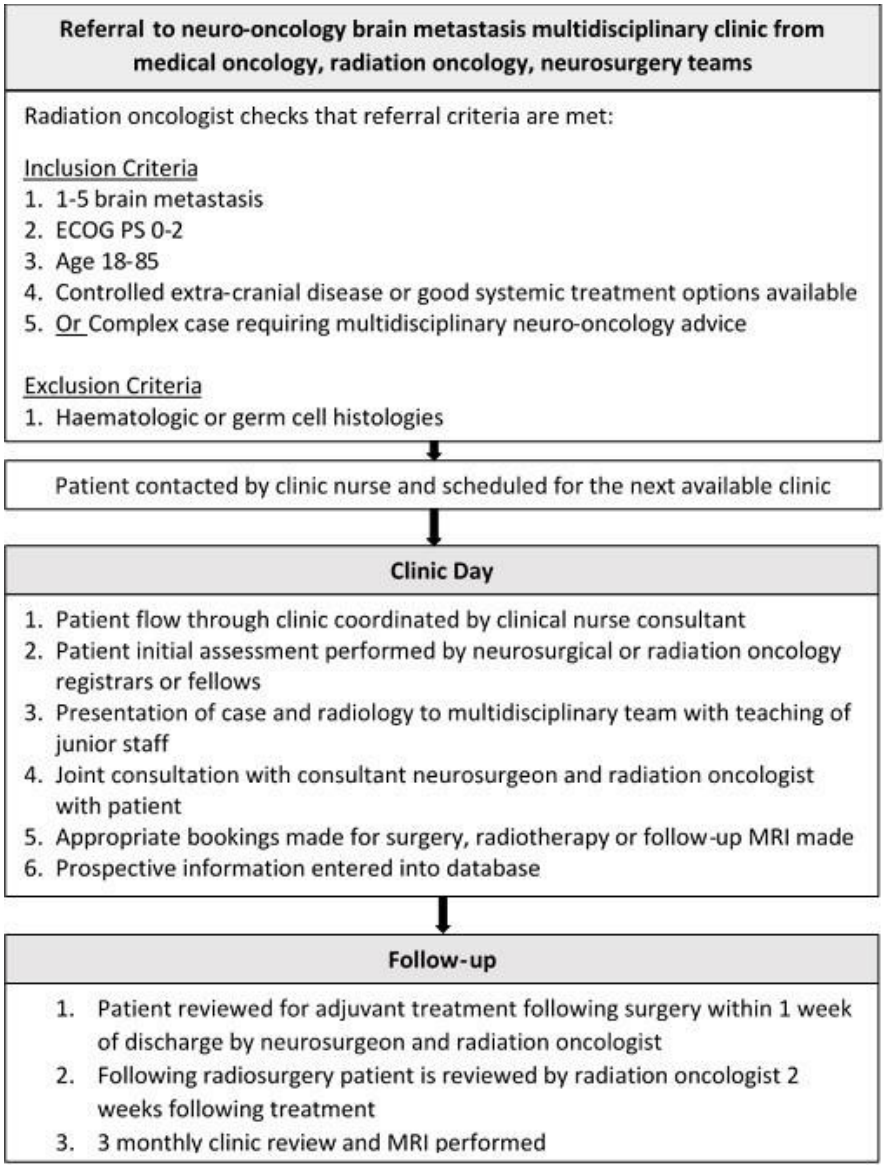


Figure 2


Referral to neuro-oncology brain metastasis multidisciplinary clinic from medical oncology, radiation oncology, neurosurgery teams
Radiation oncologist checks that referral criteria are met:
Inclusion Criteria
1. 1-5 brain metastasis
2. ECOG PS 0-2
3. Age 18-85
4. Controlled extra-cranial disease or good systemic treatment options available
5. Or Complex case requiring multidisciplinary neuro-oncology advice
Exclusion Criteria
1. Haematologic or germ cell histologies
Patient contacted by clinic nurse and scheduled for the next available clinic
Clinic Day
1. Patient flow through clinic coordinated by clinical nurse consultant
2. Patient initial assessment performed by neurosurgical or radiation oncology registrars or fellows
3. Presentation of case and radiology to multidisciplinary team with teaching of junior staff
4. Joint consultation with consultant neurosurgeon and radiation oncologist with patient
5. Appropriate bookings made for surgery, radiotherapy or follow-up MRI made
6. Prospective information entered into database
Follow-up
1. Patient reviewed for adjuvant treatment following surgery within 1 week of discharge by neurosurgeon and radiation oncologist
2. Following radiosurgery patient is reviewed by radiation oncologist 2 weeks following treatment
3. 3 monthly clinic review and MRI performed
Figure 1

	Patient seen in MDT clinic	Patients not seen in MDT clinic
Sex n (%)		
Male	16 (55.2%)	22 (39.3%)
Female	13 (44.8%)	34 (61.1 %)
Age (years)		
Median	59	64
Range	35 - 82	38 - 82
Primary Site n (%)		
Non-small cell lung cancer	14 (48.3%)	23 (41.1%)
Melanoma	5 (17.2%)	15 (26.8%)
Breast	4 (14.0%)	10 (17.9%)
Colorectal	3 (10.3%)	2 (4.7%)
Renal Cell Carcinoma	1 (3.4%)	3 (5.4%)
Small Cell Lung	1 (3.4%)	3 (5.4%)
Duodenal	1 (3.4%)	0 (0%)
Brain Metastasis Number per patient n (%)		
1	18 (62.1%)	35 (62.5%)
2	1 (3.4%)	9 (16.1%)
3	5 (17.2%)	11 (19.6%)
4	3 (10.3%)	0 (0%)
5	2 (6.9%)	3 (5.4%)
ECOG performance status n (%)		
0	21 (72.4%)	21 (37.5%)
1	4 (13.8%)	24 (42.9%)
2	3 (10.3%)	7 (12.5%)
3	1 (3.4%)	4 (7.1%)
4	0 (0%)	0
Treatment received		
Observation alone	5 (17.2%)	-
Definitive radiosurgery	4 (13.8%)	32 (57.1%)
Surgery and observation	5 (17.2%)	0 (0%)
Surgery and adjuvant cavity radiosurgery	11 (38%)	5 (8.9%)
Surgery and adjuvant whole brain radiotherapy	3 (10.3%)	19 (33.9%)
Whole brain radiotherapy alone	1 (3.4%)	-
Hippocampal avoidance whole brain radiotherapy alone	1 (3.4%)	0
Further investigation	1 (3.4%)	-

Table 1: Patient and treatment characteristics

Palliative treatment with Bevacizumab for recurrent high grade glioma

Adrian Lee[1,2], Marina Kastelan[1,2], Michael Back[1,2], Helen Wheeler[1,2]

1 Sydney Neurooncology Group, Sydney, Australia
2 Royal North Shore Hospital, Sydney, Australia

Recurrent high grade gliomas (HGGs) are usually associated with cerebral oedema which causes a number of disabling symptoms. Current standard of care for symptom relief is corticosteroids which also have significant side effects. Since 2007 we have treated 225 patients with recurrent HGG with Bevacizumab, either alone or in combination with chemotherapy to improve QOL and limit corticosteroid use. Response to Bevacizumab was based on clinical assessment and therapy was discontinued if no clinical benefit was observed.

The median age of the cohort was 58 and 65% were male. All but 1 patient had received radiotherapy, 71% had 2+ lines of chemotherapy and 53% had 2+ craniotomies for recurrent disease. All had symptomatic progression and 76% had ECOG >=2 at Bevacizumab commencement.

Median PFS from commencement of Bevacizumab was 2.8 months (0.2-37 months) and OS 5.7 months (0.6-75 months). 20% were alive at 6 months from Bevacizumab

commencement. 73% decreased corticosteroids by at least 50% within 4 weeks of commencing therapy. 10% had no benefit from Bevacizumab, 20% had minor benefit and 70% had initial significant clinical improvement. 20% were receiving LMWH at the time of commencing Bevacizumab and a further 6% developed VTE whilst on Bevacizumab. There were no major haemorrhages, but 5 had minor bleeding events. 2 patients had to cease therapy because of uncontrolled hypertension. 3 patient developed a GI perforation and 1 died from complications.

In summary, Bevacizumab is a relatively safe palliative option to improve the QOL in patients with recurrent HGG patients and reduce steroid burden. Access to this treatment remains a challenging issue due to financial restrictions in many countries.

Patients with Favourable Anaplastic Glioma who relapse after definitive intensity modulated radiation therapy have a pattern of relapse involving distant brain sites and ventricular spread

Michael Back[1,2,3,4], Dasantha Jayamanne[1], David Brazier[1,3], Marina Kastelan[1,4], Lesley Guo[1], Helen Wheeler[1,3,4]

1 Northern Sydney Cancer Centre RNSH, Sydney, Australia
2 Central Coast Cancer Centre Gosford Hospital, Gosford, Australia
3 Sydney Medical School, Sydney, Australia
4 Sydney NeuroOncology Group, Sydney, Australia

Aim: Assess patterns of failure(PoF) of patients with anaplastic glioma(AG) managed with intensity modulated radiation therapy(IMRT) and relationship to favourable(FAV) molecular subtype.

Methods: Patients with AG managed with IMRT since 2008 were entered into a prospective database with outcome assessed in regards to PoF. Patients were classified into a FAV or non-FAV cohort based on presence of oligodendroglial features, 1p19q co-deletion or IDH1mutation. From 2011 FAV patients were managed with IMRT and FET-FDGPET guided planning (PET-IMRT). Relapse Free (RFS) and Overall Survival (OS) were calculated from start RT. PoF was local, marginal or distant in relation to IMRT volume. Ventricular failure was recorded where present.

