COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

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

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# 13th COGNO ANNUAL SCIENTIFIC MEETING

## *Brain Cancer 2021: Concepts to Cure*

**Sunday 24th - Tuesday 26th October 2021**

**Virtual**

# CONFERENCE BOOKLET

COGNO

COOPERATIVE TRIALS GROUP FOR NEURO-ONCOLOGY

## CONTENTS



## 2021 ASM ORGANISING COMMITTEE

A/Prof Rosemary Harrup, Co-Convenor (Medical Oncologist, Royal Hobart Hospital)
Dr Sanjeev Gill, Co-Convenor (Medical Oncologist, Alfred Health & Cabrini Hospital)
Prof Kate Drummond (Neurosurgeon, The Royal Melbourne Hospital)
Ms Marcia Fleet (Cancer Care Coordinator, Neuro-oncology unit, The Royal Melbourne Hospital)
Prof Terry Johns (Professor of Paediatric Cancer Research and Program Head of the Telethon Kids Cancer Centre)
A/Prof Jeremy Ruben (Radiation Oncologist, The Alfred)
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Ms Danielle Massey (Project Officer, COGNO)
A/Prof Ben Chua (Radiation Oncologist, GenesisCare Rockhampton and Brisbane), 2022 ASM Co-Convenor
Dr Hamish Alexander (Neurosurgeon, Briz Brain & Spine), 2022 ASM Co-Convenor

## TWITTER

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Dear Colleagues

On behalf of the Organising Committee, it is our great pleasure to welcome you to the 13th COGNO Annual Scientific Meeting.

The theme of the meeting is 'Brain Cancer 2021: Concepts to Cure'.

We are very fortunate to warmly welcome five international guest speakers to our first Virtual meeting:

- Prof David N Louis MD
- Prof Antonio (Nino) Chiocca MD PhD FAANS
- Prof Gelareh Zadeh MD PhD FRCS(C) FAANS
- Prof Michael Jenkinson MB ChB PhD FRCSEd
- Ms Maureen Daniels BScN RN

The meeting sessions will commence with Translational Science 1 & 2, and COGNO Trials Updates on Day 1, with Meningioma, Translational Radiology, and Supportive Care on Day 2 followed by the Selected Abstracts session before the COGNO AGM.

In addition to our invited international speakers, we have representation from a broad number of disciplines across our local contributors together with many high quality submitted poster abstracts. Don't miss the Selected Abstracts session on Tuesday 26 Oct commencing at 3:15pm.

Prizes will be awarded for the Most Outstanding Oral Presentation, the Most Outstanding Poster Presentation, the Young Investigator Award, and the BTAA Lynette Williams Award for the best poster related to research into supportive care for people with brain tumours.

Our appreciation goes to all our sponsors and supporters: Cure Brain Cancer Foundation, The Brain Cancer Group, Elekta, PharmAbcine, Brain Tumour Alliance Australia, and Cancer Australia.

On behalf of the Organising Committee, we hope you enjoy the ASM.

Kind regards

A/Prof Rosemary Harrup and Dr Sanjeev Gill
Co-Convenors. COGNO ASM 2021

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

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**PROGRAM OF EVENTS** (as at 20 October 2021)
(Changes may be made to the program)

| **Sunday 24 October: Pre–ASM Satellite Meetings** | | |
|---|---|---|
| **TIME** | **MEETING** | **CHAIR** |
| 9:00am – 4:30pm | **ABCARA Scientific Research Symposium**<br>Program available here | Hui Gan / Terry Johns |
| 10:30am – 2:30pm | **BTAA Patient Education and Information Forum**<br>Program available here | |
| 5:30 – 7:00pm | **COGNO Management Committee Meeting** (closed meeting) | Eng-Siew Koh |

| **Monday 25 October: ASM Day 1** | | |
|---|---|---|
| **TIME** | **MEETING** | **CHAIR** |
| 8:00 – 10:00am | **COGNO Scientific Advisory Committee Meeting** (open to COGNO members only) | Hui Gan |
| 10:00 – 10:30am | Morning tea break | |
| 10:30 – 10:40am | **Welcome and Day 1 program overview** | Rosie Harrup |
| 10:40am – 12:30pm | **Session 1 – Translational Science Part 1** | Rosie Harrup |
| | 2021 CNS WHO classification update - *David N Louis* | |
| | Scanning the horizon for new treatments for glioblastoma - *Nino Chiocca* | |
| | Liquid biopsy in glioma - *Jordan Jones* | |
| 12:30 – 12:40pm | **COGNO Chair Update** | Eng-Siew Koh |
| 12:40 – 1:30pm | Lunch break | |
| 1:30 – 2:40pm | **Session 2 - Translational Science Part 2** | Terry Johns |
| | Drug discovery and new therapeutics - *Lenka Munoz* | |
| | Role of ion channels in high grade gliomas - *Emily Fletcher* | |
| | Chimeric Antigen Receptor T cell Immunotherapy for brain cancers: A Research update - *Misty Jenkins* | |
| | Abstract ID 22 - Correlating clinical outcomes with gene signatures using digital spatial profiling of melanoma brain metastases - *Harry Gasper* | |
| 2:40 – 2:50pm | **ABCARA Update** | Terry Johns |
| 2:50 – 3:20pm | Afternoon tea break | |
| 3:20– 5:00pm | **Session 3 – COGNO Trials Updates** | Ben Chua |

| **Tuesday 26 October: ASM Day 2** | | |
|---|---|---|
| **TIME** | **MEETING** | **CHAIR** |
| 9:00 – 9:10am | **Welcome and Day 2 program overview** | Sanjeev Gill |
| 9:10 – 10:30am | **Session 4 – Meningioma** | Kate Drummond |
| | Meningioma update from the International Collaboration on Meningioma - *Gelareh Zadeh* | |
| | Clinical trials in meningioma - *Michael Jenkinson* | |
| 10:30 – 11:00am | Morning tea break | |
| 11:00am – 12:30pm | **Session 5 – Translational Radiology** | Jeremy Ruben |
| | Neuro-oncology and radiogenomics: Time to integrate? - *Arian Lasocki* | |
| | Novel visualisations of tumour growth on MRI - *Frank Gaillard* | |
| | Ultra-high field imaging for brain tumours - *Meng Law* | |
| 12:30 – 1:30pm | Lunch break | |

| | | |
|---|---|---|
| 1:30 – 2:45pm | **Session 6 – Supportive Care** | Marcia Fleet |
| | The Gerry & Nancy Pencer Brain Tumor Centre, A Bouquet of Supportive Care; 20 Years of Evolution, Lessons Learned & Looking Ahead – *Maureen Daniels* | |
| | Online interventions for supportive care in brain tumours - *Kate Drummond* | |
| | BRAINS: assessing and addressing unmet needs in people with brain cancers & their families - *Haryana Dhillon* | |
| 2:45 – 3:15pm | Afternoon tea break | |
| 3:15 – 3:45pm | **Session 7 – Selected Abstracts** | Hamish Alexander |
| | Abstract ID 7 - From post-operative to pre-operative: neoadjuvant stereotactic radiosurgery for brain metastases - *Cristian Udovicich* | |
| | Abstract ID 23 - Quantitative volumetric tumour response in patients treated with combination Gamma Knife stereotactic radiosurgery and immunotherapy for melanoma brain metastases - *Mihir Shanker* | |
| | Abstract ID 15 - Patterns of care of adult patients diagnosed with medulloblastoma in the Australian population - *Sagun Parakh* | |
| 3:45 – 3:55pm | **ASM Summary and Close** – includes presentation of the Most Outstanding Oral Presentation, Most Outstanding Poster Presentation and Young Investigator Awards | Sanjeev Gill / Ben Chua / Hamish Alexander |
| 4:30 – 5:30pm | **COGNO Annual General Meeting** (open to COGNO members only) | Eng-Siew Koh |

## ORAL ABSTRACT LISTING

**Session 2 - Translational Science Part 2**

**22 Correlating clinical outcomes with gene signatures using digital spatial profiling of melanoma brain metastases**

Harry Gasper, Arutha Kulasinghe, Priyakshi Kalita-de Croft, Elizabeth Ahern, Samuel Foong, Anna Kuchel, Margaret Cummings, Kenneth O'Byrne, Rosalind Jeffree, Sunil Lakhani, Melissa Eastgate

**Session 7 – Selected Abstracts**

**7 From post-operative to pre-operative: neoadjuvant stereotactic radiosurgery for brain metastases**

Cristian Udovicich, Sweet Ping Ng, Nola Bailey, Damien Tange, Neda Haghighi

**15 Patterns of care of adult patients diagnosed with medulloblastoma in the Australian population**

Sagun Parakh, Amy Davies, Kerryn Westcott, Daniel Roos, Amal Abou-Hamden, Elizabeth Ahern, Peter Lau, Sowmya Cheruvu, Ganesalingam Pranavan, Andrew Pullar, James Lynam, Cecelia Gzell, Jim Whittle, Sarah Cain, Po-ling Inglis, Rosemary Harrup, Elizabeth Hovey, Hui K. Gan

**23 Quantitative volumetric tumour response in patients treated with combination Gamma Knife stereotactic radiosurgery and immunotherapy for melanoma brain metastases**

Mihir Shanker, Heath Foley, Samuel Crowley, Emma Thomson, Kendall Higgs, Christopher Bradhurst, Michael Huo, Victoria Atkinson, Matthew Foote, Mark Pinkham

## POSTER ABSTRACT LISTING

**2 The Effects of Surgery and Adjuvant Therapy on Survival Outcomes in Clear Cell Ependymomas: A Systematic Review and Meta-Analysis of Individual Patient Data**

Barry Ting Sheen Kweh, Jeffrey Victor Rosenfeld, Martin Hunn, Jin Wee Tee

**3 What matters for people with brain cancer? Selecting clinical quality indicators for an Australian Brain Cancer Registry**

Rosalind Jeffree, Misa Matsuyma, Mythily Sachchithananthan, Robyn Leonard, Michael Besser, Anna Nowak, Donna Truran, Claire Vajdic, John Zalcberg, Hui Gan, Craig Gedye, Winny Varikatt, Eng-Siew Koh, Ganessan Kichenadasse, Hao-Wen Sim, Nicholas Gottardo, Desma Spyridopoulos

**4 Standardisation of 18F-FET PET imaging quantification in neuro-oncology: a semiautomated method for background activity and biological tumour volume definition**

Caterina Brighi, Simon Puttick, Shenpeng Li, Paul Keall, David Waddington, Pierrick Bourgeat, Ashley Gillman, Michael Fay

**5 Pretreatment Neutrophil-to-Lymphocyte/Monocyte-to-Lymphocyte Ratio as Prognostic Biomarkers in Glioma Patients**

Sher Ting Chim, Paul Sanfilippo, Terence J O'Brien, Kate A Drummond, Mastura Monif

**8 The molecular profile of secondary meningiomas in survivors of childhood non-central nervous system cancers**

Catherine Corriveau-Bourque, Derek Wong, Frank van Landeghem, Matija Snuderl, Maria Spavor, Stephen Yip, David Eisenstat

**9 Atypical Meningioma: predictors of recurrence**

Mai Tran, Catherine Bettington, Lee Tripcony, Rosalind Jeffree, Craig Winter

**10 Low and Intermediate Grade Glioma Umbrella Study of Molecular Guided Therapies (LUMOS) study**

Benjamin Kong, Hao-Wen Sim, Benhur Amanuel, Bryan Day, Michael Buckland, Roel Verhaak, Sonia Yip, Terrance Johns, Zarnie Lwin, Mark Rosenthal, Anna Nowak, Elizabeth Barnes, Andrew Scott, Jonathon Parkinson, Rosalind Jeffree, Richard de Abreu Lourenco, Peter Lau, James Whittle, Elizabeth Hovey, Lawrence Cher, Ganessan Kichenadasse, Merryn Hall, Cleo Robinson, Marc Thomas, Tindaro Giardina, Emily Tu, Deepa Mathur, Mustafa Khasraw, Eng-Siew Koh, Hui Gan

**11 Clinical outcomes in CDK altered gliomas- does treatment strategy change outcome?**

Alexander Yuile, Laveniya Satgunaseelan, Kimberley L. Alexander, Subo Thavaneswaran, Michael Krasovitsky, Michael Buckland, Maggie Lee, Grace Wei, Marina Kastelan, Mark Wong, Isabella Wilson, Angela Bayly, Winny Varikat, Zarnie Lwin, Helen Wheeler

**12 A single center experience with G34R/V Histone Mutated Gliomas**

Alexander Yuile, Marina Kastelan, Madhawa De Silva, James Drummond, Michael Back, Bratati Karmakar, Helen Wheeler