Results: 155 patients with AG were included of which 122 were FAV and 33 non-FAV. Median follow-up for survivors is 29 months. 66% received sequential chemotherapy. There were 44 relapses and 34 deaths for a 5yRFS of 60.8% and 5yrOS of 65.1%. Worse survival was associated in non-FAV with 5yrOS of 31.1% vs 77.5% for FAV ($p<0.01$). Of 44 patients with relapse, 34 are deceased with a medianOS post relapse of 9.0 months.

24 FAV patients have relapsed with a medianOS post relapse of 12.0 months. Multiple relapses prior to IMRT was associated with worse survival ($p=0.05$). 46% of relapses were infield and 54% were distant. This compared with non-FAV of 70% and 25%($p=0.18$). Ventricular relapse was evident in 42% vs 15%. 15 of 24 relapsed FAV patients are deceased with a median time to death of 6.0 months.

In 59 FAV patients managed with PET-IMRT, 9 relapses occurred of which only 2 had infield component. However 8 relapses were distant, including 6 with ventricular relapse.

Conclusion: At relapse post IMRT, FAV AG patients have a higher proportion of distant brain relapse and ventricular spread.

.

POSTER ABSTRACTS

Endoscopic transsphenoidal pituitary surgery – a single surgeon consecutive series of 154 cases

Anson Chan[1], Sarah Olson[1], Ben Wallwork[1]

1 Princess Alexandra Hospital, Brisbane, Australia

Background: This audit is of a consecutive series of 154 endoscopic transsphenoidal pituitary operations performed by an experienced neurosurgeon in 3 institutions in Brisbane, Australia over a 7 year period.

Methods: All consecutive patients undergoing endoscopic transsphenoidal surgery in the period June 2008 to March 2015 at the Princess Alexandra, Greenslopes Private and Mater Private Hospitals in Brisbane were retrospectively analysed. 74 females and 68 males aged 18 to 85 years (mean age 53 years) underwent a total of 154 transsphenoidal pituitary operations. Follow-up was conducted by outpatient clinic review, chart audits and telephone interview.

Results: Pituitary lesions undergoing endoscopic transsphenoidal surgery presented most frequently in the 50-59 age bracket, with a female to male ratio of 1.09 to 1. None of the 5 metastases to the pitutary presented with diabetes insipidus. However, 4 out of 5 metastases developed permanent diabetes insipidus post-operatively. The most common histological finding was pituitary adenoma. There was one death (0.65%) due to pulmonary embolus. There was a 1.3% incidence of CSF leak requiring return to theatre and 1.94% incidence of epistaxis (all 3 cases of epistaxis had vascularized flaps intraoperatively). Diabetes insipidus was the most common complication with a temporary incidence of 16.88%; with 7.14% persistent at the 6 month follow-up. Of the 49 patients who presented with a headache, 73% reported resolution of the headache postoperatively. 10.34% of patients reported temporary loss of smell; with one reported case (0.65%) of permanent loss of smell.

Conclusions: In one surgeon's experience, a low incidence of complications can be achieved via endoscopic transsphenoidal techniques for pituitary surgery. Diabetes insipidus was the most common complication. 4 out of 5 metastases to the pituitary developed permanent diabetes insipidus. There was one case of permanent loss of smell.

Patterns of Care and survival of patients diagnosed with glioblastoma in a regional cancer centre

Glaucia Fylyk[1], James Chen[1], Zaid Househ[2], Kyaw Linnhtun[2], Elias Nasser[1], Phillip Clingan[3], Morteza Aghmesheh[3]

1 Department of Radiation Oncology, Illawarra Cancer Care Centre, Wollongong, Australia
2 Department of Anatomical Pathology, The Wollongong Hospital, Wollongong, Australia
3 Department of Medical Oncology, Illawarra Cancer Care Centre, Wollongong, Australia

Aims: To determine the patterns of care and survival outcomes of patients diagnosed with glioblastoma treated at the Illawarra Cancer Care Centre.

Methods: We performed a retrospective review of all patients with a histological diagnosis of glioblastoma between January 2006 and December 2013. Data on clinico-pathologic characteristics, treatments received and survival were recorded.

Results: One hundred and twenty-five patients were identified. Median age was 65 years (range 18-84) and 56% were males. Majority had an ECOG performance status between 0~2. The most common histology was glioblastoma NOS (74%), followed by small cell variant (21%). All tumours (98%) that were tested(1) for IDH1 mutation were negative. Sixty-one percent achieved gross total resection and 17% had biopsy only. After surgery, 74 patients (59%) were planned for radiotherapy with concomitant temozolomide (group 1), 26% of patients had radiotherapy alone (group 2) and 15% received supportive care alone (group 3). In group 1, 10 patients ceased treatment early either due to chemotherapy toxicity (7 patients) or tumour progression (3 patients). Forty-eight patients received second-line therapy (table 1) including 5 patients enrolled in clinical trials. The median survival for the entire cohort was 10 months (figure 1); 14, 7 and 2 months in group 1, 2 and 3 respectively. The one and two-year survival for group 1 was 59% and 26% respectively.

Conclusion: This is a large comprehensive report of patterns of care from an Australian regional cancer centre. Our outcomes are comparable to other patterns of care studies in Australia (2). Use of Stupp protocol (3) was the most commonly used adjuvant treatment, reflecting evidence-based practice. Treatment compliance was high, however long-term survival remains poor despite frequent use of salvage treatments.

References

1. Capper D, Weissert S, Balss J, et al. Characterization of R132H mutation-specific IDH1 antibody binding in brain tumours. Brain Pathol 2010; 20(1):245-54
2. Dally M, Rosenthal M, Drummond K, et al. Radiotherapy management of patients diagnosed with glioma in Victoria (1998-2000).A retrospective cohort study. J Med Imaging Radiat Oncol 2009; 53:318-324
3. Stupp R, Mason WP, van den bent MJ, et al. European Organisation for Research and Treatment of Cancer Brain Tumor and Radiotherapy Groups; National Cancer Institute of Canada Clinical Trials Group. Radiotherapy plus concurrent and adjuvant temozolomide for glioblastoma. N Engl J Med 2005; 52(10):987-996

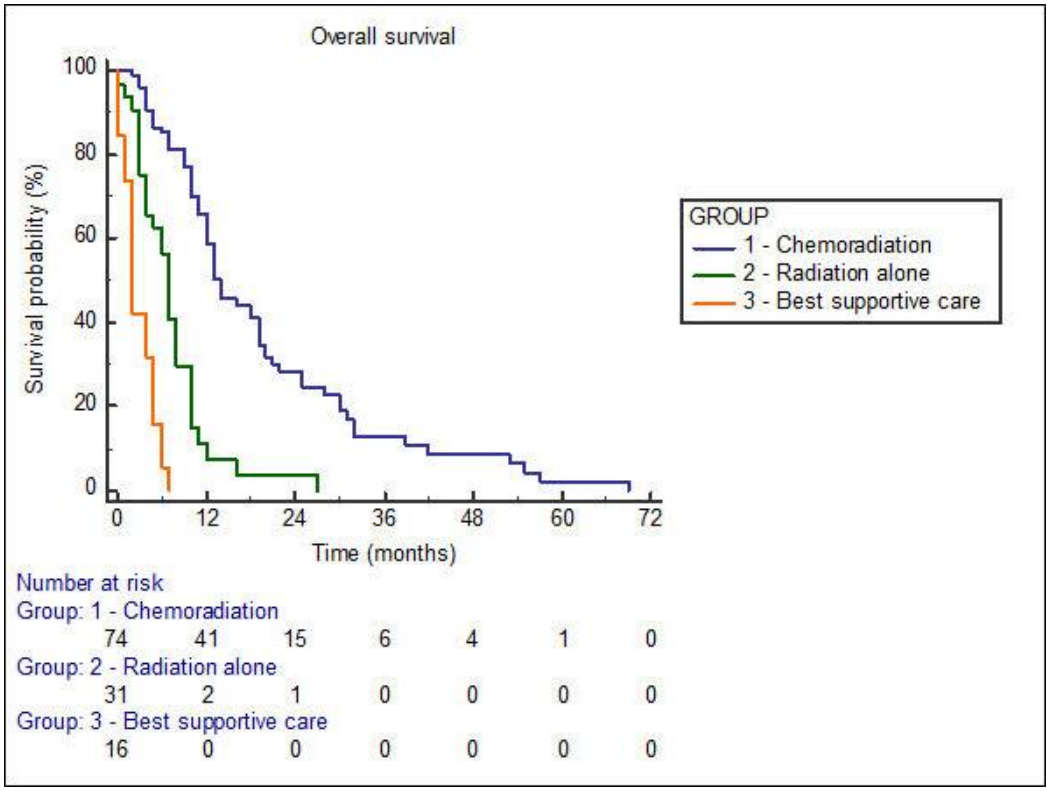


Figure 1: Kaplan Meier overall survival curves divided by groups

Further therapy	Chemoradiation (group 1) N= 61	Radiation alone (group 2) N=8	Total N=69
Second surgery§	24	1	25 (20%)
Re-irradiation	3	0	3 (2.4%)
Chemotherapy§	29	7	36 (28%)
Enrollment in trials	5	0	5 (4%)

§*Some patients had more than one salvage treatment.*

Table 1: Further therapy divided by initial adjuvant therapy group

Whole Brain Radiotherapy: Preserving Neurocognitive Function through Hippocampal Avoidance

Carly Albiez[1], Yurissa Ikeda[1], Kelli Mason[1], Minjae Lah[1]

1 Genesis Cancer Care Queensland, Brisbane, Australia

Brain metastasis heralds poor prognosis with short life expectancy for cancer patients. Yet, whole brain radiotherapy (WBRT) has contributed in symptomatic improvement and prolonged survival for these patients since the 1950s. Prophylactic use of WBRT however, has been utilised in high risk cases for CNS relapse, especially in the cases of small cell lung cancer and conclusively shown benefit towards CNS control and survival. The long term survival rates in this patient population may later be subjected to late effects of radiotherapy.

Under recent investigations, minimising the negative impact of WBRT on neurocognitive function (NCF) that has been attributed as treatment related side effects of WBRT have been undertaken. The recently reported phase III trial RTOG 0933 looked at hippocampal-avoidance WBRT as a possible approach. Using modern radiotherapy techniques, the mean dose to the hippocampus was reduced and this trial subsequently reported better preservation of NCF as indicated in the changes to patients Hopkins Verbal Learning Test scores.

At Genesis CancerCare Queensland, we have introduced hippocampal-avoidance WBRT for selected patients. In this paper, we present two examples of radiotherapy plans that utilised volumetric modulated arc therapy with hippocampal sparing for prophylactic cranial radiotherapy for small cell lung cancer.

Predicting patterns of failure in temporal lobe GBMs: possible implications on radiotherapy treatment portals

Dasantha Jayamanne[1], Helen Wheeler[1, 2], David Brazier[1], Alison Newey[1], Marina Kastelan[3], Lesley Guo[1], Michael Back[1, 2, 4]

1 Northern Sydney Cancer Centre, Royal North Shore Hospital, Sydney, Australia
2 Northern Clinical School, Sydney Medical School, University of Sydney, Sydney, Australia
3 Department of Nuclear Medicine, Royal North Shore Hospital, Sydney, Australia
4 Central Coast Cancer Centre, Gosford, Australia

Aim: Characterise patterns of failure (PoF) of Temporal Lobe (TL) Glioblastoma Multiforme (GBM) with relation to normal TL anatomy and neural pathways.

Methods: 335 GBM patients received IMRT between 03/2007 and 07/2014. 100 were located in TL. 86 had radiological progression and were included in the study.

Site of initial tumour and subsequent relapse were subdivided into 5 local TL sites (anterior, lateral, medial, posterior and superior); 5 adjacent regional sites (occipital lobe, inferior frontal lobe, caudate or internal/external capsules, fornix and trigone of ventricle or thalamus), and 5 distant failure sites (ventricles, contralateral hemisphere, brainstem, leptomeninges and spine). Extension along neural pathways at initial presentation and at time of first documented MRI failure were categorised into anterior, superior, medial and posterior pathways.

Analysis was conducted on PoF in relation to primary tumour location, failure sites and neural pathways.

Results: Median survival was 17.3months.

At initial diagnosis, 71% of tumours involved one TL site and 98% were confined to TL sites. 19% had neural pathway disease at initial pre-treatment MRI.

At first recurrence, 41% of failures were in TL sites alone, 3% in regional sites alone and 30% in both; with a total 74% having a local or regional site failure. 26% failed within distant sites and 53% patients had neural pathway involvement at time of recurrence. (Table 1)

Initial tumour location predicted for specific local site recurrence ($p<0.0001$), regional site recurrence ($p=0.004$) and neural pathway recurrence pattern ($p=0.005$), but not for distant sites ($p=0.081$)

Conclusion: Most GBM fail at local or adjacent regional sites. This study shows that recurrences occur in a predictable pattern within a local or regional site, specific to initial TL site with more than half involving anatomical neural pathways. Knowledge of tumour infiltration and failure may improve target localisation and radiotherapy treatment.

	LOCAL RECURRENCE		REG RECURRENCE		DISTANT RECURRENCE	NEURAL PATHWAY RECURRENCE	
Anterior/Pole:	Anterior	Superior	Inferior Frontal Lobe		Ventricle	Superior	
	11/22 (50)	10/22 (45)	6/22 (27)		3/22 (13)	11/22 (50)	
Lateral:	Lateral		Tail of Caudate		Contralateral Hemisphere	Superior	
	28/32 (87.5)		11/32 (34)		2/32 (6)	6/32 (19)	
Medial/Hippocampal:	Medial		Fornix	Occipital	Ventricle	Medial	Posterior
	15/23 (65)		7/23 (30)	6/23 (26)	9/23 (39)	10/23 (43)	7/23 (30)
Posterior:	Posterior		Occipital		Ventricle	Posterior	
	12/15 (80)		8/15 (53)		4/15 (27)	8/15 (53)	
Superior/Insular:	Superior		Inferior Frontal			Superior	
	15/17 (88)		4/17 (24)		0	8/17 (47)	

Table 1: Common sites of recurrence of temporal lobe tumours

Evolving management of Low Grade Glioma: No consensus amongst treating clinicians

Kathryn Field[1], Mark Rosenthal[1], Mustafa Khasraw[2], Kate Sawkins[3], Anna Nowak[4,5]

1 Royal Melbourne Hospital, Department of Medical Oncology, Melbourne, Australia
2 Geelong Hospital, Department of Medical Oncology, Melbourne, Australia
3 Cooperative Trials Group for Neuro-Oncology, NH&MRC Clinical Trials Centre, Sydney, Australia
4 School of Medicine and Pharmacology, University of Western Australia, Perth, Australia
5 Department of Medical Oncology, Sir Charles Gairdner Hospital, Perth, Australia

Aims: The de novo management of Low Grade Gliomas (LGG) is transitioning to include postoperative radiotherapy and chemotherapy after the updated RTOG-0825 study results demonstrated a survival benefit in this setting. This study assessed management strategies among Australian clinicians treating LGG during the period in which new data became incorporated into standard practice.

Methods: In 2014, Neurosurgeons, Radiation Oncologists and Neuro-oncologists who were members of the Australian Cooperative Trials Group for Neuro-oncology (COGNO) as well as additional attendants of the COGNO annual scientific meeting were surveyed. The survey presented six LGG clinical scenarios and asked respondents to select their

preferred management strategy. Additional questions included respondents' approach to 1p/19q testing and chemotherapy preferences.

Results: The response rate was 30.2% (61/202) with the majority (77%) working in tertiary referral neuro-oncology centers. There was no consensus regarding the management approach for each scenario, with observation alone post surgery remaining a popular management strategy. Only 25% of respondents reported that their institution routinely tests 1p/19q status in LGG although 69% were of the opinion that all LGG patients should be tested. The majority (81%) preferred to use temozolomide rather than PCV as first-line chemotherapy for LGG but only 44% would actually use it in this setting. Up-front chemotherapy prior to radiotherapy in certain patients with LGG would be considered by 52% of respondents.

Conclusions: This survey assessed management strategies for LGG since the updated RTOG-0825 data were presented. It demonstrates no consensus in the postoperative treatment approaches for LGG.

Trends of second surgery in GBM patients

Alysson Wann[1], Patrick Tully[2, 7], Craig Love[2], Zarnie Lwin[3, 9], Lindy Jeffree[3], Liz Barnes[4], Kate Drummond[2, 7], Hui Gan[1, 6], Mustafa Khasraw[4, 5]

1 Olivia Newton John Cancer and Wellness Centre, Melbourne, Australia
2 Royal Melbourne Hospital, Melbourne, Australia
3 Royal Brisbane and Women's Hospital, Brisbane, Australia
4 NHMRC Clinical Trials Centre, Sydney, Australia
5 Royal North Shore Hospital, Sydney, Australia
6 Latrobe University, Melbourne, Australia
7 University of Melbourne, Melbourne, Australia
8 University of Sydney, Sydney, Australia
9 University of Queensland, Brisbane, Australia

Aims: Small retrospective studies have looked at patients having second surgery at recurrence of glioblastoma multiforme (GBM). Good prognostic indicators are young age (<50 years), longer disease free interval [1], smaller tumour volume (<50 cm3), good preoperative Karnofsky Performance Status (>80%) [2]. We retrospectively explored trends and outcomes of a second surgery in GBM patients at 2 tertiary Victorian centres in Australia.

Methods: Between 2009-2014, patients with GBM that had a second surgery at first recurrence at both centres were included. Demographic data and factors including tumour location, surgeon, percentage resected were reviewed. Overall survival, time to progression and survival post second surgery were analysed.

Results: There were 99 patients in total (75 from Centre A and 24 from Centre B). There were 37 females and 62 males. Median age at first diagnosis was 55 years. At initial resection, tumours were right sided (45), left sided (42) bilateral (5) or unknown (7). Main locations included the temporal lobe (n=39), frontal (n=36) and parietal (n=29). Gross tumour resection was achieved in 27% in Centre A and 17% in Centre B.

Median time to first recurrence was 263 days. With the second surgeries, there were more right sided tumours (35 vs 27) and tumours were mainly located in the frontal (n=30), temporal (n=29) and parietal lobes (n=22). 18 surgeons were involved with the maximum number of surgeries by one surgeon (n=8) in Centre B. Median survival post second surgery was 184 days.

Discussion: Second surgery at GBM recurrence is a viable treatment option and is variably utilised in the Victorian hospitals included in this study. A further analysis comparing this group to those that didn't have surgery at recurrence, which will also include functional outcomes, is currently underway and is open to further collaborators.