**13 Patterns of care in adult histone mutated gliomas: results of an international survey**

Alexander Yuile, Mustafa Khasraw, Justin Low, Kyle Walsh, Eric Lipp, Joanne Sy, Laveniya Satgunaseelan, Marina Kastelan, Madhawa De Silva, Adrian Lee, Helen Wheeler

**14 Implementation of the Brain tumour Registry Australia: INnovation and translation (BRAIN) – Going beyond data collection**

Lucy Gately, Kate Drummond, Anthony Dowling, Claire Phillips, Robert Campbell, Rosemary Harrup, David Campbell, Simone Reeves, Elizabeth Ahern, Ronnie Freilich, Hui Gan, Peter Gibbs

**16 A prospective, multi-centre trial of FET-PET In Glioblastoma patients - the TROG 18.06 FIG Study: preliminary results of the nuclear medicine and radiation oncology credentialing program**

Alisha Moore, Eng-Siew Koh, Roslyn J. Francis, Martin A. Ebert, Hui K. Gan, Sze-Ting Lee, Eddie Lau, Alana Rossi, Andrew Grose, Sweet-Ping Ng, June Yap, Tam Ly, Peter Lin, Mark B. Pinkham, Stanley Ngai, Chris Yu, Peter Gorayski, Hien Le, Ian D. Kirkwood, Wilson Vallat, Farhan Syed, Dayanethee Krishna, Shahroz Khan, Suki Gill, Elizabeth Thomas, Michael Back, Joseph Sia, Tim Akhurst, Ramin Alipour, Ben Chua, Paul Thomas, David A. Pattison, Elizabeth H. Barnes, Brad A. Moffat, Fiona E. Scott, Lucas Adda, Farshad Foroudi, Richard De Abreu Lourenco, Anna K. Nowak, Dale L. Bailey, Andrew M. Scott

**17 Estimation of BRAF V600E mutations and its prognostic significance in high grade glioma patients**

Divyanshu Dua, Mitali Fadia, Gane Pranavan

**18 Quality of life, cognition and psychological health in patients with benign and low-grade brain tumours**

Benjamin Price, Ken Teng, Alex Prentice, Lobna Alukaidey, Shubhum Joshi, Ameer Shehab, Gurvinder Toor, Katharine Drummond

**19 Worse survival outcome for patients with IDH mutated anaplastic glioma when IMRT is delayed until time of relapse after initial surgical management**

Michael Back, Jon Parkinson, Marina Kastelan, Adrian Lee, Matthew Wong, Helen Wheeler

**20 Concordance of intra-operative frozen section and pre-operative radiological diagnosis of brain tumours with their final histopathological diagnosis – a 3-year retrospective study**

Anson Chan, Sriya Chakrabarty, Shelley Verma, Zachary Drew, Leslie Kuma, Alka Sinha, Archana Dwivedee, Eric Guazzo, David Anderson, Sarin Kuruvath

**21 Surgery and chemoradiotherapy in the management of scalp glioblastoma**

Anson Chan, Michael Collins, David Anderson

**24 Initial increase in radiological volume is associated with poorer clinical and radiological response outcomes in patients treated with stereotactic radiosurgery for melanoma brain metastases**

Mihir Shanker, Nick Gatt, Heath Foley, Samuel Crowley, Emma Thomson, Kendall Higgs, Wei Soon, Victoria Atkinson, Trevor Watkins, Michael Huo, Matthew Foote, Mark Pinkham

**25 Generation of a spatial atlas of glioblastoma tumour sections using DCNN**

Amin Zadeh-Shirazi, Mark McDonnell, Eric Fornaciari, Narjes Bagherian, Kaitlin Scheer, Michael Samuel, Mahdi Yahoobi, Rebecca Ormsby, Santosh Poonnoose, Damon Tumez, Guillermo Gomez

**26 A 3-Arm, Phase IIa Trial of Safety & Efficacy of Olinvacimab, a Monoclonal Antibody to VEGFR2 in Patients with Recurrent Glioblastoma Multiforme with Imaging and PK/PD assessments: Final report**

Adi Balasubramanian, George Iatropoulos, Anna Nowak, Lawrence Cher

## ACCEPTED ABSTRACTS

**Abstract Id: 2**

**Abstract Title**

The Effects of Surgery and Adjuvant Therapy on Survival Outcomes in Clear Cell Ependymomas: A Systematic Review and Meta-Analysis of Individual Patient Data

**Authors:** Barry Ting Sheen Kweh[1,2,3], Jeffrey Victor Rosenfeld[3,4], Martin Hunn[3,4], Jin Wee Tee[2,3,4]

[1]Royal Melbourne Hospital, Melbourne, Australia. [2]National Trauma Research Institute, Melbourne, Australia. [3]Alfred Hospital, Melbourne, Australia. [4]Monash University, Melbourne, Australia

**Abstract**

**Aims**: The survival outcomes of clear cell ependymomas is poorly understood. This study clarifies the role of surgery and adjuvant therapy when this morphologically distinct but exceedingly rare tumour is encountered.

**Methods**: A systematic search for studies relating to clear cell ependymomas was conducted. Primary outcomes were progression-free survival and overall survival. Prognostic variables were age, sex, tumour consistency, extent of resection and post-operative adjuvant therapy. Kaplan-Meier survival curves were generated and compared by the log-rank test. Multivariate Cox regression models were constructed, interrogated with Schoenfeld residuals, and utilised to identify independent prognostic factors.

**Results:** Of the 384 articles retrieved, eight published articles comprising 77 cases of clear cell ependymoma were included. Five-year overall survival and progression-free survival was 58.1% (95% CI 46.3-72.9%) and 46.3% (95% CI 34.2-62.8%) respectively (Figures 1 and 2). Kaplan-Meier analysis with the log-rank test demonstrated gross total resection was superior to subtotal resection in prolonging survival duration ($p=0.047$) and delayed time to recurrence ($p<0.01$). Multi-variate analysis confirmed gross total resection as an independent protective factor against relapse (OR 0.39, 95% CI 0.17-0.89, $p=0.03$). Age less than 50 years predicted longer overall survival (OR 0.16, 95% CI 0.05-0.49, $p<0.01$). Post-operative adjuvant therapy following gross total resection did not affect overall survival ($p=0.98$) or progression-free survival ($p=0.93$). Adjuvant therapy following subtotal resection favoured improved overall survival ($p=0.052$).

**Conclusions**: Clear cell ependymomas are particularly aggressive in those aged greater than 50 years old. Gross total resection remains the cornerstone of management. Post-operative adjuvant therapy is only likely to be of survival benefit following subtotal resection.

**Table 1** – Baseline characteristics of included cases of clear cell ependymomas with subsequent surgical and adjuvant therapy management.

| Study | Supratentorial (%) | Cystic Tumour Component (%) | WHO Grade | Gross Total Resection Achieved (%) | Receipt of Adjuvant Therapy (%) | Mean Follow-up Time (Months) |
|---|---|---|---|---|---|---|
| Figarella-Branger *et al*, 2016[1] | 20 (100) | 7 (35.0) | WHO Grade III: 20 | 90.0 | 15 (75.0) | 97.4 |
| Rickert *et al*, 2006[2] | 12 (92.3) | 9 (69.2) | WHO Grade III: 7<br>WHO Grade II: 5 | 61.5 | 11 (84.6) | 39.0 |
| Hashmi *et al*, 2015[3] | 11 (100) | 7 (63.6) | WHO Grade III: 9<br>WHO Grade II: 2 | 54.5 | 10 (90.9) | 13.6 |
| Fouladi *et al*, 2003[4] | 9 (90.0) | 5 (50.0) | Not Reported | 70.0 | 6 (60) | 54.7 |
| Kawano *et al*, 1999[5] | 0 (0) | 6 (75.0) | Not Reported | 100 | 0 (0) | 103.5 |
| Min *et al*, 1997[6] | 8 (100) | 5 (62.5) | Not Reported | 100 | 5 (62.5) | 63.5 |
| Kawano *et al*, 1989[7] | 2 (50.0) | 2 (50.0) | Not Reported | 75 | 4 (100) | 25.3 |
| Jain *et al*, 2008[8] | 3 (100) | 3 (100) | Not Reported | 0 | 3 (100) | 58.7 |
| **Overall** | **65 (84.4)** | **44 (57.1)** | **36 (83.7)** | **58 (75.3)** | **54 (70.1)** | **61.9** |

**Figure 1** – Kaplan-Meier Curve depicting overall survival of total study population with clear cell ependymoma (A) where shaded area represents 95% confidence interval. Results of Kaplan-Meier subgroup analyses stratified by sex (B), age with a threshold of 50 years (C), tumour composition (D), extent of tumour resection (E) and receipt of adjuvant therapy (F). The log-rank test was used to compared the survival distributions between dichotomized cohorts. Statistically significant reduced overall survival was noted in patients younger than 50 years of age (p=0.019), tumours of cystic rather than solid composition (p=0.033), and those who underwent subtotal rather than gross total resection (p=0.047).

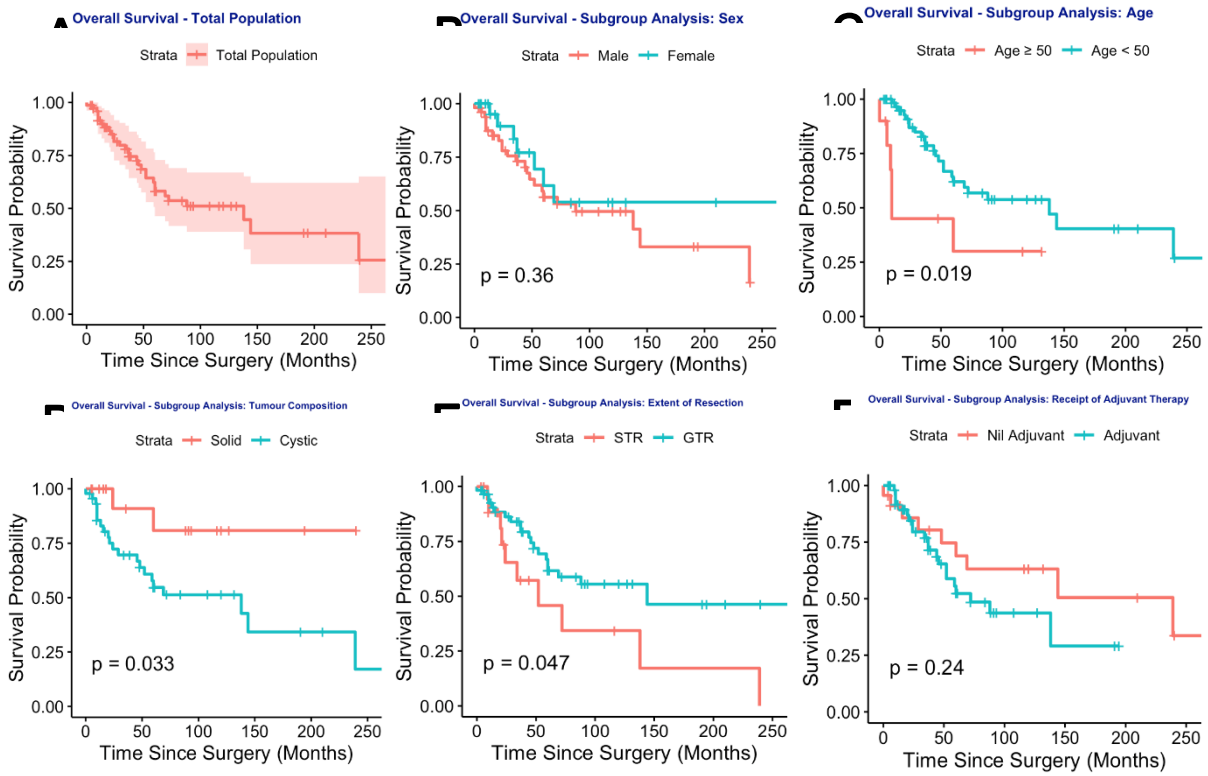
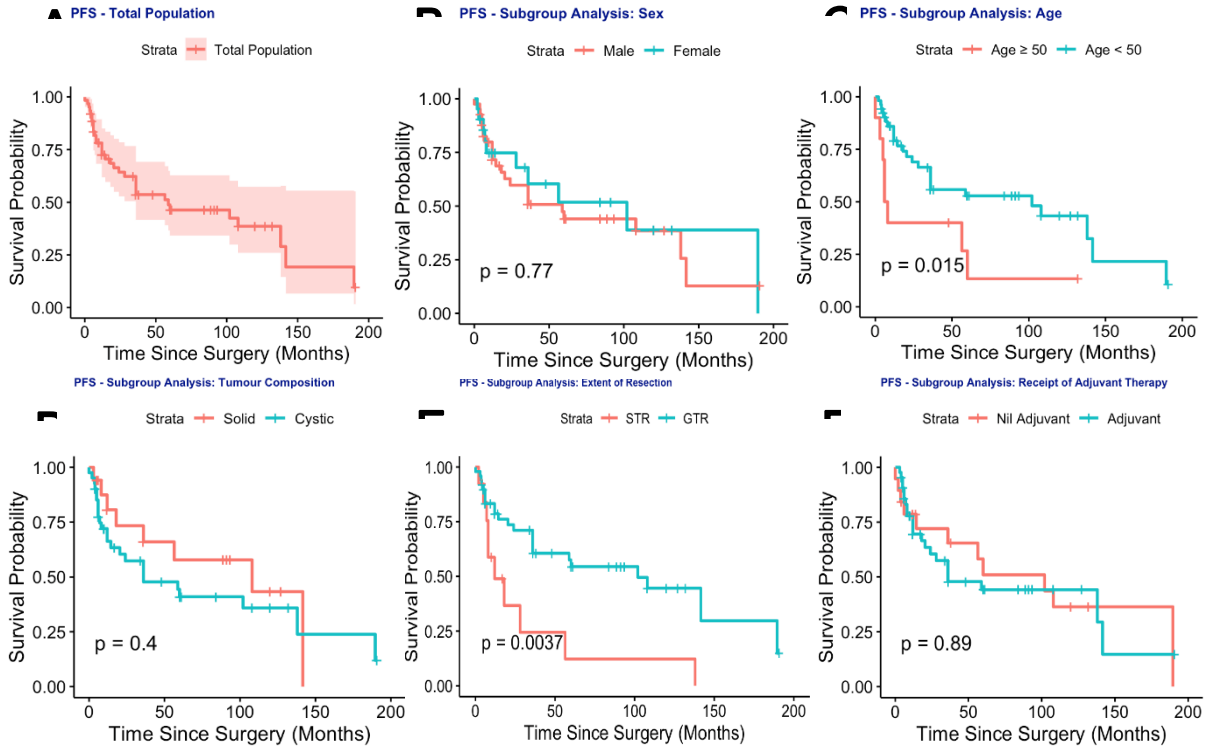