	Time to first recurrence (days)	Survival from second surgery (days)
Median	263	184
Range	15-3662	2-1374

Median survival

	Location of tumours	
	At first surgery	At second surgery
Right sided	45	35
Left sided	42	27
Bilateral	5	9
Frontal	36	30
Temporal	39	29
Parietal	29	22
Occipital	6	7
Others	15	13

Location of tumours

Anaplastic oligodendroglioma treated with adjuvant radiation and concurrent and maintenance Temozolomide

Haresh KP[1], Subhash Gupta[1], Supriya Mallick[1], Ajeet Gandhi[1], Nikhil Joshi[1], Dayanand Sharma[1], Pramod Kumar Julka[1], Goura Kishor Rath[1]

1 All India Institute of Medical Sciences, New Delhi, India

Background: Temozolomide (TMZ)-based adjuvant chemo-radiation have been inadequately explored in anaplastic oligodendroglioma.

Methods: We analyzed our database between 2007 and 2011. All had maximally safe surgical resection followed by post-operative radiation (60 Gy in 30 fractions). All received chemoradiation with concurrent daily TMZ (75 mg/m2) then four weeks later, adjuvant TMZ started at 150 mg/m2 day 1 to 5 every 28 days and escalated to 200 mg/m2 after the 2nd cycle. An event was described as death, progression/recurrence, or neuro-deterioration. Log-rank test was used to compare event-free survival (EFS) distribution.

Results: Total 57 patients. Median age was 38 years (Range: 24-77 years); Male: Female ratio was 40:17. 38 patients had frontal lesion, 8 had parietal, 6 temporal, and 5 in other areas. Symptoms: Headache in 25, seizure in 18, vomiting in10 patients. 5 patients had limb weakness and 2 patients each had speech difficulty and visual complaints. Median symptom duration was 18 months (Range: 0.2-120 months). 27 (47%) underwent gross/near total resection; 29 (51%) underwent a subtotal resection. Median MIB labeling index 18.5 (Range: 5-45). The median number of adjuvant TMZ cycles was 6 (range: 0 to 12). Median follow-up was 27 months (range: 4 to 79 months). 9 patients did not receive maintenance Temozolomide after concurrent RT+CT. Estimated Median DFS: 61.7 months and estimated 5year DFS: 57%. Estimated Median OS: NR and estimated 5year OS: 66.4%. 3 year survival 68% patients with frontal vs. 38% temporal tumor however (p= P=0.164). All but one patients tolerated the planned Radiation well; Grade III and IV thrombocytopenia was noted in 10% cases, and 2% had grade III and IV neutropenia with 3 patients required hospitalization. PFS were not significantly different for age<40 years, sex, and extent of surgery.

Conclusion: Adjuvant Temozolomide with radiation is a safe and feasible in anaplastic oligodendroglioma.

Craniopharyngioma – Demography and treatment outcomes – a single institution experience

Subhash Gupta[1], Haresh K P[1], Prashanth Giridhar[1], Umesh Velu[1], Dayanand Sharma[1], P K Julka[1]

1 Department of Radiation Oncology, All India institute of Medical sciences, New Delhi, India

Introduction: Craniopharyngioma are rare tumors of the sellar region. Data on demographic details, symptomatology, treatment and response is limited from the Indian sub-continent.

Methods: Patients included in the retrospective analysis were those who presented to the neuro-oncology clinic after surgery between years 2003 and 2015. The treatment charts were reviewed and the demographic, treatment details and outcomes were retrieved using predesigned pro-forma.

Results: A total of 42 patients were treated. The median age of presentation was 17 years (Range 2 – 34 years). The sex distribution was Male: Female of 31 : 11. The presenting symptom was visual symptoms in 31 patients, hormonal imbalance in 3, neurological deficit in 1 patient and raised intracranial tension in 7 patients. Lesion size was < 4 cm for 26 patients and > 4 cm for 16 patients. Baseline TSH levels were available for 34 patients (Raised – 1; Decreased – 3). Baseline GH levels were available for 32 patients (Raised – 0; Decreased – 3). Baseline prolactin levels were available for 29 patients (Raised – 3; Decreased – 1). Radiation was delivered by 3 D- CRT in 39 patients. IMRT in 2 patients and SRT in 1 patient. Radiation dose was 50.4 Gray in 28 fractions over 5.5 weeks. 35 patients had a complete response, 5 patients a partial response. 1 stable disease and 1 progressive disease. 7 patients recurred at local site. 6 patients underwent surgery. 4 of those patients had progressive disease at last follow up. No grade 3 or 4 toxicity was documented. Univariate analysis did not detect any association of age, sex, hormonal perturbations or lesion size with response to primary therapy at six months or recurrence.

Conclusion: Craniopharyngioma are effectively treated with a combination of surgery and radiation.

A new venture for the Hunter Cancer Biobank - Establishment of sequential blood collection for brain cancer research

Pia Laegdsgaard[1,2], Sarah Nielsen[1,3], Amanda Koegelenberg[1,2], Susan Goode[1,2], Rick Thorne[1,2], Demi Lund[1,2], Craig Gedye[1,2,4], Fiona Day[1,2,4], Rodney Scott[1,2,3]

1 Hunter Cancer Research Alliance, Newcastle, Australia
2 University of Newcastle, Newcastle, Australia
3 Pathology North, Newcastle, Australia
4 Calvary Mater Newcastle, Newcastle, Australia

The Hunter Cancer Biobank (HCB) was established in 2012 to meet the needs of cancer researchers for high quality tissue specimens linked to clinical data. The HCB collects a range of tumour and adjacent normal tissue from adult patients having cancer-related procedures in the Hunter New England (HNE) region. Now with support from the Mark Hughes Foundation the HCB has established a dedicated Brain Cancer Biobank to create a high value resource for future brain cancer research.

With recent technical advances in molecular biology, computing and bioinformatics allowing for the detection of trace amounts of cancers circulating within blood samples, the biobank is investigating the feasibility of collecting sequential blood samples from patients with brain cancer. The aim of the study was to test the feasibility of collecting and storing sequential blood samples for the Brain Cancer Biobank. Banking sequentially collected blood samples,

together with solid tumour samples, adds power and utility, but also complexity, to the biobanking process. Innovative procedures were developed for: patient recruitment and tracking to collect samples at multiple clinically relevant time-points during their cancer treatment; use of specialised tubes for blood collection; prospective clinical data collection to accompany samples; timely processing of blood samples and appropriate storage to maximise utility for future research; assays to test the range of utility of stored blood samples. Since June 2015, blood samples sequentially collected from patients with brain cancer have been processed and stored as aliquots of plasma and buffy coat. Data will be presented on the key performance indicators used in establishing the processes for patient consent and tracking, collection of multiple blood samples, processing techniques and sample utility. The Brain Cancer Biobank has been successful in establishing processes to collect and store sequential blood samples and is working to ensure the utility of these samples for future research.

Genomically unstable Glioblastoma (U-GBM) show exquisite sensitivity to Parp (poly[ADP-ribose] polymerase) inhibition

Kerrie McDonald[1], Swapna Joshi[1], Toni Jue[1], Lisette Schroder[1], Julia Yin[1], Mustafa Khasraw[2]

1 Cure Brain Cancer Foundation Biomarkers and Translational research Group, Sydney, Australia
2 Royal North Shore Hospital, Sydney, Australia

Aims: The development of effective targeted drugs for the treatment of glioblastoma (GBM) represents a major unmet need. Veliparib (ABT-888; Abbvie) inhibits both PARP1 and PARP2. The successful clinical application of veliparib and other PARP inhibitors (PARPi) will be assisted by the identification of predictive biomarkers.

Methods: We performed whole genome sequencing (WGS) on ten GBM specimens with matched normal DNA. Mutations were detected using qSNP and GATK and indels called with Pindel and GATK. Somatic structural variants were identified using the qSV package. We tested the efficacy of the combination of veliparib and radiotherapy (RT) in vitro using patient derived cell lines (PDCLs) and in vivo using our patient derived xenograft (PDX) models.

Results: Strikingly, in 2 patient samples denoted as G89 and G54, the mutation rate was at least 16-fold higher compared to the other 8 participants. G89 and G54 exhibited a large number of single nucleotide variants (SNVs), insertions, deletions and structural variant (SV) events when compared to the other 8 patient samples. The scale of genomic instability suggested defects in DNA maintenance, which could potentially define sensitivity to DNA damaging agents. We designated these GBM as U-GBM class. We found the U-GBM class of tumours, G89 and G54 to be hypersensitive to the combination of veliparib and RT, both in vitro and in vivo.

Conclusions: Mutations in DNA maintenance pathways may be a method for selecting patients for therapies involving the combination of DNA damaging agents such as radiotherapy, and PARP inhibitors. Additionally, the signature associated with genomically unstable GBM may be a method of identifying potential responders to PARP inhibitor therapy in clinical trials.

A lab-based hospital for personalising treatment for glioblastoma patients

Kerrie McDonald[1], Sylvia Chung[1], Sheri Nixdorf[1], Wendy Ha[1], Swapna Joshi[1], Julia Yin[1], Martina Hochwartner[1], Manuri Gunawardena[1], Charlie Teo[2], Jacob Fairhall[3], Raj Reddy[3]

1 Cure Brain Cancer Foundation Biomarkers and Translational research Group, Sydney, Australia
2 Centre for Minimally Invasive Neurosurgery, Sydney, Australia
3 Prince of Wales Hospital, Sydney, Australia

Aims: Increasingly, the development of novel therapies involves defining drug-diagnostic combinations where the presence of a molecular target or marker identifies patients who are more likely to respond to a specific therapy. This model of developing treatment and diagnostic/companion biomarker combinations is the emerging paradigm for novel diagnosis and therapies. In this study we aim to identify new therapies based on genomic targets in individual patients using lab based models.