**Figure 2**– Kaplan-Meier Curve depicting progression free survival (PFS) of total study population with clear cell ependymoma (A) where shaded area represents 95% confidence interval. Results of Kaplan-Meier subgroup analyses stratified by sex (B), age with a threshold of 50 years (C), tumour composition (D), extent of tumour resection (E) and receipt of adjuvant therapy (F). The log-rank test was used to compared the survival distributions between dichotomized cohorts. Statistically significant reduced progression-free survival was noted in patients who underwent subtotal rather than gross total resection (p=0.0037) or were aged greater than or equal to 50 years of age (p=0.015).



**Abstract Id: 3**

**Abstract Title**

What matters for people with brain cancer? Selecting clinical quality indicators for an Australian Brain Cancer Registry

**Authors:** Rosalind Jeffree[1,2,3], Misa Matsuyma[1,3], Mythily Sachchithananthan[1], Robyn Leonard[1], Michael Besser[1], Anna Nowak[1,4,5], Donna Truran[1,6], Claire Vajdic[1,7], John Zalcberg[1,8,9], Hui Gan[1,10,11,12], Craig Gedye[1,13,14], Winny Varikatt[1,15,16], Eng-Siew Koh[1,17,18,19], Ganessan Kichenadasse[1,20,21], Hao-Wen Sim[1,22,23,24], Nicholas Gottardo[1,25,26,27], Desma Spyridopoulos[1]

[1]Brain Cancer Biobanking Australia, NHMRC Clinical Trials Centre, The University of Sydney, Sydney, Australia. [2]Kenneth G. Jamieson Department of Neurosurgery, Royal Brisbane and Women's Hospital, Brisbane, Australia. [3]Faculty of Medicine, The University of Queensland, Brisbane, Australia. [4]Medical School, The University of Western Australia, Perth, Australia. [5]Department of Medical Oncology, Sir Charles Gairdner Hospital, Perth, Australia. [6]Australian e-Health Research Centre, CSIRO, Brisbane, Australia. [7]Centre for Big Data Research in Health, University of New South Wales, Sydney, Australia. [8]Faculty of Medicine, Nursing and Health Sciences, School of Public Health & Preventive Medicine, Monash University, Melbourne, Australia. [9]Department of Medical Oncology, Alfred Health, Melbourne, Australia. [10]Cancer Therapies and Biology Group, Centre for Research Excellence in Brain Cancer, Olivia Newton-John Cancer Research Institute, Austin Health, Melbourne, Australia. [11]Centre for Research Excellence in Brain Cancer, Monash University, Melbourne, Australia. [12]Cancer Clinical Trials, Austin Hospital, Melbourne, Australia. [13]Medical Oncology, Calvary Mater Newcastle, Newcastle, Australia. [14]Hunter Medical Research Institute, Newcastle, Australia. [15]Sydney Medical School West precinct, The University of Sydney, Sydney, Australia. [16]Tissue Pathology and Diagnostic Oncology, ICPMR, Westmead Hospital, Sydney, Australia. [17]Liverpool and Macarthur Cancer Therapy Centres, Sydney, Australia. [18]University of New South Wales, Sydney, Australia. [19]Collaboration for Cancer Outcomes, Research and Evaluation, Ingham Institute for Applied Medical Research, Sydney, Australia. [20]Department of Clinical Pharmacology, College of Medicine and Public Health, Flinders University, Adelaide, Australia. [21]Department of Medical Oncology, Flinders Centre for Innovation in Cancer, Flinders Medical Centre, Adelaide, Australia. [22]St Vincent's Clinical School, University of New South Wales, Sydney, Australia. [23]Department of Medical Oncology, The Kinghorn Cancer Centre, Sydney, Sydney, Australia. [24]Department of Medical Oncology, Chris O'Brien Lifehouse, Sydney, Australia. [25]Telethon Kids Institute, Perth Children's Hospital, Perth, Australia. [26]Centre for Child Health Research, University of Western Australia, Perth, Australia. [27]Department of Oncology, Princess Margaret Hospital, Perth, Australia

**Abstract**

**Purpose:** The goal of a clinical quality registry is to deliver immediate gains in survival and quality of life by delivering timely feedback to practitioners, thereby ensuring every patient receives the best existing treatment. We are developing an Australian Brain Cancer Registry (ABCR) to identify, describe and measure the impact of the variation and gaps in brain cancer care from diagnosis through to end of life.

**Methodology:** To determine a set of Clinical Quality Indicators (CQIs) for the ABCR, a database and internet search was used to identify relevant guidelines, which were then assessed for quality using the AGREE II Global Rating Scale. Potential indicators were extracted from 21 clinical guidelines, ranked using a modified Delphi process completed in two rounds by a panel of experts and other stakeholders, including consumers, and refined by a multidisciplinary Working Party.

**Results:** Nineteen key quality reporting domains were chosen, specified by 57 CQIs detailing the inclusion (denominator) and outcome (nominator) characteristics to be reported. Of the 57 indicators, 42 were supported by moderate or strong evidence. The modified Delphi process took place over 11 months. The selected CQIs include structural measures such as performing surgery in tertiary centres and availability of neuro-oncology care coordinators, process measures such as availability of specific molecular tests, discussion at an MDT and rehabilitation referral, and outcome measures such as extent of resection and days spent in hospital between diagnosis and death.

**Conclusion:** The selected CQIs will form the basis for the ABCR, provide a framework for data collection, and specify best practice for patients and health care providers, with a view to improving care and outcomes for brain cancer patients. Pilot data collection is underway to determine the feasibility of collecting each indicator.

**Abstract Id: 4**

**Abstract Title**

Standardisation of 18F-FET PET imaging quantification in neuro-oncology: a semiautomated method for background activity and biological tumour volume definition

**Authors:** Caterina Brighi[1], Simon Puttick[2], Shenpeng Li[3], Paul Keall[1], David Waddington[1], Pierrick Bourgeat[2], Ashley Gillman[4], Michael Fay[5,6]

[1]ACRF Image X Institute, The University of Sydney, Sydney, Australia. [2]Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organization, Brisbane, Australia. [3]Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organization, Melbourne, Australia. [4]Australian e-Health Research Centre, Commonwealth Scientific and Industrial Research Organization, Townsville, Australia. [5]GenesisCare, Newcastle, Australia. [6]The University of Newcastle, School of Medicine and Public Health, Newcastle, Australia

**Abstract**

**Aims:** The recognition of the important role of $^{18}$F-Fluoroethyl-L-tyrosine ($^{18}$F-FET) PET imaging in the management of glioma patients has highlighted a need for standardised methods of data acquisition and analysis.[1] $^{18}$F-FET uptake normalised against background in the contralateral brain is emerging as a standard imaging technique to delineate the biological tumour volume (BTV). Quantitative analysis of $^{18}$F-FET PET images requires a consistent and robust background activity. Currently, defining background activity involves the manual selection of an arbitrary region of interest, a process that is subject to large variability. This study aims to eliminate methodological errors in background activity definition through the introduction of a semiautomated method for region of interest selection.

**Methods:** A new method for background activity definition, involving the semiautomated generation of mirror-image (MI) reference regions, was compared with the current state-of-the-art method, involving following guidelines to manually drawing crescent-shape (gCS) reference regions (Figure 1).[2] The MI and gCS methods were tested by measuring values of background activity and resulting BTV of $^{18}$F-FET PET scans of six patients with recurrent glioblastoma multiforme generated from inputs provided by six readers. To assess intra-reader variability, each scan was evaluated six times by each reader. Intra- and inter-reader variability in background activity and BTV definition was assessed by means of coefficient of variation (CoV).

**Results:** Compared to the gCS method, the MI method showed significantly lower intra- and inter-reader variability (median CoV values of 0%, Figure 2) both in background activity and in BTV definition.

**Conclusions:** The semiautomated MI method minimises intra- and inter-reader variability, providing a valuable approach for standardisation of $^{18}$F-FET PET quantitative parameters both in the evaluation of multicentre clinical trials and in routine clinical decision-making processes, including radiotherapy treatment planning and assessment of treatment response in neuro-oncology patients.

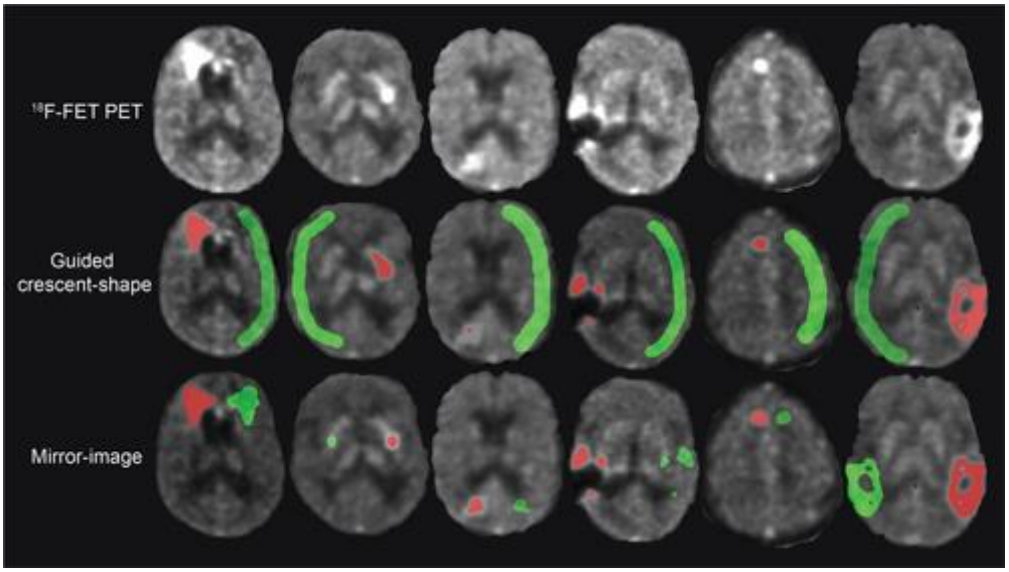



**Figure 1.**

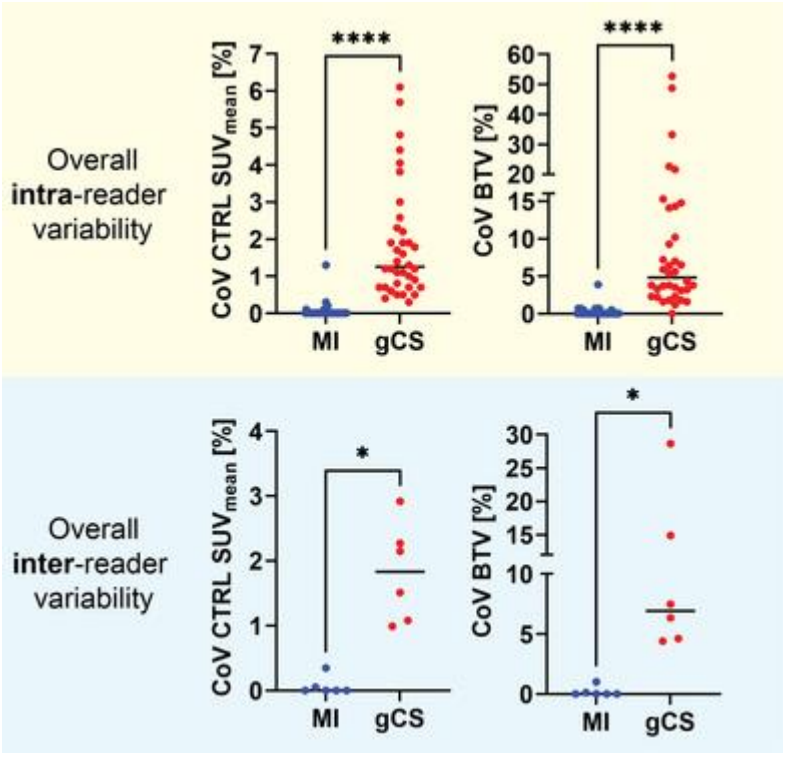



**Figure 2.**

**References**

1. Galldiks N, Niyazi M, Grosu AL, et al. Contribution of PET imaging to radiotherapy planning and monitoring in glioma patients - a report of the PET/RANO group. *Neuro Oncol*. 2021;(February):1-13. doi:10.1093/neuonc/noab013

2. Unterrainer M, Vettermann F, Brendel M, et al. Towards standardization of 18F-FET PET imaging: do we need a consistent method of background activity assessment? *EJNMMI Res*. 2017;7(1):48. doi:10.1186/s13550-017-0295-y

**Abstract Id: 5**

**Abstract Title**

Pretreatment Neutrophil-to-Lymphocyte/Monocyte-to-Lymphocyte Ratio as Prognostic Biomarkers in Glioma Patients

**Authors:** Sher Ting Chim[1,2,3], Paul Sanfilippo[4], Terence J O'Brien[1,2,5,4], Kate A Drummond[6,7], Mastura Monif[1,2,3,5,4]

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**Abstract**

**Background:** In the glioma microenvironment, elevations in immune cell ratios are posited to reflect the host's systemic response to malignancy. Given the dearth in clinically significant molecular markers to predict prognosis, there is potential for peripheral immune cell ratios to serve as low-cost and readily available prognostic markers.

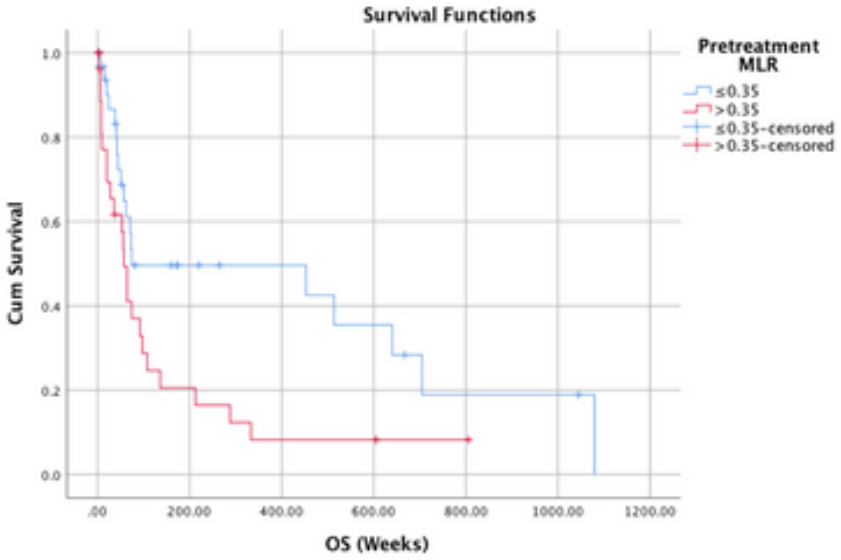
**Objectives:** This study evaluated the ability for pretreatment peripheral immune cell ratios (Neutrophil-to-Lymphocyte Ratio, NLR, and Monocyte-to-Lymphocyte Ratio, MLR) to predict overall survival (OS) and modified Rankin Scale (mRS) at admission, 6 months and 12 months post-diagnosis. It also explored relationships between immune cell ratios and clinicopathological parameters (tumour location, tumour size, tumour grade, IDH-1 mutation and MGMT promoter methylation status).

**Methods:** Pretreatment NLR and MLR, defined as NLR and MLR from the first presentation with glioma symptoms to the last blood count before treatment, were analysed retrospectively in 64 glioma patients from Royal Melbourne Hospital. OS was evaluated with the Kaplan-meier method. Prognostic factors for OS and mRS were evaluated with univariate and multivariable regression analyses.

**Results:** Higher pretreatment NLR (>4.7), compared to lower pretreatment NLR (≤ 4.7), predicted higher mean admission mRS (mean 3.31 vs 2.40, p<0.001) and 6-month mRS (mean 3.60 vs 2.44, p=0.019). Higher pretreatment NLR was associated with poor functional outcome (mRS 3-6) at admission (p<0.001) and 6 months (p=0.001). Higher pretreatment MLR (>0.35) predicted poorer OS in glioma patients (median 57.0 ± 6.6 weeks, 95% CI 43.4-70.6, p=0.024) (Fig. 1). Higher NLR was associated with larger tumour diameter (≥5cm) (p=0.02).

**Conclusion:** To our knowledge, this was the first study to evaluate the association between immune cell ratios and mRS in glioma patients. This study demonstrated that NLR and MLR can serve as prognostic markers to predict functional outcomes and OS in glioma patients, which allows us to identify high-risk patients in need of further treatment.

Fig. 1. Kaplan-Meier OS analysis of pretreatment MLR. Abbreviations: OS, overall survival; MLR, monocyte-to-lymphocyte ratio



**Abstract Id: 7**

**Abstract Title**

From post-operative to pre-operative: neoadjuvant stereotactic radiosurgery for brain metastases

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**Abstract**

**Aims:** Post-operative stereotactic radiosurgery (PoSRS) following resection of brain metastases is currently the standard of care. However, rates of leptomeningeal disease (LMD) after PoSRS have been reported >30%. Neoadjuvant radiosurgery (NaSRS) has been proposed as an alternative treatment approach to decrease this risk. The aim of the study was to report the local control (LC) and LMD rates in patients undergoing NaSRS.

**Methods:** Consecutive patients planned for SRS followed by resection of intracranial lesions with a confirmed primary malignancy were included in our retrospective multi-centre case series. Concurrent SRS alone to other intracranial lesions was permitted. Exclusion criteria included previous local treatment to that particular lesion and ECOG≥3. Outcomes reported included LC, distant control (DC), overall survival (OS), LMD and radionecrosis (RN) rates.

**Results:** Overall, 28 patients with 29 lesions were eligible for analysis. Median follow up was 12.8 months. The mean age was 62.5 years (range 43-80) and 55% were ECOG 0-1. The most common primary malignancies included non-small cell lung cancer (43%) and melanoma (32%). Hypofractionated NaSRS was utilised in 62.1%. The 12-month LC and LMD rates were 91.3% and 4.0%, respectively. The 12-month RN, DC, and OS rates were 5.0%, 51.5%, and 60.1%, respectively.

**Conclusions:** Compared to post-operative SRS, our study suggests that NaSRS leads to comparable local control with a decreased risk of LMD and RN. This is the first NaSRS series with a majority of patients treated with fractionated SRS. NaSRS is a promising approach for appropriate patients where surgical resection is a component of local therapy.

**Abstract Id: 8**

**Abstract Title**

The molecular profile of secondary meningiomas in survivors of childhood non-central nervous system cancers

**Authors:** Catherine Corriveau-Bourque[1], Derek Wong[2], Frank van Landeghem[1], Matija Snuderl[3], Maria Spavor[1], Stephen Yip[2], David Eisenstat[1,4]

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**Abstract**

**Introduction:** Cranial irradiation remains part of childhood cancer therapy and secondary meningiomas are a late effect. Secondary meningiomas are reported in patients who received low and high dose cranial irradiation and arise ~20 years post exposure. The molecular and genetic profile of primary meningiomas has been well studied; however, only a few studies describe these in radiation-induced meningiomas (RIM).

**Methods:** We identified patients followed at the Childhood Cancer Survivor Clinic, Stollery Children's Hospital who had a history of non-central nervous system malignancies and received cranial irradiation who developed meningiomas between clinic inception in 1971 and June 2013. Whole exome sequencing (WES) as well as DNA methylation profiling were performed for patients where tumor and germline DNA were available.

**Results:** Of 96 patients who received cranial irradiation, 16 (16.7%) developed symptomatic meningiomas. This patient cohort is unique; all 16 patients received 2000-2400 cGy, suggesting a threshold dose. 9/16 (56%) had WHO Grade 2 meningiomas or greater and 7/16 (44%) were infiltrative. Post-surgical recurrences occurred in 43%. Patients experienced considerable morbidities directly attributable to the meningiomas or their treatment. 14 patients had samples suitable for further analysis. Preliminary results revealed that NF2 mutations were the most common (5). Other meningioma related genes with mutations identified in our patient cohort include TRAF7, AKT3, MSH4 (2), KMT2C (2), TET1 (2), KDM6A, and MLH3. Copy number alternations were noted with increased frequency on chromosomes 1p, 22q, 19q. 850k methylation analysis did not conclusively show any clustering. Ongoing studies include assessment of tumor mutation burden, RNAseq, and the mutational profile.

**Conclusions:** This study examined RIM in patients who received similar doses of radiation for their childhood cancer. To date, our findings are consistent with previously described primary and RIM mutations. Enhanced knowledge in secondary meningiomas is crucial for accurate patient counseling, prognostication, and treatment.

**Abstract Id: 9**

**Abstract Title**

Atypical Meningioma: predictors of recurrence

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**Abstract**

**Introduction:** Meningiomas comprise of up to one third of primary central nervous system tumours. Approximately 20% of these are atypical (WHO grade II). Atypical meningiomas are associated with a 30-50% risk of local recurrence after Simpson 1 resection/ gross tumour resection (GTR)[1]. Adjuvant radiotherapy may reduce recurrence but its role is not clearly defined. Histologic parameters may stratify the risk of recurrence and guide the use of adjuvant radiotherapy[2].

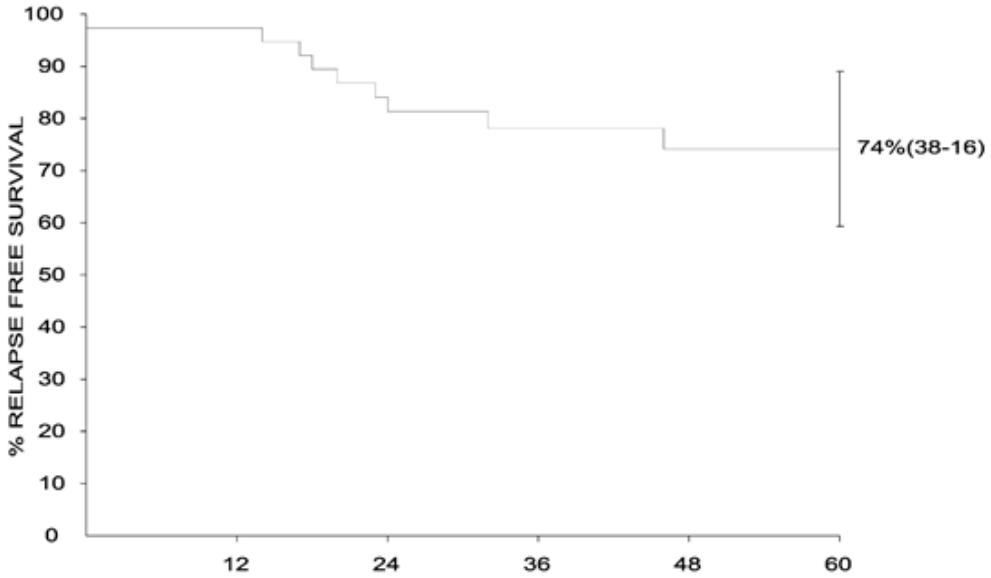
**Aims**: To assess the prognostic value of histopathological features of atypical meningiomas in determining recurrence risk and to assess the impact of adjuvant radiation therapy.