Methods: We used a four-tiered system of tumour tissue collection and storage: (1) part of the tumour was cryofrozen; (2) part of the tumour was embedded in paraffin; (3) a cell line was established and (4) cells were intracranially injected into Nod-SCID-gamma mice. In a subset of tumours, DNA was sent for whole genome sequencing (WGS). Mutations and structural variations were validated in the cell line and the cells were subsequently treated with an appropriate targeted treatment.

Results: We have generated 158 patient derived cell lines from GBMs (initial and recurrent) and low-grade gliomas. We have developed 29 patient-derived xenografts models. Finally, approximately 15 patient models have been sequenced using WGS . The genomic landscape of GBM significantly varies from one patient to the next. In one patient we identified a translocation event encompassing the MDR2 gene and GNPDA1 gene. This tumour displayed exquisite sensitivity to anti-glycolytic drugs. In another tumour, deregulation of the DNA repair genes was evident. This tumour, when treated with PARP inhibitors in culture and in vivo showed remarkable sensitivity.

Conclusions: We have established a dynamic pipeline that can form a platform for developing personalized treatment approaches for patients.

CABARET Biomarker Study: Identifying biomarkers associated with longer overall survival in recurrent GBM after treatment with Bevacizumab

Kerrie McDonald[1], Liz Barnes[2], John Simes[2], Sheri Nixdorf[1], Kathryn Field[3]

1 Cure Brain Cancer Foundation Biomarkers and Translational research Group, Sydney, Australia
2 NHMRC Clinical Trials Centre, Sydney, Australia
3 Royal Melbourne Hospital, Melbourne, Australia

Aims: There are no effective systemic treatments available for patients with recurrent glioblastoma (GBM). Bevacizumab (Avastin) is FDA approved as a second line therapy for recurrent GBM and is used in some patients in Australia. Key questions cloud the value of Bevacizumab for recurrent GBM: (1) Why is benefit from Bevacizumab seen only in some patients? (2) How do we preselect these patients? To date no biomarkers have been identified to select patients who will benefit from this treatment.

Methods: The CABARET clinical trial: a randomized phase II study of Carboplatin and Bevacizumab in Recurrent GBM provides the linkage of clinical specimens to trial data. We used the CABARET dataset as a discovery cohort to identify the molecular phenotype (candidate molecular signature) of patients who responded to Bevacizumab. We tested tissue (n=56) for the expression level of 19 pre-selected proteins using immunohistochemistry. To identify novel biomarkers associated with response to Bevacizumab, we used whole genome sequencing (WGS). We extracted DNA from blood and tissue of the top ten poor responders and positive responders (defined by survival percentiles) and performed WGS.

Results: Methylation of the MGMT gene promoter measured using pyrosequencing was found to be significantly associated with longer survival. Despite statistical significance not being reached, high levels of two proteins, VEGFR2 and cMET were associated with longer survival. No other biomarkers were related to survival. Results of WGS will be available for presentation in October.

Conclusions: There are obvious benefits for patient stratification to avoid unnecessary toxicity in patients who fail to respond to the particular treatment; to reduce healthcare costs; and to better understand drug resistance. To improve drug selection, a more durable treatment response and improved survival will ensue.

Targeting CDK4 and 6 in the Classical Subtype of Glioblastoma

Kerrie McDonald[1], Daniel Madani[1], Mustafa Khasraw[2]

1 Cure Brain Cancer Foundation Biomarkers and Translational research Group, Sydney, Australia
2 Royal North Shore Hospital, Sydney, Australia

Aims: Glioblastoma is highly refractory to conventional treatment approaches. Since the introduction of concomitant and adjuvant temozolomide and radiotherapy, patients with glioblastoma have shown little improvement in the median survival time of just 15 months. Inhibitors that target the cell cycle of the tumour present an exciting prospect for glioblastoma, in particular the classical subtype. Overexpression of the cyclin dependent kinases (CDK) 4 and 6 as well as the homozygous deletion of CDNK2A are common events in glioblastoma.

Methods: We have developed over 15 patient derived xenograft (PDX) models with whole genome sequencing data. We identified the PDX models (n=4) that were of a "classical" subtype i.e. harbored mutations and amplification of EGFR, homozygous deletion of CDKN2A and wildtype for TP53 and RB1. We also measured the protein expression levels of CDK4/6 to confirm overexpression. We tested a highly specific and potent antiproliferative CDK4/6 inhibitor on this preselected panel of patient derived glioblastoma cells. We tested the efficacy of the CDK4/6 inhibitor as a monotherapy and in combination with radiotherapy (RT).

Results: We found, as a monotherapy, the CDK4/6 inhibitor to be highly effective in causing cell death on the preselected PDX cell lines (IC50: 515µM). Increases in efficacy were observed when we combined the inhibitor with RT. In vivo analysis of the drug and in combination with RT is currently underway.

Conclusions: This study demonstrated in vitro efficacy of CDK 4/6 inhibition alone or in combination with RT in glioblastoma. This study presents a new potential clinical strategy for patients with classical glioblastoma.

Crossing the great divide: aptamer engineering for targeted brain metastasis treatment

Joanna Macdonald[1], Patrick Houghton[1], Wei Duan[1], Sarah Shigdar[1]

1 School Of Medicine Deakin University, Melbourne, Australia

Classified as the most frequent cancer in the central nervous system, brain metastases are ten times more common than primary brain tumours. Situated within the safe sanctuary of the brain, protected by the blood brain barrier (BBB), current management strategies are limited, thus the overall survival for diagnosed patients is very poor. A novel strategy to overcome this barrier is to hijack active transport mechanisms present on the BBB to transport large molecules into the brain. A receptor of particular interest is the transferrin receptor (TfR), given its high expression. Nucleic acid based aptamers are ideal for this purpose given the ability to generate them against a vast range of targets, their stability and safety profile. This project aims to generate a bi-functional aptamer capable of transcytosing through the BBB by targeting the TfR and specifically delivering a cytotoxic payload to the tumours. This was achieved through the fusion of two mono-functional aptamers targeting the TfR and EpCAM,a glycoprotein overexpressed in a number of solid tumours with a high incidence of metastasing to the brain. The specificity and selectivity of these aptamers was confirmed against a number of cells lines expressing the TfR, EpCAM or neither using flow cytometry and confocal microscopy. Following

this we have demonstrated the ability of this aptamer to enter the brain in a living system using an in vivo mouse model, with the results showing specific internalisation within 10 minutes of tail vein injection. Intercalation of the common chemotherapeutic doxorubicin, showed no influence on aptamer specificity, with the conjugate specifically internalised within the targeted cells following 1 hour incubation. These results demonstrate the great potential this bi- functional aptamer doxorubicin conjugate has for the specific treatment of brain metastases in addition to the possibility of mitigating the neurotoxic effects on healthy brain tissue.

Bevacizumab in Neurofibromatosis type 2 (NF2) related vestibular schwannomas: a UK nationally coordinated approach to delivery and prospective evaluation

Katrina Morris[1,2], Martin McCabe[3], Shazia Afridi[4], Raj Jena[5], Claire Blesing[2], John Golding[6], Dorothy Halliday[2], Rosalie Ferner[4], D Gareth Evans[7], Patrick Axon[8], Pieter Pretorius[2], Allyson Parry[2]

1 University of New South Wales, Sydney, Australia
2 Oxford University Hospitals NHS Trust, Oxford, UK
3 Institute of Cancer Studies, University of Manchester, Manchester, UK
4 Dept of Neurology, Guys and St Thomas's Hospital, London, UK
5 University of Cambridge, Department of Oncology, Cambridge, UK
6 University of Westminster, London, UK
7 Central Manchester NHS Foundation Trust, Manchester, UK
8 Addenbrookes Hospital, Cambridge, UK

Background: Neurofibromatosis type 2 (NF2) patients develop multiple nervous system tumors including bilateral vestibular schwannomas (VS). The tumors and their surgical treatment are associated with deafness, neurological disability and mortality.

Medical treatment with bevacizumab has been reported to reduce VS growth and to improve hearing. In addition to evaluating these effects this study also aimed to determine other important consequences of treatment including patient reported QOL and the impact of treatment on surgical VS rates.

Methods: Patients treated with bevacizumab underwent serial prospective MRI, audiology, clinical, CTCAE-4.0 adverse events and NFTI-QOL quality of life assessments. Tumor volumetrics were classified according to the ReiNs criteria and annual VS surgical rates reviewed.

Results: 61 patients (59% male), median age 25 years (range 10-57) were reviewed. Median follow-up was 23 months (range 3-53). Partial volumetric tumor response was seen in 39% and 51% had stabilization of previously growing tumors. Age and pre-treatment growth rate were predictors of response. Hearing was maintained or improved in 86% of assessable patients. Mean NFTI-QOL scores improved from 12.0 to 10.7 ($p<0.05$). Treatment was generally well tolerated. Hypertension was observed in 30% and proteinuria in 16%. 12 treatment breaks occurred due to adverse events. The rates of VS surgery decreased after the introduction of bevacizumab.