**Methods**: Patients with histologically confirmed atypical meningioma diagnosed between January 2000 and December 2020 at a single, tertiary hospital in Brisbane, Australia were identified. Data on patient, tumour and treatment characteristics were retrospectively collected. Specific histological features were identified: sheet like growth, high nuclear to cytoplasmic (N/C) ratio, prominent nucleoli, necrosis, increased cellularity, mitoses and brain invasion. These parameters were correlated with overall survival (OS) and relapse free survival (RFS).

**Results**: A total of 56 patients were identified, with data for 49 available. The median age at diagnosis was 57 years, 24/49 (49%) were female. The median follow up period was 166 months. GTR was performed in 38 patients. Of these, 9 received adjuvant radiotherapy. Sheet like growth was seen in 10/38, increased cellularity 6/38, high N/C ratio 3/38, necrosis 25/38, prominent nucleoli 6/38, brain invasion 17/38 and mitosis ³4 23/38. Following GTR, the 5 year RFS and OS was 74% (95%CI 59-89) and 87% (95%CI 74-99), respectively as seen in graphs 1 and 2. Pathologic parameters and adjuvant radiotherapy were not predictive of RFS on univariate analysis.

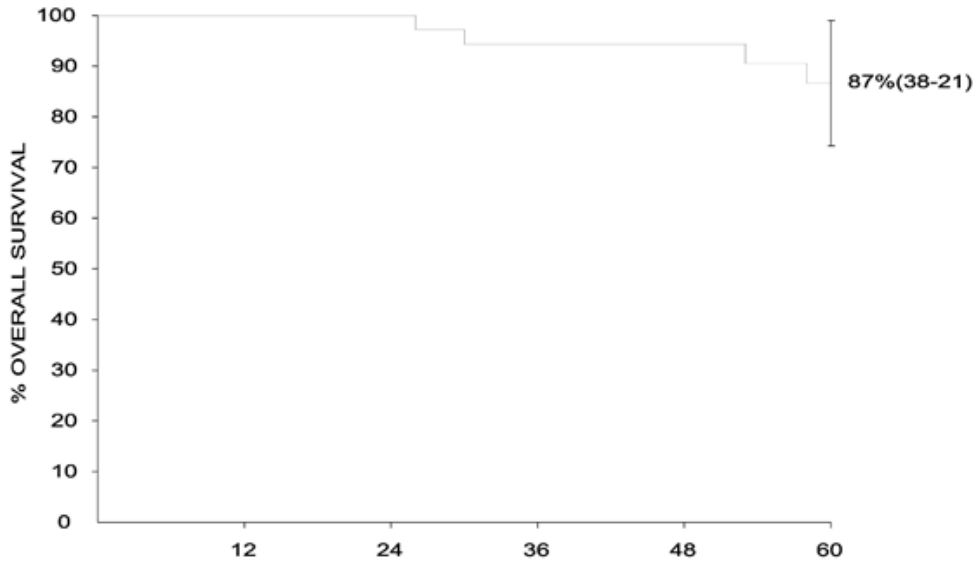
**Conclusions**: Recurrence free survival following GTR is significant and consistent with reported literature. Further study is required to identify patients at highest risk of recurrence.

Atypical Meningioma - GTR




| Subjects at risk | | | | | | 95% CI |
|---|---|---|---|---|---|---|
| 38 | 37 | 31 | 24 | 19 | 16 | [ 59, 89 ] |

Atypical Meningioma - GTR




| Subjects at risk | | | | | | 95% CI |
|---|---|---|---|---|---|---|
| 38 | 38 | 37 | 32 | 27 | 21 | [ 74, 99 ] |

**References**

1. Aghi MK, Carter BS, Cosgrove GR, et al (2009) Long-term recurrence rates of atypical meningiomas after gross total resection with or without postoperative adjuvant radiation. Neurosurgery 64 (1):56-60; discussion 60. doi:10.1227/01.NEU.0000330399.55586.63

2. Lamba N, Hwang WL, Kim DW, et al (2020) Atypical Histopathological Features and the Risk of Treatment Failure in Nonmalignant Meningiomas: A Multi-Institutional Analysis. World Neurosurgery 133:e804-e812. doi.org/10.1016/j.wneu.2019.10.002

**Abstract Id: 10**

**Abstract Title**

Low and Intermediate Grade Glioma Umbrella Study of Molecular Guided Therapies (LUMOS) study

**Authors:** Benjamin Kong[1,2], Hao-Wen Sim[1,3,4,5], Benhur Amanuel[6], Bryan Day[7,8], Michael Buckland[9], Roel Verhaak[10], Sonia Yip[1], Terrance Johns[11], Zarnie Lwin[12,13], Mark Rosenthal[14,15], Anna Nowak[16,17,18], Elizabeth Barnes[1], Andrew Scott[19,20,21], Jonathon Parkinson[22], Rosalind Jeffree[13,23], Richard de Abreu Lourenco[24], Peter Lau[16,17], James Whittle[14,15], Elizabeth Hovey[25,26], Lawrence Cher[27], Ganessan Kichenadasse[28,29], Merryn Hall[1], Cleo Robinson[6,18], Marc Thomas[6], Tindaro Giardina[6], Emily Tu[1], Deepa Mathur[1], Mustafa Khasraw[30], Eng-Siew Koh[31,32], Hui Gan[19,20,33,34]

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**Abstract**

**Background:** Grade 2 and 3 (G2/3) gliomas are the second largest group of brain tumours in adults. The prognosis for G2/3 gliomas at relapse mirrors that of glioblastoma, but few trials address the complex molecular heterogeneity of relapsed glioma [1].

**Methods**: LUMOS was a national multi-centre pilot study for patients with relapsed G2/3 gliomas designed to establish the feasibility of an umbrella approach to type tissue and match it with targeted therapies. Tumour tissue (formalin-fixed paraffin embedded) underwent next generation sequencing (TST170, Illumina). A Molecular Tumour Advisory Panel (MTAP) with subspecialty neuro-oncology expertise was formed to interpret genomic information and provide a recommendation to the treating physician.

**Results:** Ten patients (median age 42; range 32-62; four G2 astrocytoma, one G3 astrocytoma, three G2 oligodendroglioma, one G3 oligodendroglioma, one G2 mixed tumour) were enrolled in this study. Eight patients had surgery within 6 months prior to study entry whilst two underwent surgery during the study. The study identified potentially targetable alterations in all participants (10 *IDH*, 3 *FGFR,* 2 *PIK3K*, *CCND3*, *NRAS, CDK4, PTPRZ1-MET* fusion and *MET* amplification). Of the two patients who received matched therapies via compassionate access schemes, one patient with a PIK3K mutation had stable disease 12 months after study enrolment and another with CDK 4/6 copy number gain had stable disease for 12 weeks prior to progressing. Overall, 6 of 10 patients remained alive with median follow up time of 12.2 months. The median time from participant consent to MTAP reporting was 7.0 weeks (range 5.1–9.7 weeks) but 4.9 weeks when lag time for sample retrieval and shipping was omitted.

**Conclusion**: LUMOS confirmed that this design was feasible in the Australian setting with turnaround times comparable to previous studies [2]. These findings support moving to a larger study using contemporaneous tissue samples matched with targeted therapies.

**References**

1. Barthel, F.P., et al., *Longitudinal molecular trajectories of diffuse glioma in adults.* Nature, 2019. **576***(*7785): p. 112-120.

2. Luchini, C., et al., *Molecular Tumor Boards in Clinical Practice.* Trends Cancer, 2020. **6**(9): p. 738-744.

**Abstract Id: 11**

**Abstract Title**

Clinical outcomes in CDK altered gliomas- does treatment strategy change outcome?

**Authors:** Alexander Yuile[1], Laveniya Satgunaseelan[2], Kimberley L. Alexander[3,4,5], Subo Thavaneswaran[6,7,8], Michael Krasovitsky[7,8], Michael Buckland[2], Maggie Lee[2], Grace Wei[2], Marina Kastelan[9], Mark Wong[10], Isabella Wilson[11], Angela Bayly[12], Winny Varikat[12], Zarnie Lwin[13], Helen Wheeler[14]

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**Abstract**

**Background**: IDH-mutant glioma is recognized as a distinct pathological entity. A subset have significantly worse outcomes. The cIMPACT-NOW group has identified homozygous deletions of *CDKN2A/CDKN2B* as indicators of poor prognosis independent of tumour grade. The re-classification of IDH-mutant gliomas with high grade histologic features or *CDKN2A/B* homozygous deletions as grade IV IDH-mutant astrocytomas is therefore recommended. The impact this change in classification has on the selection of treatment (Stupp versus CATNON-radiotherapy and sequential temozolomide) is unknown. Here, we present data related to treatment outcomes for patients with IDH-mutant, *CDKN2A/B* heterozygous or homozygous deleted gliomas.

**Methods**: With HREC approval, molecular and clinical data concerning IDH-mutant glioma patients +/- *CDKN2A/B* alterations was accessed from RNSH, GIMR, RPAH, Westmead Hospital, RBWH and Sydney Brain Tumour Bank.

**Results**: We identified 19 patients with *CDKN2A/B* alterations recorded between January 2016-May 2021. Thirteen were histologically grade 2 (n=4) and grade 3 (n=9) astrocytomas. Median age was 30 years (20-74 years) and two were female. Homozygous *CDKN2A* deletions were detected in five patients (three *CDKN2B* co-deleted); the remainder showed heterozygous deletion. Survival data was available for 16 patients; 14 had disease progression (median PFS=2 years; 0.3-10 years) and 10 patients were deceased (median OS=2.8 years; 0.3-16 years). Of these 16 patients, 19% (n=3) were treated with Stupp and 38% (n= 6) with radiotherapy followed by sequential temozolomide. Median OS for Stupp treated patients was 2.6 years (0.5-2.7 years) and 2.8 years (0.3–6 years) after sequential temozolomide. Using IDH-mutant *CDKN2A* wildtypes as controls, median OS was 6.5 years for astrocytomas (n=18, 0.9-22.3 years), and 3.6 years for glioblastomas (n=6, 1.9-11.6 years).

**Conclusion**: This early data shows similar outcomes for patients with *CDKN2A/B* deleted IDH-mutant gliomas with either concurrent or sequential regimens. However, larger studies are required to further define optimal treatment for these gliomas.

**Abstract Id: 12**

**Abstract Title**

A single center experience with G34R/V Histone Mutated Gliomas

**Authors:** Alexander Yuile[1], Marina Kastelan[2], Madhawa De Silva[3], James Drummond[4], Michael Back[5], Bratati Karmakar[6], Helen Wheeler[1]

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**Abstract**

**Background**: Histone mutated gliomas (HMGs) form a newly recognized distinct pathologic entity. A subset of HMGs are those with G34R/V mutations. These gliomas are universally IDH wildtype and almost all have mutations in ATRX and high p53 expression. Adult G34 HMG gliomas are seen in younger patients and pose a poor prognosis (median age 25 years and median overall survival of 12.4 months according to recent case series). This being said evidence of clinical outcomes of this glioma type remains limited. In this single centre case series we report on the Australian experience of G34 gliomas, in hopes to further define the clinical outcomes of this HMG subset.

**Methods**: With Human Research Ethics Committee approval, data from patients at Royal North Shore Hospital with a known G34R/V mutated glioma presenting between February 2016 and end of February 2021 was retrieved. Clinicopathologic, radiologic and treatment outcomes were extracted for correlation.

**Results**: Six patients fitting the selection criteria were identified and reported. All had G34R mutations, all were IDH wild type, 2 had ATRX loss, 2 retained, 1 indeterminate and 1 not tested. One case was histologically an anaplastic astrocytoma, 1 was classified as GBM-primitive ectodermal tumor with the remainder being glioblastomas. The median age at diagnosis was 20 years (17-24 years) and 4 were female. The most common presenting symptoms were headaches/symptoms of raised intracranial pressure and seizures (n= 3 and n=2 respectively). The median overall survival was 1.2 years months (0.39-3.5 years), 3 patients are currently alive.

**Conclusion**: This case series reports the outcomes of adult patients with G34 mutated gliomas, a new and undescribed patient cohort. Ongoing studies are required to further characterize the histopathological and clinical differences to other glioma types.

**Abstract Id: 13**

**Abstract Title**

Patterns of care in adult histone mutated gliomas: results of an international survey

**Authors:** Alexander Yuile[1], Mustafa Khasraw[2], Justin Low[2], Kyle Walsh[2], Eric Lipp[2], Joanne Sy[3], Laveniya Satgunaseelan[3], Marina Kastelan[4], Madhawa De Silva[5], Adrian Lee[1], Helen Wheeler[1]

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**Abstract**

**Background**: Histone mutated gliomas (HMG) with *H3F3A* K27M and G34R/V mutations are recognized as biologically discrete entities with poor prognosis and a younger age at presentation. There is paucity of data regarding treatment of adult HMG patients and no consensus for management. This study aims to identify patterns of Australian and US neuro-oncology clinical practice for this entity.

**Methods**: Following institutional approvals, a patterns of care survey was circulated through COGNO in Australia and the CARIS Precision Oncology Alliance in the US. The findings were then augmented with an Australia based survey addressing local testing practices, circulated through the Royal College of Australian Pathologists (RCPA).

**Results**: Between 4/ 2021 and 6/ 2021, responses were collected. 72% (n= 26) were medical/neuro-oncologists, 17% (n= 6) were radiation oncologists and 11% (n= 4) were neurosurgeons. 25% (n= 9) tested all patients for HMGs routinely; 44% (n= 16) tested in select patients. The common indications for testing selected patients were midline anatomic location (n= 16) and age (n= 9) (majority <50 years). 15 used molecular sequencing, 17 used IHC at their centres (all used H3K27M IHC). These findings were further supported by results from a separate RCPA survey of 22 pathologists.

With regards to management (Table 1), 25% (n=9) participants stated knowledge of histone mutation did not affect management, 22% (n=8) stated on recurrence, 56% (n=20) stated it affected management of midline K27M patients, 25% (n=9) participants stated it affected management of non-midline K27M mutations and 6% (n=2) felt it affected management of G34R/V mutated gliomas.

**Conclusion**: Here we present the first description of global patterns of care of adult histone mutated gliomas. Through establishing standard approaches to these entities, we hope to allow for future standardization to guidelines and trial protocols.

| | **BSC** | **RT Alone** | **TMZ alone** | **RT+TMZ-Stupp protocol** | **RT+TMZ-other protocol** | **Clinical Trials** | **Other** |
|---|---|---|---|---|---|---|---|
| **Midline *K27M* glioma-Initial** | 3 Rarely | 2 Sometimes | 1 Sometimes | 34 Usually | 3 Sometimes /Rarely | 7 Sometimes | 1 Rarely |
| **Midline *K27M* glioma-recurrent** | 10 Sometimes /Usually | 4 Sometimes | 13 Sometimes | 1 Usually | 0 | 12 Sometimes | 18 Usually |
| **Non-midline *K27M* glioma-initial** | 3 Rarely | 3 Sometimes | 2 Sometimes | 32 Usually | 5 Usually | 3 Sometimes | 1 Not stated |
| **Non-midline *K27M* glioma-recurrent** | 10 Sometimes /Usually | 7 Sometimes | 13 Sometimes | 0 | 0 | 7 Usually | 16 Usually |
| ***G34R/V* glioma-initial** | 3 Rarely | 3 Sometimes | 1 Not stated | 31 Usually | 2 Sometimes | 1 Not stated | 0 |
| ***G34R/V* glioma-recurrent** | 9 Sometimes /Usually | 5 Sometimes | 11 Sometimes | 1 Sometimes | 1 Usually | 5 Usually | 18 Usually |

**Table 1-** Selected treatment regimens for initial and recurrent HMGs (number of participants using regimen; most common frequency (always, usually, sometimes, rarely, never) at which regimen used by participants)

**Abstract Id: 14**

**Abstract Title**

Implementation of the Brain tumour Registry Australia: INnovation and translation (BRAIN) – Going beyond data collection

**Authors:** Lucy Gately[1,2], Kate Drummond[3,4], Anthony Dowling[5,4], Claire Phillips[6,4], Robert Campbell[7], Rosemary Harrup[8], David Campbell[9], Simone Reeves[10], Elizabeth Ahern[11,12], Ronnie Freilich[13,14], Hui Gan[15], Peter Gibbs[1]

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**Abstract**

**Background:** Real-world data collected in clinical registries has been embraced as a means to answer clinical and policy-relevant questions, including many that are unlikely to be answered by clinical trials. Traditionally, registries are stand-alone initiatives, whereas registry data has the potential to support a broad range of collaborative research projects. Given the relatively low incidence of brain tumours and the decentralisation of cancer treatment in Australia, a multisite effort is paramount for high impact research. Here we describe the development and implementation of a dedicated brain tumour registry collecting comprehensive data across a variety of tumour types, informing our understanding of real-world treatment and outcomes, and integrating with multiple research efforts.

**Methods:** BRAIN (Brain tumour Registry Australia: INnovation and translation) was developed in collaboration with BIOGRID, a secure data repository that links and de-identifies data from multiple sources whilst protecting privacy and intellectual property. Leveraging this infrastructure, BRAIN is a cloud-based platform capturing comprehensive clinical information regarding adult patients with brain tumours from diagnosis through treatment until death. Independent expert opinion was sought to determine the breadth and nuances of data collection.

**Results:** BRAIN was developed between August 2017 and February 2021. Currently there are 11 sites across Victoria/Tasmania actively contributing patients, including private hospitals and regional sites. Since deployment in February 2021, 179 patients have been added. Figure 1 shows the breakdown by tumour type. Median age is 59 (range 19-87years) with 50% male. BRAIN is supporting multiple research efforts, including EX-TEM, a registry-based randomised trial, and BioBRAIN, a patient-derived tumour organoid program.

**Conclusion**: To our knowledge, this is the first multi-state initiative for brain tumour clinical data collection in Australia. BRAIN is currently being scaled nationally with plans to support more research efforts over time, driving clinical and translational research efficiency.

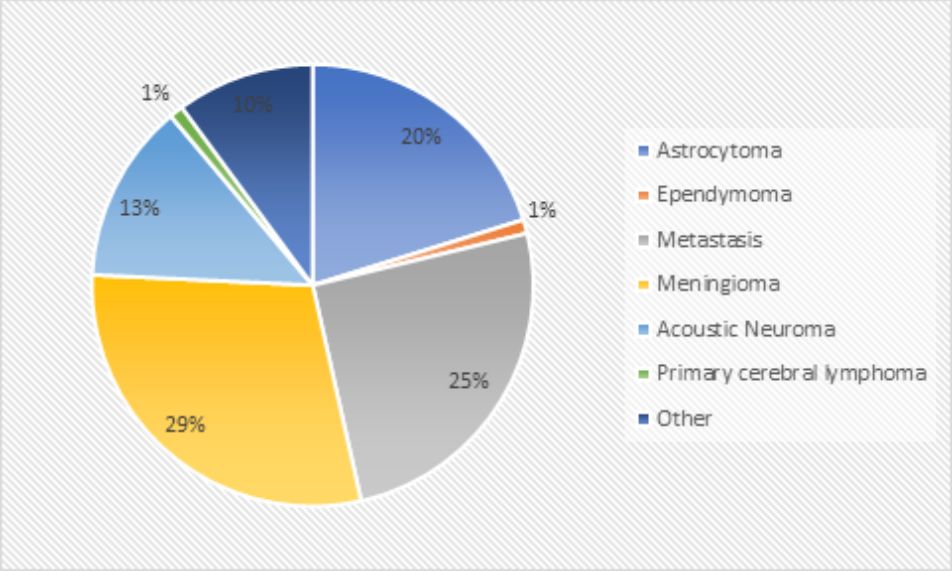


**Figure 1: Spread of tumour types**

**Abstract Id: 15**

**Abstract Title**

Patterns of care of adult patients diagnosed with medulloblastoma in the Australian population

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**Abstract**

**Background:** Adult medulloblastoma is a rare primary brain tumour with no accepted standard of care. We reviewed patterns of care and outcomes of adult patients diagnosed with medulloblastoma in the Australian population.

**Methods:** We retrospectively assessed patients treated between January 2010 - December 2019 across major neuro-oncology centres in Australia. Clinicopathologic and treatment parameters were collected. Kaplan-Meier estimates of overall survival (OS) were analysed.

**Results:** Interim analysis of 36 patients are reported with median follow up of 59 months. The median age was 26 (range 18 – 53) years and the majority male (58%). Histological subtypes were classic 4 (11%), NOS 3 (8%), desmoplastic/nodular 6 (17%), extensive nodular 3 (8%), large cell anaplastic 5 (14%), and not recorded in 15 (42%). Molecular subtyping was performed in 15 (42%) and of these sonic hedgehog (SHH) subtype was the most common 5 (33%). As per the Chang staging system, the majority were T1 12 (33%) or T2 19 (53%). Most patients had gross total resection 23 (64%) and 12 (33%) had residual tumour. Nearly all patients, 35/36 (97%), received craniospinal radiotherapy with 6 patients (17%) receiving concurrent chemoradiotherapy. The majority (59%) received 36 (range 23.4 – 54)Gy craniospinal irradiation and 36% received boost to the tumour bed (range 18 – 59.4Gy). Adjuvant chemotherapy regimens varied significantly with 8 different protocols used and 8 (22%) did not receive adjuvant chemotherapy. In 10 patients who relapsed, treatments included re-resection and chemotherapy, radiotherapy alone and chemotherapy alone. Median OS was 56 months (IQR 21-113), while the median OS was 15.5 months after developing recurrent disease.

**Conclusion:** This is the largest Australian dataset to date. Significant variability in practice exists with no standardised adjuvant chemotherapy regimen utilised. Our findings are consistent with other smaller studies, highlighting the need for national guidelines on molecular profiling and age-adapted treatment strategies.

**Abstract Id: 16**

**Abstract Title**

A prospective, multi-centre trial of FET-PET In Glioblastoma patients - the TROG 18.06 FIG Study: preliminary results of the nuclear medicine and radiation oncology credentialing program

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**Abstract**

**Background:** FIG is an Australian prospective multi-centre study across 10 sites evaluating impact of serial [18F] fluoroethyl-L-tyrosine positron emission tomography (FET-PET) imaging on the management of up to 210 glioblastoma patients. Participants undergo FET-PET imaging at three time-points: pre-chemo-RT (FET-PET1), one month post-chemo-RT (FET-PET2) with FET-PET3 triggered at suspected clinical and/or radiological progression. FET-PET image analysis is both qualitative and quantitative including biologic target volume (BTV) delineation by Nuclear Medicine (NM) physicians. Radiotherapy (RT) is per standard care with the Radiation Oncologist (RO) deriving hybrid RT volumes using the BTV only after RT completion. We describe preliminary outcomes of the comprehensive NM, RO/RT quality assurance (QA) credentialing program.

**Methods:** FIG site credentialing requires documentation detailing equipment, processes, independent audits and completion of multiple benchmarking cases. Benchmarking is completed by at least 2xNM physicians (n=6 cases each) and 1xRO (n=4 cases each) per site, with central review assessing protocol compliance (Table.1). NM cases span 3xFET-PET1 delineation of BTVs and 3xFET-PET3 cases involving response criteria interpretation. RO cases include 1xPlanning case and 3xCases delineating hybrid volumes and organs-at-risk (OAR).

**Results:** Of eight sites analysed to date, NM FET-PET1 and FET-PET3 case interpretation resulted in an overall pass-rate of 76.7% (92/120), with 36.7% (FET-PET1: 22/60) and 38.3% (FET-PET3: 23/60) with some form of violation (Table.2). Predominant resubmission reasons were incorrect delineation of background region-of-interest and gross tumour volume (GTV) (Table.2). RO credentialing results (Table.3) showed 92.6% (25/27 cases) were acceptable for hybrid volume and 85.2% (23/27 cases) for OAR delineation respectively with no major violations noted. The MR-derived-GTV (GTV_MR) contour was, however, non-evaluable/missing in 51.8% of cases.

**Conclusions:** A robust FIG study credentialing program has resulted in increased national capacity, expertise, and familiarity with FET-PET interpretation. Key QA aspects will be incorporated into the prospective recruitment phase of the study.

Table 1: Summary of Nuclear Medicine and Radiation Oncology / Therapy Credentialing Activities Per Site

| Pre-Trial Quality Assurance Activities | | |
|---|---|---|
| **Activity – Radiation Oncology** | **Number of Cases** | **Assessment Criteria** |
| Phantom Dosimetry Audit | 1 | Evidence of appropriate Level III dosimetric audit |
| Facility Questionnaire | 1 | Appropriate site radiation therapy facilities and processes |
| Benchmarking Exercise -Radiation Therapy Treatment Planning (one per site) | 1 | Ability to meet protocol planning and dosimetry constraints |
| CASE 1 (at least one RO per site)<br>PART A) Standard Contour Delineation Benchmarking Exercise,<br>PART B) FET-PET Image Interpretation and incorporation into RT Target Volume Delineation | 1 | Ability to meet protocol contouring guidelines (standard RT volumes).<br>Ability to derive protocol defined hybrid target volumes using a biologic target volume |
| CASE 2 and 3 -Benchmarking Exercise - FET-PET Image Interpretation and incorporation into RT Target Volume Delineation (at least one RO per site) | 2 | Ability to derive protocol defined hybrid target volumes using a biologic target volume |
| **Activity – Nuclear Medicine/Radiology** | **Number of cases** | **Assessment Criteria** |
| FIG - Technical survey; Nuclear Medicine and Radiology capacities | 1 | Appropriate site NM and radiology capacity |
| Benchmarking Exercise - FET-PET Image Interpretation Target Volume Delineation (x2 NM Physicians per site) | 3 | Ability to derive protocol defined biologic target volume using MIM Workflow |
| Benchmarking Exercise - FET-PET Imaging Interpretation and Response criteria/scoring (x2 NM Physicians per site) | 3 | Ability to interpret response criteria, scoring and assessment of disease status using FET-PET imaging |
| **Activity – Nuclear Medicine/Radiology** | **Number of cases** | **Assessment Criteria** |
| ARTnet PET-CT/PET-MR Certification | 1 | Evidence of ARTnet PET-CT/PET-MR Certification |
| RANZCR MRI Accreditation | 1 | Evidence of RANZCR (or equivalent) MRI Accreditation |

Table 2: FET-PET NM Credentialing Results Summary

| FET-PET1 NM Credentialing Results Summary n=60 | | | |
|---|---|---|---|
| | **Key Assessment Criteria: Biologic Target Volume Contour Acceptable** | **Violation Reasons** | **Frequency** |
| **Acceptable** | 63.3% | Background ROI incorrectly contoured | 47.8% |
| **Minor** | 18.3% | Excessive GTV Contour | 39.1% |
| **Major** | 18.3% | Documentation | 8.7% |
| | | Inadequate GTV Contour | 4.4% |
| **FET-PET3 NM Credentialing Results Summary n=60** | | | |
| | **Key Assessment Criteria: Interpretation of FET-PET3** | **Violation Reasons** | **Frequency** |
| **Acceptable** | 61.7% | Inadequate GTV contour | 37.5% |
| **Minor** | 25% | Incorrect FET-PET image interpretation | 33.3% |
| **Major** | 13.3% | Background ROI incorrectly contoured | 16.7% |
| | | Documentation | 12.5% |

Table 3: FET1 RO Credentialing Results Summary - Target Volume Delineation

| FET-PET RO Credentialing Results Summary n=27 | | | | | | | |
|---|---|---|---|---|---|---|---|
| | **Clinical GTV Contour** | **GTV_MR Contour** | **Clinical CTV Contour** | **Clinical PTV Contour** | **Hybrid GTV Contour** | **Hybrid CTV Contour** | **Hybrid PTV Contour** |
| **Acceptable** | 92.6% | 48.2% | 88.9% | 88.9% | 100.0% | 92.6% | 92.6% |
| **Minor** | 0.0% | 0.0% | 3.7% | 3.7% | 0.0% | 7.4% | 7.4% |
| **Major** | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| **Missing/Not Evaluable** | 7.4% | 51.9% | 7.4% | 7.4% | 0.0% | 0.0% | 0.0% |

**Abstract Id: 17**

**Abstract Title**

Estimation of BRAF V600E mutations and its prognostic significance in high grade glioma patients

**Authors:** Divyanshu Dua[1,2], Mitali Fadia[3,2], Gane Pranavan[3,2]

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**Abstract**

**Background:** High grade gliomas are aggressive with no major breakthrough in the gliomas over the past 20 years. Hence there is a need for target approach.

VE – BASKET study was an open labelled, non-randomised, multicohort study of BRAF v600 mutant non melanoma cancers which included 24 patients primary brain cancers were treated Vemurafenib 960 mg twice a day continuously until disease progression, withdrawal or intolerable adverse effects. The ORR was 25% and median PFS as 5.5 months. In the high grade glioma group, 1 patient had a partial response and 2 of the patients had stable disease for >12 months.

There is lack of data involving the BRAF mutation in high grade gliomas and needs prospective data.

**Aims:** a. To establish the incidence BRAF mutation in high grade glioma patients currently seen at the Canberra Hospital using the Qiagen Therascreen platform. b. Prospective Analysis of Progression free Survival and Overall Survival in BRAF V600E mutation positive and wild type.

**Methods:** a. All newly diagnosed high grade gliomas being reviewed or managed at the Canberra hospital approached and consented for the screening for BRAF V600E mutation patients. b. The clinical and demographic information to be collected on the database for prospective analysis.

**Results:** The study started to recruit since January 2020 and so far, 30 patients have been recruited. 14 patients have been tested for the BRAF V600E mutation with 1 patient being tested positive for BRAF V600E mutation. The estimated patient numbers expected for this study is 100 patients. The updated results to follow as study is ongoing.

**Conclusions:**

- There is lack of evidence of BRAF mutation incidence in high-grade gliomas.
- The BRAF inhibitors may be a suitable target approach for selected patients with high-grade gliomas.

**References:** Kaley T, Touat M, Subbiah V et al. BRAF Inhibition in *BRAF*$^{V600}$-Mutant Gliomas: Results From the VE-BASKET Study. J Clin Oncol. 2018 Dec 10;36(35):3477-3484.

**Abstract Id: 18**

**Abstract Title**

Quality of life, cognition and psychological health in patients with benign and low-grade brain tumours

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**Abstract**

**Introduction:** Impairments in health-related quality of life (HRQoL) are well documented in acoustic neuroma (AN), meningioma (M) and low-grade glioma (LGG) patients. Early results from our ongoing largest prospective, cross-sectional cohort study have identified a significant impairment in perceived cognitive functioning. We aim to further assess the correlation between subjective and objective cognition, and any other HRQoL factors involved to develop risk stratification methods and identify therapeutic targets.

**Method:** Adults postoperative for AN, M or LGG and in follow-up at a large tertiary centre underwent HRQoL assessment using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire (EORTC-QLQ-C30 and BL20). Cognition was tested by a computerised cognitive testing battery and psychological health was assessed using the Hospital Anxiety and Depression Scale (HADS). Two-tailed T tests and Spearman's correlation were used for statistical analysis.

**Results**: There were a total of 612 participants (AN=163, M=290, LGG=159). AN, M and LGG patients show significant HRQoL impairments post-resection, most markedly in subjective cognitive function ($p<0.0001$). A marked discrepancy can exist between patients' perception of their cognition and their performance on objective testing. Patients with impaired subjective cognition (despite normal objective testing) show significantly worse HRQoL across all domains. Poor emotional functioning and fatigue significantly correlate with impaired perception of cognition. HADS score, and the subset depression score, significantly correlate with impaired subjective cognition but show no correlation with objective deficits.

**Conclusion**: Post-resection AN, M and LGG patients have significantly impaired HRQoL across all domains and worst in the cognitive domain. Most patients do not have a true cognitive deficit despite reporting poor cognition and it is this perceived cognitive deficit that is associated with impaired psychological health and overall HRQoL. Therefore, cognitive functioning may represent the first actionable domain to treat HRQoL impairments in this vulnerable cohort.

**Abstract Id: 19**

**Abstract Title**

Worse survival outcome for patients with IDH mutated anaplastic glioma when IMRT is delayed until time of relapse after initial surgical management

**Authors:** Michael Back[1,2,3,4], Jon Parkinson[5,4], Marina Kastelan[1,4], Adrian Lee[1,3], Matthew Wong[2], Helen Wheeler[1,4]

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**Abstract**

**Aim:** Assess impact on survival for IDH mutated anaplastic glioma (AGmut) managed with radiation therapy either upfront(IMRTinit) or delayed(IMRTdelay) until time of subsequent relapse after neurosurgical management of lower-grade glioma .

**Methods:** Patients with AGmut managed with IMRT between January2008-March2021 were audited with timing of IMRT described as IMRTinit or IMRTdelay (first, second or later after surgery for lower-grade glioma). Survival was calculated from IMRT start and prognostic factors assessed by log-rank analysis. Site of relapse was categorised as local or distant in relation to surgical cavity/residual disease. Survivorship endpoints were CTCv4.0 late events, ECOG and employment.

**Results**: Of 187 patients the median age was 43years; 100 patients classified as AAmut whilst 87 with AOD. Residual disease at IMRT was present in 77% patients with >20mm in 61%; and 85% received temozolomide. Timing of RT was upfront in 56%; whilst 24%,12% and 8% were managed at first, second or later relapse with median time from initial diagnosis of 64.5 months. Median follow-up for survivors was 6.5 years.

The 8yPFS was 62.6% and 8yrOS was 70.4%. Worse PFS was noted with AAmut ($p<0.01$), worse ECOG ($p=0.03$) and delayed IMRT($p=0.04$); but not age ($p=0.34$) or residual disease ($p=0.10$). Specifically IMRTinit had 8yPFS of 62.6% versus IMRTdelay of 50.0% ($p<0.01$); and proportion of distant relapse was 26.9% and 45.4% respectively($p=0.14$). For AAmut subgroup the impact was greater with 8yrPFS from IMRTinit and IMRTdelay of 66.7% and 43.8%($p=0.02$).

Overall survival was also negatively impacted by IMRTdelay($p=0.02$).

Of 71 assessable patients with 5years PFS there was good survivorship with 97% ECOG0,1; 94% seizure-free; and equivalent employment from Year1 postIMRT.

**Conclusion:** Delaying IMRT until relapse was associated with worse outcome. This may have implications for counselling patients with lower-grade glioma on a delayed intervention strategy, including in the EORTC IWoT Study.

**Abstract Id: 20**

**Abstract Title**

Concordance of intra-operative frozen section and pre-operative radiological diagnosis of brain tumours with their final histopathological diagnosis – a 3-year retrospective study

**Authors:** Anson Chan, Sriya Chakrabarty, Shelley Verma, Zachary Drew, Leslie Kuma, Alka Sinha, Archana Dwivedee, Eric Guazzo, David Anderson, Sarin Kuruvath

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**Abstract**

**Aims:** Radiological and pathological diagnoses are of utmost importance in the management of neurosurgical patients with brain tumours. We reviewed the accuracy of both pre-operative radiology and intra-operative frozen section diagnoses and explored the reasons for non-concordance.

**Methods**: We performed a three-year retrospective audit of all patients who underwent neurosurgery for brain tumours at the Townsville University Hospital (TUH) between January 2017 and December 2019. The data was analysed using SPSS software.

**Results**: A total of 134 patients underwent surgery for brain tumours in the study period. Concordance between frozen section and final histopathology diagnoses was achieved in 110 cases. We demonstrated 95% accuracy for meningiomas, 90% for metastases and 70% for glioma. A discrepancy between frozen section and final histopathology was observed in 10 cases – 8 of these cases involved glioma. Concordance between radiological and final histopathology diagnoses was achieved in 96 cases. The most accurate pre-operative radiological diagnoses were metastases (88%) and meningiomas (87%). Glioma were found to have a lower rate of pre-operative radiological diagnosis (57%) and all 3 lymphoma cases were not diagnosed on pre-operative radiology.

**Conclusions**: The overall concordance of intra-operative frozen section and the final histopathological diagnosis of brain tumour patients treated at TUH during the past 3 years was high at 82%. This was in context of the accepted challenges of frozen section interpretation which include volume of tissue sent for analysis, distortion due to cautery and availability of clinical and radiological data. The accuracy of pre-operative radiological diagnosis was found to be 72%. Gliomas were associated with a lower accuracy rate in both frozen section and radiological diagnoses.

**Abstract Id: 21**

**Abstract Title**

Surgery and chemoradiotherapy in the management of scalp glioblastoma

**Authors:** Anson Chan, Michael Collins, David Anderson

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**Abstract**

**Aims:** Scalp glioblastoma metastases are rare and are associated with a poor prognosis. We present a case of early scalp metastasis treated with surgical excision followed by chemoradiotherapy and explore the associated challenges. To our knowledge, combination treatment has been previously reported in only one case and was associated with improved survival.

**Case report:** A 59-year-old man was diagnosed with left temporal lesions after presentation with headaches. He underwent debulking surgery and histopathology returned as glioblastoma, WHO grade IV, IDH wild-type, ATRX+. He underwent adjuvant radiotherapy and temozolomide. On post-operative day 78, a 2.5 cm nodule within his craniotomy incision was discovered. Computed tomography (CT) confirmed a subgaleal nodule. He proceeded to wide local excision which confirmed scalp glioblastoma thus radiotherapy was commenced to the excised region (with unavoidable overlap of previously irradiated skin) along with concurrent temozolomide. At his last review 5 months post completion of radiotherapy to the scalp metastasis there was no clinical evidence of recurrence at the scalp.

**Literature review**: Scalp glioblastoma metastases are rare; our literature review found 9 previous reports in the English literature.[1-9] The mean time to onset of scalp metastasis was at 7.89 months in this group. Our patient was diagnosed with a scalp metastasis at only 2.5 months post treatment. The mean survival after diagnosis of scalp glioblastoma metastasis reported in the literature was 4.79 months; treatment with excision alone had a mean survival of 3.4 months. Notably, the only case to be treated with excision, radiotherapy and chemotherapy (as in our case) was reported to have survived 14.5 months after diagnosis of scalp metastasis.

**Conclusions**: Scalp glioblastoma metastases may be encountered increasingly as survival in primary glioblastoma improves with contemporary treatment protocols. Radiotherapy to previously treated fields warrants special consideration given to consent and techniques.

**References**

1. Pérez-Bovet J, Rimbau-Muñoz J. Glioblastoma multiforme metastases to the masticator muscles and the scalp. *J Clin Neurosci*. 2018;53:237–239.
2. Ginat D, Kelly H, Schaefer P, et al. Recurrent scalp metastasis from glioblastoma following resection. *Clin Neurol Neurosurg*. 2013;115:461–463.
3. Jain N, Mirakhur M, Flynn P, KA Choudhari KA. Cutaneous metastasis from glioblastoma, *Br J Neurosurg*, 2005;19:1, 65–68.
4. Forsyth T, Bi W, Abedalthagafi M, et al. Extracranial growth of glioblastoma multiforme. *J Clin Neurosci*. 2015;22:1521–1523.
5. Goyal R, John P, Bhatoa S, Arora R. Extracranial metastasis in a IDH- wild type glioblastoma. *Indian J Pathol Microbiol*. 2019;62(3):495–497.

6. Ozturk N, Erdim M, Sonmez A, Bayramicli M. Scalp metastases of glioblastoma multiforme: case report. *Eur J Plast Surg*. 2007;29:303–306.
7. Allan RS. Scalp metastasis from glioblastoma. *J Neurol Neurosurg Psychiatry*. 2004;75:559.
8. Figueroa P, Lupton JR, Remington T, et al. Cutaneous metastasis from an intracranial glioblastoma multiforme. *J Am Acad Dermatol*. 2002;46:297–300
9. Houston SC, Crocker IR, Brat DJ, et al. Extraneural metastatic glioblastoma after interstitial brachytherapy. *Int J Radiat Oncol Biol Phys*. 2000;48:831–836

**Abstract Id: 22**

**Abstract Title**

Correlating clinical outcomes with gene signatures using digital spatial profiling of melanoma brain metastases

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**Abstract**

**Aims**: Melanoma brain metastases present a therapeutic challenge, with poorer outcomes in patients treated with modern systemic therapies. Barriers to effective therapy include lack of penetration of the blood brain barrier, the unique brain immune environment and the tumour microenvironment. Our discovery cohort study seeks to explore gene signatures using digital spatial profiling that may hold prognostic and predictive value in melanoma brain metastases.

**Methods**: Archival resected brain tissue from 109 patients with melanoma brain metastases was identified and 1mm cores extracted into a tissue micro array. Concurrent clinical annotation for demographics, tumour characteristics, burden of disease, treatment received, and clinic-pathological outcomes was performed.

We examined the composition of assessable patient tumours (n=38) using Nanostring GeoMX Digital Spatial Profiling (DSP). Using the human whole transcriptome atlas (WTA) assay, 18000 mRNAs targets were analysed within separate tumour or stroma compartments of each TMA core, and our analysis utilised unbiased approaches to identify factors that may influence patient response.

**Results**: 109 patients were identified, of which 38 had adequate tissue for WTA. Median age of the whole cohort was 57 with 69 (63%) of male sex. Resection of the tumour was complete in 84 (77%), 40 (36%) had BRAF mutation 38 of which were V600E or K. Modern systemic therapy in the form of BRAF-targeted therapy was received by 29 patients whilst 51 patients received immune-checkpoint inhibitors in a line of therapy  Median overall survival (95% confidence interval, CI) for the overall cohort was 11.4 months (9.1-18.4) and 5-year survival was 22%, whereas median PFS was 6.3 months (95% CI, 5.1-8.0). WTA sequencing has been performed and results are currently undergoing analysis, to be presented.

**Conclusion**: High-plex digital spatial profiling of the tumour and microenvironment is likely to identify gene signatures which are predictive/prognostic for melanoma brain metastasis.

**Abstract Id: 23**

**Abstract Title**

Quantitative volumetric tumour response in patients treated with combination Gamma Knife stereotactic radiosurgery and immunotherapy for melanoma brain metastases

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**Abstract**

**Introduction**: Stereotactic radiosurgery (SRS) confers excellent local control for melanoma brain metastases (MBM). This study examines the MRI volumetric tumour response over time of melanoma brain metastases following Gamma Knife SRS, and aims to synthesize a predictive model of volumetric change following treatment.

**Methods**: A retrospective single-institution analysis was performed of patients who received single-fraction Gamma Knife SRS for melanoma brain metastases. Predictive factors relating to patient characteristics, tumour factors, SRS dose, volume and systemic therapy treatment factors were collected. Treatment volume was delineated on a T1-weighted Gadolinium contrast enhanced MRI at baseline and each follow-up scan. A repeated measures ANOVA was used to assess for differences in mean volumetric change between interpolated 3-month intervals with a two-tailed significance of $\alpha$=0.05.

**Results**: 101 patients with 425 melanoma BM were treated with SRS in the study period. Median follow-up was 29.2 months (IQR 19.7-39.8). Median dose was 20Gy (IQR 18-20). Median baseline volume and lesion diameter were 0.24cc (IQR 0.06-1.02) and 7.7mm (IQR 4.8-12.4) respectively. 77% of patients received concurrent immunotherapy. There was a statistically significant decrease in lesion size in the 0-3 and 3-6 month interval ($p<0.0001$). 89.7% of treated lesions had durable local control on MRI at last follow-up. 5% of patients experienced symptomatic radionecrosis and 19% had any grade 3 or higher toxicity. Every 1mm increase in maximal lesion diameter was associated with a 1.5% (95%CI 0.04-2.9, p=0.04) and 2% (95%CI 0.4-3.7%, p=0.016) greater reduction in volume at 3- and 6-months. Patients receiving concurrent immunotherapy had a significantly greater regression in tumour volume at 3-months (37% superior [95%CI 6.0-68.1%, p=0.02] and 6-months (48% superior [95%CI 7.4-89.5%, p=0.02] compared to those commencing >4 weeks post-SRS.

**Conclusion**: This study demonstrates a significantly greater volumetric regression with concurrent immunotherapy and SRS in melanoma brain metastases in the initial 6-months following treatment.

**Abstract Id: 24**

**Abstract Title**

Initial increase in radiological volume is associated with poorer clinical and radiological response outcomes in patients treated with stereotactic radiosurgery for melanoma brain metastases

**Authors:** Mihir Shanker[1,2], Nick Gatt[3], Heath Foley[3], Samuel Crowley[3], Emma Thomson[3], Kendall Higgs[3], Wei Soon[3], Victoria Atkinson[3,1], Trevor Watkins[3], Michael Huo[3,1], Matthew Foote[3,1], Mark Pinkham[3,1]

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**Abstract**

**Introduction**: Stereotactic radiosurgery (SRS) demonstrates excellent local control for melanoma brain metastases (MBM) in the order of 75-95%. This study aimed to assess factors associated with the clinical and radiological responses of 1) complete/partial response and 2) progression of disease using RANO-BM criteria in patients receiving combined modality immunotherapy treated with Gamma Knife® SRS for MBM at a single tertiary institution.

**Methods**: A retrospective single-institution analysis was performed of patients who received single- or multi-fraction Gamma Knife® SRS for MBM. Predictive factors relating to patient characteristics, treatment factors and systemic therapy timing was collected. Efficacy outcome data was stratified as per the RANO-BM working group clinical and radiological criteria. Response assessment was characterised radiologically using MRI 3 monthly post SRS. Hazard ratios (HR) with their respective 95% confidence intervals (CI) were determined with Cox proportionate hazards modelling.

**Results**: On multivariate analysis for local control, concurrent immunotherapy with SRS was significant when adjusting for BRAF status, volumetric change at initial post SRS MRI and age at time of SRS; HR=0.27(95%CI 0.08-0.9, p=0.04) and volumetric increase of lesions on *initial* MRI was significantly associated with progression when adjusting for age, immunotherapy status and BRAF status; HR=3.8(95%CI 1.7-8.5, p=0.0015). Multivariate cox regression analysis demonstrated that patients receiving concurrent SRS-IT maintained a higher chance of achieving a complete / partial response when adjusted for BRAF status, symptoms at time of SRS, ECOG performance status, dexamethasone use and MRI volumetric characteristics at initial 3-month post-SRS imaging. On multivariate analysis, patients demonstrating any increase in volume on *initial* post-SRS imaging were significantly less likely to achieve an ultimate CR or PR as per RANO-BM criteria; HR=0.048 (95%CI 0.007-0.345,p=0.0026).

**Conclusion**: Combined modality immunotherapy and SRS provides a high degree of local control for MBM. Initial 3-month MRI volumetric change post-treatment is predictive of final response.

**Abstract Id: 25**

**Abstract Title**

Generation of a spatial atlas of glioblastoma tumour sections using DCNN

**Authors:** Amin Zadeh-Shirazi[1], Mark McDonnell[2], Eric Fornaciari[3], Narjes Bagherian[4], Kaitlin Scheer[1], Michael Samuel[1], Mahdi Yahoobi[5], Rebecca Ormsby[6], Santosh Poonnoose[7], Damon Tumez[1], Guillermo Gomez[1]

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**Abstract**

**Background:** Spatial characterization of gene signatures and the cell types expressing these signatures in different glioblastoma tumour locations is lacking.

**Methods:** We have used DCNN as a semantic segmentation model to segment tumour regions in digitised glioblastoma histopathological slides. Correlation analysis between segmentation results from tumour images and matched RNA expression data was performed to identify genetic signatures and cell types that are specific to different tumour regions.

**Results**: We found that spatially resolved gene signatures were strongly correlated with survival. Further in silico cell ontology analysis along with single-cell RNA sequencing data from resected glioblastoma tissue samples showed that these tumour regions had different gene signatures, whose expression was driven by different cell types in the tumour microenvironment. Our results pointed to a key role for interactions between microglia/pericytes/monocytes and tumour cells that contribute to poor survival in glioblastoma.

**Conclusions:** This work identified key histopathological features that correlate with patient survival and detected spatially associated genetic signatures that contribute to tumour-stroma interactions and which should be investigated as new targets in glioblastoma.

**References:** Zadeh Shirazi, A., McDonnell, M.D., Fornaciari, E. *et al.* A deep convolutional neural network for segmentation of whole-slide pathology images identifies novel tumour cell-perivascular niche interactions that are associated with poor survival in glioblastoma. *Br J Cancer* **125,** 337–350 (2021). https://doi.org/10.1038/s41416-021-01394-x

**Abstract Id: 26**

**Abstract Title**

A 3-Arm, Phase IIa Trial of Safety & Efficacy of Olinvacimab, a Monoclonal Antibody to VEGFR2 in Patients with Recurrent Glioblastoma Multiforme with Imaging and PK/PD assessments: Final report

**Authors:** Adi Balasubramanian[1], George Iatropoulos[1], Anna Nowak[2], Lawrence Cher[1]

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**Abstract**

The VEGF pathway has been an important target in Glioma given the vascular nature of the tumour, the role of angiogenesis and the autocrine aspects of VEGF signalling in Glioblastoma. This report analyses the role of Olinvacimab in recurrent GBM assessing safety, dosing schedules and efficacy. Olinvacimab (TTAC-0001) is a VEGFR2 Mab that binds and inhibits the receptor.

In this study we assessed three dosing schedules, 8 mg/kg and 12mg/kg weekly for 3 weeks of 4 and 12 mg/kg for weekly for each week of 4 weeks. Assessments were performed for safety of each cohort prior to progressing to the next level. The main toxicity was the presence of cutaneous haemangiomas. PlGF-VEGFR1 pathway may be the cause of cutaneous hemangioma combining IHC of hemangioma tissue and PlGF concentration. The common toxicities seen with other VEGF directed therapies including Ramucirumab, such as hypertension, impaired wound healing, and proteinuria were not seen in this cohort.

Efficacy was assessed by MRI using RANO criteria. 6 month PFS was 17%, with Disease control rate of 25%, with steroid dose reduction. The longest response was 15 months.

On DCE MRI, there was no significant difference in perfusion parameters between baseline and 1st follow-up MRI comparing those with stable disease and progression.

Pharmacokinetics showed decreased clearance rate (CL) and resulted in increased half-life compared to Phase I study. Pharmacodynamic studies showed much higher levels of a range of serum concentrations particularly of VEGF-A in those treated at 12mg/kg vs arm 1. In addition, concentrations of VEGF-A, C and D were elevated in the 3 patients with SD compared to those with PD.