Conclusion: Treatment with bevacizumab in this UK-wide cohort decreased VS growth rates, improved hearing and QOL. The potential risk of surgical iatrogenic damage was also reduced due to an associated reduction in VS surgical rates. However, careful patient selection is important given the risks of prolonged treatment in a young population. Ongoing follow-up of this cohort will determine the long-term benefits and risks of bevacizumab treatment.

Behaviour of ependymomas in UK neurofibromatosis type 2 (NF2) patients on Bevacizumab

Katrina Morris[1,2], Shazia Afridi[3], Dorothy Halliday[4], Anke Hensiek[5], John Ealing[6], Mark Kellet[6], Pieter Pretorius[7], D Gareth Evans[6], Allyson Parry[2]

1 University of New South Wales, Sydney, Australia
2 Department of Neurology, John Radcliffe Hospital, Oxford, UK
3 Department of Neurology, Guy's & St Thomas's Hospital, London, UK
4 Department of Genetics, Churchill Hospital, Oxford, UK
5 Department of Clinical Neurosciences Addenbrookes Hospital, Cambridge, UK
6 Central Manchester NHS Foundation Trust, Manchester, UK
7 Department of Neuroradiology, John Radcliffe Hospital, Oxford, UK

Background: Bevacizumab has been reported to have positive effects on hearing and volumetric tumour reduction in NF2 patients.1 A group of NF2 patients in the UK with rapidly growing schwannomas have been commenced on Bevacizumab since August 2010. This patient group often has significant disability from multiple peripheral and cranial nerve schwannomas, meningiomas and spinal cord ependymomas.

Aim: To explore the effect of Bevacizumab on ependymomas in NF2 patients treated for rapidly growing schwannomas.

Methods: The records of the 61 patients commenced on Bevacizumab in the UK between August 2010 and December 2013 for rapidly growing schwannoma were reviewed. Retrospective analysis of co-existent intrinsic spinal tumours was performed.

Results: The available spinal MRI scans are not appropriate for volumetric analysis. Replicable methods for measurement of both solid enhancing and cystic components of the observed ependymomas were developed. Adjacent cord oedema and syrinx were assessed where present.

30% of the cohort had intrinsic spinal tumours identified. Cystic components and adjacent syrinxes had the most dramatic reduction in size.

A correlation between changes in tumour and clinical outcomes was undertaken.

Discussion: Ependymomas in NF2 patients often are slow growing over prolonged periods and are usually asymptomatic at the time of identification. However, at times they can become symptomatic and cause disability. Both the solid and cystic components of the ependymoma can create clinical deterioration. Evaluating the effects of Bevacizumab on NF2 associated ependymomas in a prospective fashion, with dedicated serial imaging, is worthy of consideration.

Reference:

1. Plotkin SR Merker VL, Halpin C et al Bevacizumab for Progressive Vestibular Schwannoma in Neurofibromatosis Type

2: A Retrospective Review of 31 Patients Otol Neurotol 2012 33:1046-1052

Risk adapted single or fractionated stereotactic radiotherapy using the Novalis system for management of Pituitary adenoma

Raghav Murali-Ganesh[1], Daniel Ashrafi[1], Lani Attwood[1], Benjamin Jonker[2,3], Nitya Patanjali[1]

1 Department of Radiation Oncology, Chris O'Brien Lifehouse, Sydney, Australia
2 Department of Neurosurgery, Royal Prince Alfred Hospital, Sydney, Australia
3 Brain & Mind Research Institute, University of Sydney, Sydney, Australia

Aim: The aim of this study was to evaluate local control and toxicity following single (SRS) or fractionated stereotactic radiotherapy (fSRT) using the Novalis Tx Linear accelerator for management of pituitary adenoma at a single institution.

Methods: Between October 2011 and June 2015, 28 patients (table1) with pituitary adenomas (20 functioning and 8 non-functioning) with a median age of 57 (range 29-84) were retrospectively evaluated following a treatment protocol of SRS (12 patients) and fSRT (16 patients) with the discriminatory feature being size of lesion (fSRT for >2cm) and proximity to the optic chiasm (OC) (fSRT if <3mm from OC). 25 (89%) patients underwent surgery prior to SRS/fSRT. All patients were treated on a dedicated linear accelerator (Novalis, Heimstetten, Germany). SRS doses were 15Gy to non-functioning tumours and 20Gy to functioning tumours. For fSRT (Gross Tumour Volume with 2mm expansion for Planning Target Volume (PTV)) a median isocentre dose of 50.4Gy was delivered in 28 fractions, with 95% of PTV covered by the 100% isodose. Plan parameters including dose to PTV and organs at risk are appraised (fig1). Treatment outcome parameters including local control, endocrine outcomes and toxicity are measured.

Results: With a median follow-up time of 24 months, the radiological local control rate was 100%. Of patients with normal pituitary function at baseline, 31% (5/16) experienced ≥ 1 hormone deficiencies after fSRT and 25% (3/12) after SRS. Of the 8 functioning adenomas, 2 patients had complete normalisation of hormone function and 6 patients had >50% decrease of hypersecreted hormone. Hypopituitarism was observed in 8/28 patients (29%) as the commonest late side effect. Although 57% (16/28) of optic chiasms were at least partially within the PTV, no radiation-induced optic neuropathy was noted.

Conclusion: SRS/fSRT is an effective and well tolerated option for the control of residual or recurrent pituitary adenomas.

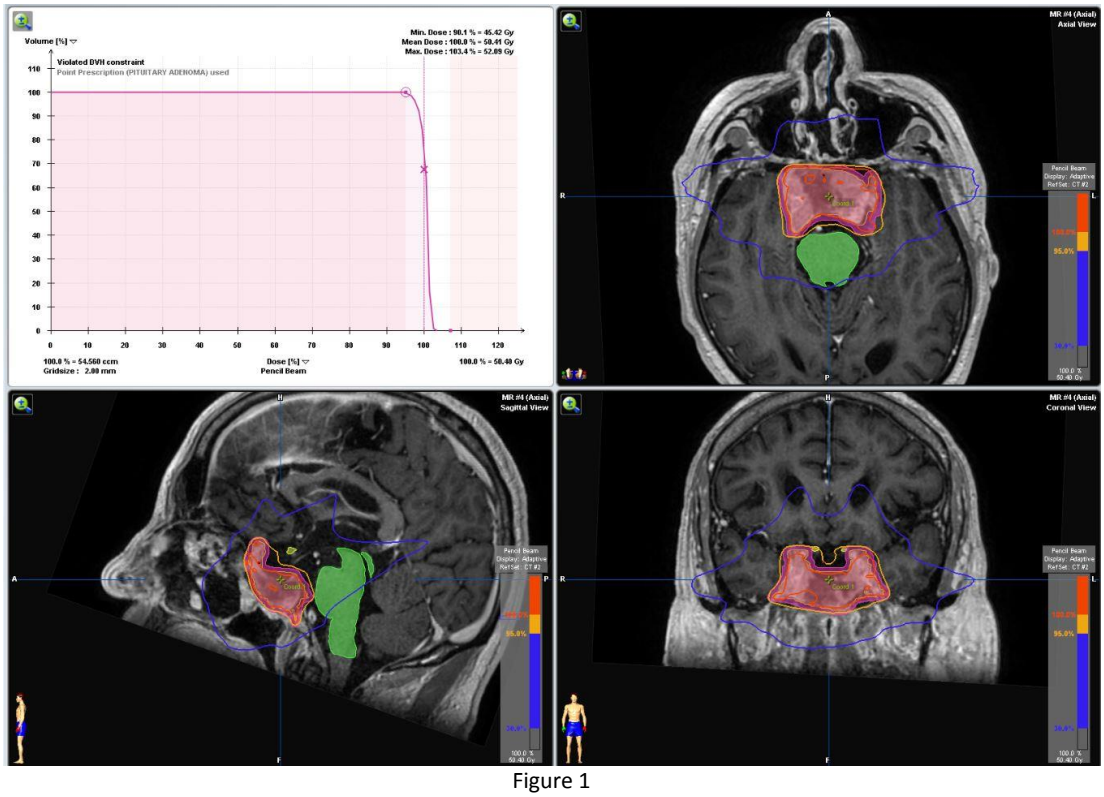


Figure 1

Age		
- **Mean**	57.1	
- **Range**	29 to 84	
- **Median**	56.5	
Patients	28	
- **Male**	16	60.7%
- **Female**	12	46.4%
Initial Hormone Status		
- **Nonfunctioning**	20	71.4%
- **Functioning**	8	28.6%
Adenoma Subtype at diagnosis		
- **Non-functioning**	20	71.4%
- **ACTH-secreting**	3	10.7%
- **Prolactin**	3	10.7%
- **GH-secreting**	2	7.1%
Type of last surgery:		
- **Trans-sphenoidal**	23	85.7%
- **Trans-cranial**	2	7.1%
- **No histology**	3	7.1%
Tumour Extent Pre-RT		
- **Intra-sellar**	9	32.1%
- **Extra-sellar**	18	64.3%
- **Unknown**	1	3.6%
Visual Defect Pre-RT		
- **Present**	10	35.7%
- **Absent**	18	64.3%
Hormone status pre-RT		
- **Normal**	14	50.0%
- **Abnormal**		0.0%
- **1**	7	25.0%
- **2**	0	0.0%
- **>3**	7	25.0%
RT Type		
- **SRS**	12	42.9%
- **fSRT**	16	57.1%
Median months follow up	24	

Table 1

Glioblastoma brain cancer invasion: how different subclasses move through the brain

Thomas Grundy[1,2], Ellen De Leon[1], Brett Stringer[3], Bryan Day[3], Andrew Boyd[3], Justin Cooper-White[4], Geraldine O'Neill[1,2]

1 Children's Cancer Research Unit, The Children's Hospital, Sydney, Australia
2 Discipline of Paediatrics and Child Health, University of Sydney, Sydney, Australia
3 Brain Cancer Research Unit & Leukaemia Foundation Research Unit, QIMR Berghofer, Brisbane, Australia
4 Tissue Engineering and Microfluidics Laboratory, Australian Institute for Bioen, Brisbane, Australia

Solid tumours are frequently detected by physical palpation and the tumour stiffness that is evidenced by the ability to distinguish the tumour from surrounding tissue by touch has emerged as a significant factor in the promotion of cancer malignancy. There are conflicting reports over whether glioblastoma (GBM) cells are rigidity-dependent (induced to invade in response to increasing external tissue stiffness) or rigidity-independent (invade irrespective of local tissue rigidity). Since GBM constitutes molecularly and prognostically distinct subclasses, we hypothesized that the conflicting reports may be due to different responses between the subclasses. To address this hypothesis, we analysed the rigidity-response of primary GBM lines representative of proneural, neural and mesenchymal subclasses, based on cluster analysis of microarray expression data as previously reported. Cells were plated on poly-acrylamide gels of defined rigidity, corresponding to the reported range of Young's modulus values for brain tissue (0.2, 1.0 and 8.0 kPa) and 50 kPa (~stiffness of fibrotic tissue). Time-lapse imaging and cell tracking revealed that proneural cell migration speed is rigidity-dependent,

mesenchymal cell migration speed exhibits an intermediate response and neural cell migration is rigidity-independent. Moreover, we show corresponding differences in actin stress fibre formation correlating with the differences in rigidity responses. Our data reveal differential responses between GBM subclasses to the external mechanical environment that may determine invasive capacity. While stratification of GBM patients into different risk groups can inform treatment decisions, the even greater promise of such stratification is if we can find approaches to specifically target the different patient groups. Our data has revealed subclass specific invasion mechanisms that may provide a key to new approaches to successfully treat GBM from different subclasses.

Experience of Procarbazine, Lomustine and Vincristine (PCV) Chemotherapy in Low-Grade and High-Grade Glioma in the real-world setting

Geoffrey Peters[1,3], Po-ling Inglis[1,3], Zarnie Lwin[1,3], Rosalind L Jeffree[2,3], Catherine Bettington[1], MIchael Colditz[2,3]

1 Cancer Care Services, Royal Brisbane and Women's Hospital, Brisbane, Australia
2 Department of Neurosurgery, Royal Brisban and Women's Hospital, Brisbane, Australia
3 University of Queensland, Brisbane, Australia

Introduction: PCV chemotherapy has re-emerged since the EORTC 26951 and RTOG 9402 clinical trials reported improvement in overall survival for low grade and anaplastic glioma.

Objectives: We explored treatment-related toxicities of PCV and any impact on quality of life (QoL), in the real-world setting

Methodology: Patients with intra-cerebral tumour who underwent surgical resection or biopsy at our institution from August 2007-2014 were identified through detailed theatre lists. Patients with confirmed WHO histological grade II and III glioma were selected for retrospective review, to capture those receiving at least 1 cycle of PCV during their treatment. Electronic chemotherapy prescribing and dispensing software were interrogated to cross-match patient selection. Hospital charts were then manually reviewed to collect data on treatment, toxicities and any documented impact on QoL during their chemotherapy schedule and outpatient appointments.

Results: Nineteen patients received at least 1 cycle of PCV, 9 had WHO grade II, 8 had grade III, 2 had glioblastoma. Median age was 35 years, Ten had 1p19q co-deletion. Eight (42%) completed the planned 6 cycles. Haematologic toxicity of grade 1-2 and grade 3-4 occurred in 84% and 32%, respectively. One patient experienced grade 4 hepatotoxicity. Fourteen (74%) required dose reductions. Four had doses omitted and 11 had dose delays. Seven required hospital admissions. Six patients ceased treatment due to disease progression. Four patients missed appointments. Patients or carers reported reduced QoL in 8 documented encounters.

Conclusions: Our data highlights real-world toxicity and impact on QoL with PCV. Benefits and risks need to be explained to patients for shared decision making.

Fluorescence in situ hybridisation (FISH) probe ratio independently predicts survival in 1p19q co-deleted gliomas

Mark Pinkham[1], Tom Liptrot[2], Catherine McBain[3], Nick Telford[4], Fran O'Neill[4], Rao Gattamaneni[3], Anna Tran[3], Gillian Whitfield[3]

1 Department of Radiation Oncology, Princess Alexandra Hospital, Brisbane, Australia
2 Clinical Outcomes Unit, The Christie NHS Foundation Trust, Manchester, UK
3 Department of Clinical Oncology, The Christie NHS Foundation Trust, Manchester, UK
4 Department of Oncology Cytogenetics, The Christie NHS Foundation Trust, Manchester, UK

Aims: 1p19q co-deletion is associated with improved survival. Co-deletion status is considered a binary result but determined by FISH probe ratio, a continuous variable. We assessed whether survival for co-deleted gliomas varies according to this ratio.

Methods: Consecutive patients with WHO grade II and III gliomas undergoing 1p19q analysis using FISH at Christie Hospital between 2006-2014 were included. Minimum follow-up was 6 months unless death occurred sooner. A dual locus-specific probe ratio ≤0.8 indicated chromosome deletion. Patients were stratified by ratios ≤0.6, 0.6 to ≤0.8, 0.8 to ≤1.0 and >1.0 for both chromosomes. Kaplan Meier survival curves were compared using the Log Rank test. Prognostic factors were evaluated using a multivariate Cox model.

Results: 243 patients were identified. Median age 46yr (range 18-83) and median follow-up 3.5yr (range 33days-22yr). 151 tumours were WHO grade II and 58% co-deleted. 92 tumours were WHO grade III and 45% co-deleted. For grade II and III tumours with versus without co-deletion, median survival was 13.5yr versus 12.1yr (p=0.42) and 12.9yr versus 2.0yr (p<0.0001), respectively. As expected, age, performance status (PS), WHO grade and co-deletion predicted survival on multivariate analysis.

Of 131 patients with co-deletion, 5yr survival was similar when one or both ratios >0.6 (p=0.62) but worse if both ratios ≤0.6 (63%, 95%-CI 44-78%) compared to the rest (91%, 95%-CI 77-97%, p=0.005). On multivariate analysis, probe ratios ≤0.6 (p=0.026) and initial chemotherapy use (p=0.028) correlated with survival but age, PS and WHO grade did not.

Conclusions: The prognostic relevance of WHO grade in co-deleted gliomas, where survival is markedly improved overall, is uncertain. For co-deleted gliomas, FISH probe ratios ≤0.6 independently predicted inferior survival. The mechanism is unclear but may relate to higher tumour cell density. Initial chemotherapy use appears beneficial, consistent with emerging trial reports at extended follow-up.

Volumetric-Modulated Arc Therapy (VMAT) for adult craniospinal irradiation

Esther Sim[1,2], Michael Buchanan[1], Minjae Lah[1], Marisa Xinis[1]

1 Genesis CancerCare Queensland, Brisbane, Australia
2 The University of Queensland, Brisbane, Australia

Aims: For tumours of the central nervous system (CNS) with high risk of neuraxis recurrence, treatment of the entire CNS with radiotherapy can be an effective treatment option. However, this technique is technically challenging and complex. In adults, the length of the target volume further complicates treatment planning. Traditional 3D-conformal craniospinal irradiation (CSI) does not spare any critical organs, resulting in both acute and late toxicity. We present a volumetric-modulated arc therapy (VMAT) technique for CSI, examining the dose conformity and homogeneity in the planning target volume (PTV) and dose to the organs at risk (OAR).

Methods: We retrospectively identified a 33 year old female patient with a diagnosis of medulloblastoma. The entire craniospinal neuraxis was treated to a dose of 36Gy in 20 fractions utilising conventional 3D-conformal (3DCRT) technology. A VMAT plan was generated and optimised and this was compared to the 3DCRT plan.

Results: The Piddick Conformity Index was 0.45 and 0.94 for the 3DCRT and VMAT plans respectively. This represents significantly better conformity with the VMAT technique. Figure 1 illustrates the dose distributions using 3DCRT and VMAT techniques. Examination of the dose-volume histograms (DVHs) showed dose to all OARs was acceptably low. In particular, the utilisation of VMAT compared with 3DCRT resulted in significant reductions in doses to the thyroid (10Gy vs 26Gy respectively), oesophagus (12Gy vs 28Gy respectively) and heart (4Gy vs 12Gy respectively). The VMAT technique does however result in a greater volume of the lung, liver and kidney receiving low doses of radiation.

Conclusion: Utilising a RapidArc technique for CSI achieved a highly conformal treatment. Doses to OARs were within acceptable values, with a significant reduction in mean dose to organs such as the thyroid, oesophagus and heart.

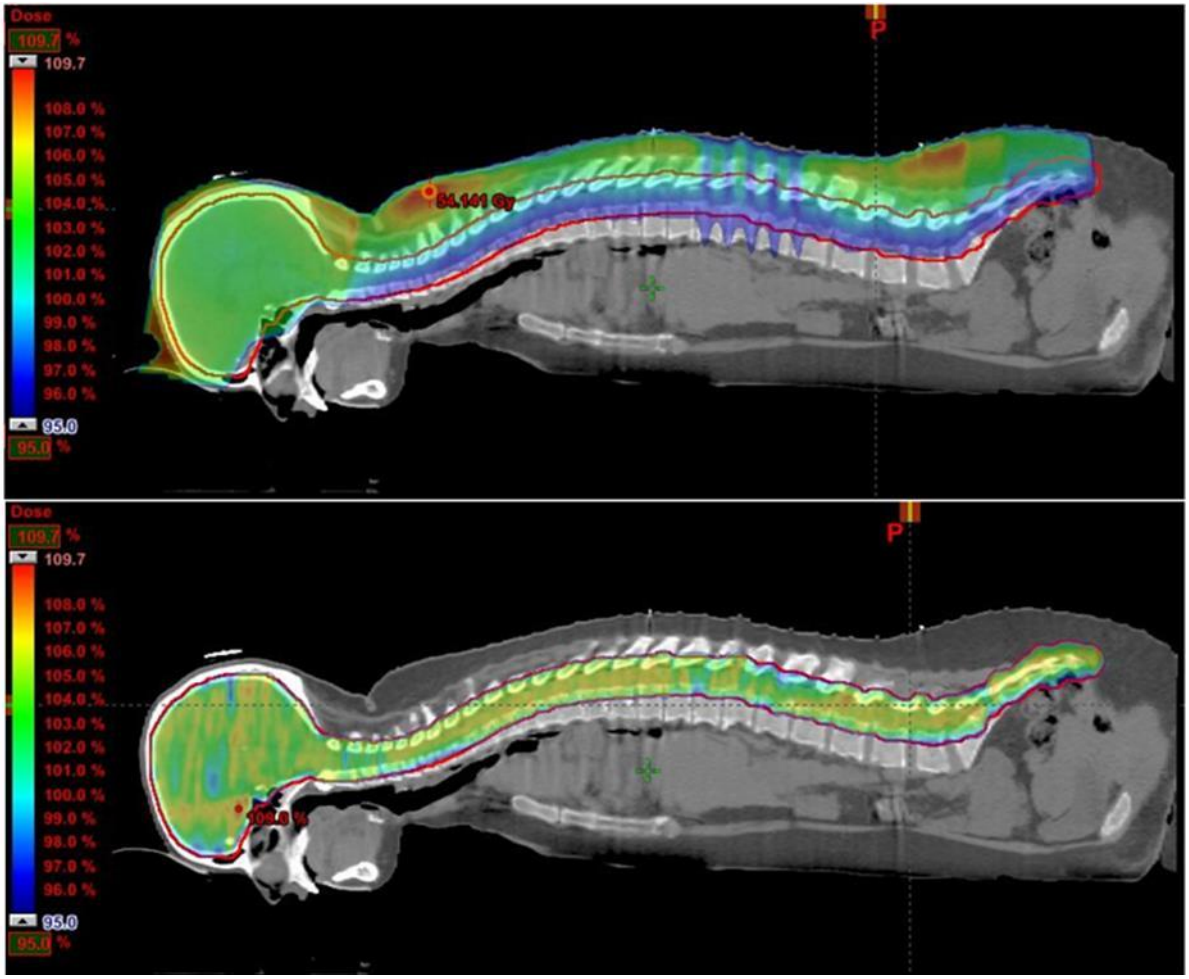


Figure 1 3DCRT v VMAT

Caesar Trial: Assessing effectiveness of Levetiracetam prophylaxis at reducing seizure incidence in patients undergoing craniotomy, with no previous seizure history

Bhavneet Singh[1], Sarah Olson[1], Bruce Hall[1], Helen Brown[2], Caroline Airey[2], Aleksander Dionisio[2], Peter Pillans[3], Thomas Campbell[1]

1 Department of Neurosurgery, Princess Alexandra Hospital, Brisbane, Australia
2 Department of Neurology, Princess Alexandra Hospital, Brisbane, Australia
3 Dept of Clinical Pharmacology, Princess Alexandra Hospital, Brisbane, Australia

Introduction: Seizures in Neurosurgical patients are pathological phenomenon which are associated with poor clinical outcomes, reduced quality-of-life and predispose to unprovoked seizures in later life [1]. The clinical basis of anticonvulsant prophylaxis post-craniotomy stems from early 1900s observations that craniotomy promotes cerebral oedema and haemorrhage. However, conclusions from current retrospective data worldwide indicates anticonvulsant prophylaxis confers no benefit[2]. This prospective study aims to determine if prophylactic anticonvulsant administration reduces seizure incidence in the post-supratentorial craniotomy patient, with no previous seizure history. Prophylactic agent used for this study is Levetiracetam.

Methods: Ethics approval received in 2014 to commence recruitment over 2 years, based on inclusion/exclusion criteria. Patients randomised to either Cases, to receive 1g Levetiracetam at induction, then 500mg BD for 7-days total, or Controls, with no prophylaxis. All patients monitored for clinical factors which could promote seizure incidence, and for Levetiracetam side-effects. All trial patients followed up for 6-weeks total.

Results:
total n=81 (case=39, control=42), to date.
seizure incidence: cases=0, control=1 (focal seizures, progressing to status epilepticus)
tumour surgery=75
aneurysm=2
haematoma evacuation=4

Discussion: This study is in the early stages of 2-year recruitment and data collection. The current trends show patients without seizures pre-operatively do not benefit from seizure prophylaxis. This would support the conclusions of current worldwide retrospective data that seizure prophylaxis is not indicated post-operatively in patients without seizures pre-operatively.

1. You G, Sha Z, Jiang T. The pathogenesis of tumor-related epilepsy and its implications for clinical treatment. Seizure. 2012;21(3):153–9.

2. Glantz MJ, Cole BF, Forsyth PA et al. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000;(54):1886–1893

Determining a cut point for Ki-67 proliferation that predicts for poorer survival in high-grade glioma

Eugene Ho-Lam Wong[1, 3], Purnima Sundaresan[2], Najmun Nahar[2], Thomas Ng[2], Val Gebski[2], Winny Varikatt[2], Jayasingham Jayamohan[2]

1 Northern Sydney Local Health District, Sydney, Australia
2 Sydney West Area Health Service, Sydney, Australia
3 University of Newcastle, Newcastle, Australia

Aims: Ki-67 index is used to assess cell proliferation during histopathological assessment of various tumours including high grade gliomas (HGG): Anaplastic astrocytoma, Anaplastic Oligodendroglioma and Glioblastoma Multiforme (GBM). We aimed to determine if there is a correlation between percentage staining of Ki-67 and overall survival in patients with HGG and determine a cut-point for percentage staining of Ki-67 that predicts for poorer survival.

Methods: Records of adult patients diagnosed with HGG on histopathological specimens examined at the Institute of Clinical Pathology and Medical Research at Westmead Hospital, NSW, between 1st of January 2002 and 31st of July 2012 were identified. The specimens of these patients were examined for quantification of Ki-67 staining by two independent pathologists. Patient, disease, treatment and survival data were collected from hospital and cancer care service records. Descriptive statistical analyses were performed on the patient, disease and treatment data. Survival curves were constructed using Kaplan Meier methods. Using the minimum p value approach we obtained a cut-point for Ki-67 percentage staining that predicts for poorer survival.

Results: Of the eligible 78 patients (median age = 57, range 18 - 87) 46 (59 %) were males and 32 (41%) were females. 59 (76%) patients were of ECOG performance status 0 -1. Seven patients had anaplastic astrocytoma or anaplastic oligodendroglioma and the rest had GBM. There was a clear inverse correlation between Ki-67 percentage staining and overall survival. In patients with Ki-67 ≤ 30% (n=18), 5 year survival was approximately 50% compared to those with Ki-67 >30% (n=60) with survival of 10% (logrank P-value 0.02, HR 0.39, 95% CI 0.17 – 0.88).

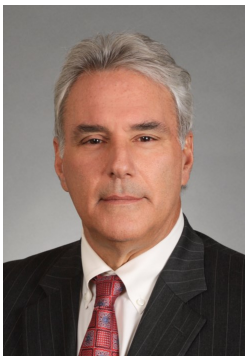
Conclusion: There appears to be a correlation between percentage staining of Ki-67 and overall survival in patients with HGG. Percentage staining of Ki-67 > 30% appears to predict for poorer survival in HGG.

Notes

2016 ASNO / COGNO ASM

CONFIRMED INTERNATIONAL SPEAKERS

PROF ROGER STUPP MD



PROF MITCH BERGER MD

PROF PAUL MISCHEL MD

ASSOC PROF ARJUN SAHGAL
BSC, MD, FRCPC

PROF W. K. ALFRED YUNG MD

PROF GREGORY RIGGINS MD PHD

ASST ADJ PROF MARY LOVELY
PHD, RN, CNRN

COGNO
COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

COOPERATIVE TRIALS **G**ROUP FOR **N**EURO-**O**NCOLOGY

The achievement of better health outcomes for patients and those affected by brain tumours through clinical trials research

2016: SAVE THE DATE!

11th-15th SEPTEMBER 2016

SYDNEY, AUSTRALIA

13TH ASIAN SOCIETY FOR NEURO-ONCOLOGY (ASNO) MEETING / 9TH COGNO ANNUAL SCIENTIFIC MEETING

"Neuro-Oncology: is the landscape changing?"

Register for updates by emailing cogno@cogno.org.au

COGNO

COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY