

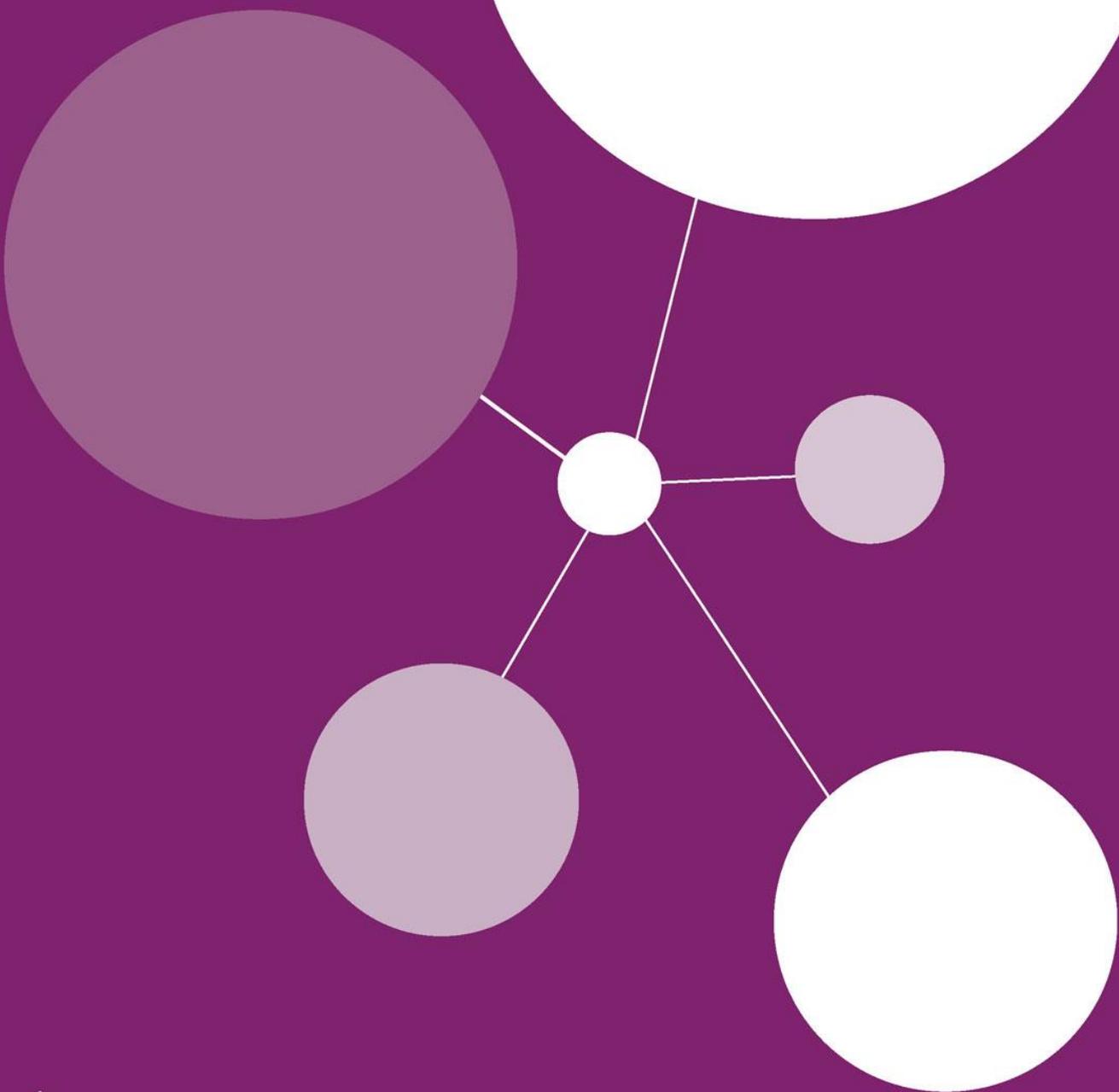


**NCRI**

National  
Cancer  
Research  
Institute

# **NCRI Brain Group**

**Annual Report 2019-20**



Partners in cancer research

**The NCRI Group Annual Reports 2019/2020** span the time period April 2019 – March 2020. The reports were submitted during a challenging time for all in the healthcare sector due to the COVID-19 pandemic. This has had an unprecedented impact on the activity of both the Research Group itself and wider research activities, ranging from the time available for research work versus clinical commitments to the funding of new trials and the recruitment of existing trials. Due to this the NCRI significantly extended the deadline for submission of annual reports and allowed the Groups to submit reduced reports, if time permitted, with the following sections at a minimum:

- Achievements (section 1 of the report)
- Funding Submissions over the last 12 months (section 5)
- Priorities and Challenges (section 7)

In addition to this, Consumer representatives of each Group were asked to only complete their sections if they feel able to. Most of our Consumers have submitted reports, however where reports have *not* been submitted this was due to extended periods of ill health, or additional work/home life constraints, as a result of COVID-19.



## NCRI Brain Group Annual Report 2019-20

### 1. Top 3 achievements in the reporting year

#### **Achievement 1**

We have developed several new trials funded by NIHR and charities. STOP 'EM is a large multi-centre meningioma trial that will open in 15-20 centres and recruit ~1000 patients. BRIOCHE and iWOT are multi-centre glioma trials that will answer important questions about the role or re-irradiation in recurrence (BRIOCHE) and adjuvant radiotherapy in low grade gliomas (iWOT). Two single site quality of life studies have also been funded (SCARF BT and QUALMS).

#### **Achievement 2**

The ROAM trial (Clinical Investigator: Professor Michael Jenkinson) has reported the qualitative research component (doi: 10.1634/theoncologist.2019-0571). This identified the key challenges in conveying equipoise in trials comparing adjuvant radiotherapy versus monitoring, after surgical resection of meningioma. Strategies to improve recruitment are described and the results are generalisable across other trials and will have an impact on future study design.

The KEATING trial (CI: Professor Jenkinson) has reported (doi: 10.1007/s11060-020-03417-8). The trial established that patient selection is a key part of establishing those suitable for diet therapy. Patients are able to stay on diet for around 6 weeks. This will inform future trial design for phase 3 studies.

The PRaM-GBM study (CI: Mr Stephen Price) has reported (doi: 10.1259/bjr.20190441) on using semi-automated construction of patient individualised radiotherapy planning techniques. This has the potential to impact on radiotherapy planning for glioblastoma.

#### **Achievement 3**

The main Group and Subgroups are working more effectively following interaction with the wider neuro-oncology network. This has been facilitated by the refreshed membership and as a result we have successfully converted some of the incubator days and workshops into grant applications submitted to NIHR. Furthermore, the NCRI Brain Group, Society of British Neurological Surgeons (SBNS) tumour section and British Neuro-Oncology Society (BNOS) now

have shared representation across all three organisations which facilitates stronger networking.

## 2. Structure of the Group

The structure of the Group and Subgroups is unchanged. Professor Jenkinson continues as chair. Several experienced members rotated off: Professor Silvia Marino – neuropathology after 6 years; Professor Oliver Hanneman – neurology and Dr Paul Sanghera – clinical oncology after 3 years. This enabled us to appoint some new members who are already study investigators: Dr Jillian Maclean (clinical oncologist), Mr Puneet Plaha (neurosurgeon), Dr Meera Nadnhabalan (clinical oncologist). Professor Sebastian Brandner (neuropathologist) was appointed for 3 years only and given the remit to find a new academic neuropathologist (rather than the role rotating between him, Professor Marino and Dr Kathreena Kurian, as has been done for the past 10+ years). Ms. Jessica Sass (PPI) left the Group due to change in career direction and was replaced by Ms. Zoe Faulkner and Miss Paula Smallwood.

The main and Subgroups have a good mix of expertise and appropriate geographic and gender diversity. We retained our existing scientific member (Dr Igor Vivanco) and did not feel the need to appoint an additional scientist in this rotation.

## 3. Brain Cancer Group & Workstream strategies

### Brain Group

#### **Portfolio development**

Several new studies have been funded and will be adopted onto the portfolio:

- STOP 'EM (Surgical Trial Of Prophylaxis for Epilepsy in Meningioma). NIHR HTA funded. CI: Professor Jenkinson. Multi-centre.
- BRIOCHE (Brain irradiation or chemotherapy – randomised phase 2 trial). Funded by Jon Moulton Charitable Foundation. CI: Dr Louise Murray. Multi-centre.
- iWOT (IDH mutated 1p/19q intact lower grade glioma following resection: wait or treat?). Funded by EORTC charity arm. UK CI: Dr Sara Erridge. Multi-centre.
- SCARF BT (Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour). Funded by NIHR RfPB. CI: Mr Price. Single site.
- QUALMS (Quality of life outcomes in patients with incidental and operated meningiomas: a cross-sectional cohort study). The Brain Tumour Charity Funded. CI: Professor Jenkinson. Single site.

### **Raising the Group's Profile**

The Brain Group's continues to engage with aligned professional societies. The Brain Group chair now has a standing position on the BNOS council. A reciprocal arrangement is in place to have a BNOS council member join the Brain Group. Mr Puneet Plaha was appointed to the Brain Group and is also the lead for the Tumour Section of the SBNS. Professor Jenkinson is chair of the Academic Committee of the SBNS and is neurosurgery sub-speciality lead for The Royal College of Surgeons of England (RCSEng). Both these roles are complementary to the activities of the Brain Group and have led to increasing awareness of the Brain Group activities.

### **Strengthen UK wide and international working**

With the refreshed main and Subgroup membership the neuro-oncology research network in the UK continues to increase. Several new Cis have been developed (e.g. Dr Murray – BRIOCHE trial; Mr Puneet Plahah – FUTURE GB tria). International networking continues, e.g. with opening of the iWOT study (UK CI: Dr Erridge) and continued recruitment into the ROAM trial (with EORTC and TROG). Professor Jenkinson is also a member of the EORTC meningioma research committee which ensure that any EORTC initiated studies are also opened in the UK.

### **Research Group structure and function**

Over the last 2 years (since new chair appointed) membership of the main and Subgroups has been extensively refreshed. The Subgroups are actively working up new clinical studies for funding, as well as working closely with other NCRI Groups (Breast, Lung, Skin). The Subgroups meet 3-4 times per year by teleconferences and face-to-face meetings.

### **Patient and public involvement and impact**

We have a Public and Patient Involvement (PPI) representative from a patient with a glioma who provided fantastic contribution at the main Group meeting in October 2019. Although she is still receiving treatment she continues to contribute to Group activity where possible. Mr Usama Ali makes excellent contributions to the meningioma Subgroup. Ms. Faulkner was on the National Institute for Health and Care Excellence (NICE) brain tumour guidelines committee and brings a wealth of consumer experience to the Group.

## **Glioma Subgroup (Chair, Dr Sara Erridge)**

### **Develop new trials within the Group for glioma and ensure areas of unmet need included**

Several studies are being developed by the Subgroup:

- Re-irradiation for recurrent gliomas: A workshop was held in Leeds in the Autumn 2019. The Group agreed to define different Groups of recurrence (e.g. early relapsers versus late relapsers). The BRIOCHE study is funded (CI: Dr Murray) and was cited as an example of success for the Group. A further study is proposed to address the role of re-irradiation. A study of re-irradiation + PARP inhibitor and has submitted to a pharma company for costings (CI: Dr Dusan Milanovic).
- Dr Erridge secured funding to open the EORTC iWOT study. This has achieved UK ethics approval.
- Drug development: Dr Vivanco is looking into Capmatinib (also known as INCB28060 and INC280, is an orally bioavailable inhibitor of cMET) which could be an interesting agent in glioma. The Edinburgh team are working with Oxford and MIT (Dr Juanita Lopez also inputting) are developing a large scale drug screening programme – they will use 6-8 cells lines which represent a cross section of biological subtypes.
- Proton v photon radiotherapy for G2/3 co-deleted glioma was a joint study developed by Dr James Powell & Professor Susan Short and has been submitted for funding.

### **Provide feedback for non-Group member studies**

Feedback was provided for several studies:

- Surgical trial for low grade glioma (Samandouras). There were concerns about early re-operation for these patients and additional PPI work was advised. A survey of surgeons identified that most were interested in the surgical question (i.e. the clinical dilemma) and that they would recruit to the trial.

### **Widen the access to trials throughout the UK through a neuro-oncology network**

This objective has been achieved though greater integration of research active sites with smaller sites. The CNS Bootcamp (run by Dr Sarah Jeffries) has further facilitated networking between centres and head led to a number of new investigators.

## **Meningioma, Metastases & Other Tumours Subgroup (Chair, Mr Thomas Santarius)**

### **Support and develop new clinical trials for patients with meningioma**

- Professor Jenkinson developed STOP 'EM – a multicentre trial of prophylactic antiepileptic drugs for seizure naïve patients undergoing surgery for meningioma. This has been funded by NIHR HTA (£1.61M) and will be a multi-centre UK trial.
- Professor Jenkinson developed QUALMS – a quality of life studies for patients with incidental and operated meningioma. This is a single site study that will recruit ~300 patients. A follow-up multi-site study is planned.

### **Support and develop new clinical trials for patients with metastases**

Six study proposals were discussed in a cross-Group workshop in February 2020. The workshop was led by the Brain Group with contribution from lung, breast and skin. Studies in development are:

- EDAM-BRAIN (screening lung cancer patients for brain metastases). Led by Lung Group with Brain Group support. Submitted to NIHR RfPB March 2020 – not funded.
- Melanoma platform trial. Multi-arm study assessing combination of drug and radiosurgery. Developed jointly by Brain and Skin Group. A further 1-day meeting is planned to finalise study design. NIHR Health Technology Assessment (HTA) funding application planned for 2021.
- SUPARMAN. Surgical resection trial in brain metastases with radiotherapy component. This has been in development for 2 years and is proving difficult to agree on protocol. A further meeting is planned in 2020.
- SAFER. Seizure management in brain metastases. Early concept. Further development needed but suitable for NIHR funding stream.
- SMARTIE. Radiotherapy for large unresectable brain metastasis. Early concept that needs multi-user input into study design. Brain Group supporting but low priority project.
- HER2 breast cancer screening. Early concept that is similar to EDAM-BRAIN proposal.

### **Establish links with other Clinical Studies Groups for brain metastases trials**

A cross-group (Brain, Lung, Breast, Skin) workshop was held in February 2020. Six trial proposals were discussed. EDAM-BRAIN (screening lung cancer patients for brain metastases) has been submitted for funding to NIHR RfPB in March 2020. The remaining studies require further development with a view to submitting to NIHR funding streams in 2020/2021.

## Supportive & Palliative Care Subgroup (Chair, Dr Robin Grant)

### Encourage development of high quality clinical trials in the top 10 priority areas

NCRI brain S&PC Subgroup members have developed high quality clinical trials.

- NCRI Brain S&PC continues to support SPRING (Seizure PRophylaxis IN Glioma) which is recruiting and encouraging centre involvement. (CI: Dr Grant) NIHR HTA funded.
- NCRI Brain S&PC supported BT Life, developed through NCRI Incubator days. This has finished and results are being analysed. (CI: Dr Alasdair Rooney). Brain Tumour Charity funded.
- NCRI Brain S&PC fed back comments on SCARF BT Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour. (PI: Dr Price) NIHR RfPB funded.
- NCRI brain S&PC fed back comments on FuTuRE-GB (a non-randomised multicentre learning and evaluation phase Phase IIB study) followed by prospective, phase III, multicentre randomised controlled trial using “standard techniques” versus “new techniques (DTI and Intra-operative Ultrasound. (PI: Mr Plaha). NIHR EME funded.
- NCRI brain S&PC fed back comments on SHIPPING study. Scanning Headache to Identify Positive Predictive factors for use IN Guidelines. (Co-PIs: T Ham/Dr Grant). Being developed for NIHR HSDR.
- NCRI brain S&PC fed back comments on Core Outcome Measures. (PI: Dr Anthony Byrne) Submitted to TBTC (Under consideration).
- PREPARED – Providing resources to Engage Patient and Relative in End of Life care Decisions – (PI: Dr Florian Boele: (under consideration).

### Provide early advice on study applications

NCRI brain S&PC Subgroup have advised on submissions from outside the Group.

- Comments on: CaPaBLE - a small, multi-centre non-randomised study exploring the use of better tools for QoL measures in patients with HGG. (PI: M Williams).
- Comments on: LGG surgical trial – (PI: G Samandouras).
- Comments on: BRAINpower: Brain Patient Outcomes With Enhanced Radiotherapy: (PI: N Burnett).
- Comments on: SCAN-LGG - Symptom correlates and neuroimaging in low-grade glioma. (PI: G Thompson).
- Comments on: Neurotoxic-Oncology SALT Rehabilitation: (PI: S Andrew).

### Support Research Design Service and key Clinical Trials Units involvement

We have encouraged researchers developing studies for submission to large funders (NIHR, TBTC) to involve RDS, a CTU and PPI advice in trial development.

#### **Work collaboratively with relevant NCRI Groups**

- We have been liaising with Living with and Beyond Group members (Professor Sara Faithful) on Neurotoxic –Oncology Rehabilitation (NIH funding application (unsuccessful) and potential research planned speech therapy in Intra-operative language testing in awake craniotomy.
- NCRI Brain S&PC Group led an “Incubator Day” with NCRI Living with and Beyond Group led by Professor Anne Marie Nelson.
- NCRI brain S&PC Group have also been in discussion with Professor Mike Hawkins, NCRI TYA Quality of Life and Survivorship Subgroup to work to develop a joint proposal on later effects of CNS treatment Incubator Day which was to be held in Glasgow on 28th April 2020.
- We continue to work with Cochrane Neuro-Oncology on the NIHR Systematic Review Programme Grant.
- The “Incubator Day on Quality of Life MDM” led by NCRI Brain S&PC Subgroup and NCRI Living with and Beyond Group included representatives from the Tessa Jowell Brain Cancer Mission on 28th January 2020 to plan research and development of Quality of Life MDM in Neuro-Oncology.

#### **4. Task Groups/Working parties**

The Brain Group have had no task Groups or working parties during the reporting year.

## 5. Funding applications in last year

**Table 2 Funding submissions in the reporting year**

Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
<b>Cancer Research UK</b>					
<b>May 2019</b>					
IMAGE-ID: Image-guided Multi-modal Annotation of Genetics and tumour micro-Environment In patients with Diffuse glioma	Experimental Medicine Award (full)	Dr Matthew Grech-Sollars	Not Supported	Supported	
<b>Other committees</b>					
Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
Surgeons Trial Of Prophylaxis for Epilepsy in Meningioma (STOP 'EM).	NIHR HTA	Michael Jenkinson	Funded	Developed by Group	£1,641,896
A randomised phase II study of baseline MRI brain scanning versus no MRI brain scanning in patients with stage IV non small cell lung cancer without neurological symptoms. Early Detection of Asymptomatic Metastases – the EDAM-BRAIN trial.	NIHR RfPB	Simon Paige	Submitted March 2020. Not funded	Cross Group study. Led by lung, supported by brain. Michael Jenkinson is co-applicant	£350,000
SCARF BT (Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour).	NIHR RfPB	Stephen Price	Funded	Supported by Group	£239,569

## 6. Consumer involvement

### Usama Ali

No consumer report submitted - please refer to page 2.

### Zoe Faulkner

No consumer report submitted – please refer to page 2.

### Paula Smallwood

No consumer report submitted – please refer to page 2.

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## 7. Priorities and challenges for the forthcoming year

### **Priority 1**

Continue to increase the number of interventional and observational studies on the portfolio across all brain tumours types. We need to translate the brain metastases workshop in February 2020 into successful grant applications.

### **Priority 2**

Ensure that the trainee members are involved in working up studies and are co-applicants on any funding applications.

### **Priority 3**

Ensure that closed and completed portfolio studies are published so patients can benefit from the impact of the research e.g. GALA-5 and GALA-BIDD studies are still pending publication.

### **Challenge 1**

COVID-19 has stopped all recruitment into trials. It jeopardises funding on existing and new studies as Charities will have lost fundraising income streams and required to pay staff, or contract to within expected resource budget.

### **Challenge 2**

Designing multi-centre studies for meningioma and low-grade glioma – these often need international collaboration.

### **Challenge 3**

Increase the number of multi-centre studies that can be opened in all UK centres – important to engage with those centres not currently recruiting to the portfolio.

## 8. Collaborative partnership studies with industry

The FUTURE GB trial involves collaboration with industry to provide intra-operative ultrasound and image-guidance systems for participating neurosurgery units to the value for approximately £1.7M. This industry support was essential to ensure the requested funds from NIHR Efficacy and Mechanism Evaluation (EME) represented value for money.

## 9. Appendices

Appendix 1 – Brain Cancer Group strategies

A – Brain Cancer Group Strategy

B – Glioma Subgroup

C – Meningioma, Metastases & Other Tumours Subgroup

D – Supportive & Palliative Care Subgroup

Appendix 2 – Top 5 publications in reporting year & Group involvement with NICE appraisals

**Professor Michael Jenkinson (Brain Group Chair)**

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## Appendix 1

### Brain Cancer Group and Subgroup Strategies

#### A – Brain Cancer Group Strategy

Patients with brain tumours continue to suffer from poor clinical outcomes because of under-developed clinical research infrastructure, pre-clinical models that do not accurately represent clinical disease and a limited scientific base in the UK.

#### Aims

- To promote and support the development of clinical trials for patients with all types of brain tumours through disease-focused Subgroups.
- To promote research into survivorship, quality of life and patient reported outcomes through a specific Subgroup.
- To work more closely with scientists to generate added value from clinical trials and develop mechanistic and discovery science.
- To support, promote and advocate on behalf of brain tumour patients and their carers.

To achieve these aims, we have:

- Re-organised the Subgroup structures to better reflect clinical research priorities.
- Appointed basic scientists to the Group and Subgroups to encourage synergy between science and clinical trials.
- Appointed clinical trainees to the Group to encourage the clinical investigators of tomorrow.
- Engaged with patient representative through Group PPI members and brain tumour charities to support clinical trial development and prioritise what matters to patients.
- Worked with all our stakeholders to improve recruitment and identify barriers to recruitment into clinical trials.

The challenges of neuro-oncology research in the UK and planned strategy have been published: Brain tumor research in the United Kingdom: current perspective and future challenges. A strategy document from the NCRI Brain Group

Kathreena M. Kurian, Michael D. Jenkinson, Paul M. Brennan, Robin Grant, Sarah Jefferies, Alasdair G. Rooney, Helen Bulbeck, Sara C. Erridge, Samantha Mills, Catherine McBain, Martin G. McCabe, Stephen J. Price, Silvia Marino, Erica Moyes, Wendy Qian, Adam Waldman, Babar Vaqas, Debbie Keatley, Peter Burchill, and Colin Watts  
Neuro-Oncology Practice. 5(1), 10–17, 2018 | doi:10.1093/nop/npx022

The timelines below outline the strategic objectives, actions, Group leads and outcomes for each element of the strategy.

## Brain Tumours CSG Strategy: April 2018 – April 2021

This strategy timeline has been produced to support the Brain Tumour CSG research strategy. It runs from April 2018 until April 2021, and will be reviewed and updated (by MDJ, SJ and RG) on a regular basis.

The document is composed of the following:

Page 2 – 4: NCRI Brain Tumour CSG Strategy: plan of implementation, containing agreed strategic objectives (1-5), specific actions, CSG leads and proposed deadlines.

Strategy document agreed by CSG on 19.4.18

Brain Tumour CSG members		Glioma subgroup		Meningioma & metastasis subgroup		Supportive & Palliative care subgroup	
MDJ	Michael Jenkinson	SJ	Sarah Jeffries (chair)	PS	Paul Sanghera (co-chair)	RG	Robin Grant (chair)
DK	Debbie Keatley	CMcB	Catherine McBain	TS	Tom Santarius (co-chair)	AA	Ann Arber
HB	Helen Bulbeck	EH	Estelle Healey	MDJ	Michael Jenkinson	AB	Anthony Byrne
IV	Igor Vivanco	GT	Gerry Thompson	DK	Debbie Keatley	CMcB	Catherine McBain
KK	Kathreena Kurian	HB	Helen Bulbeck	GW	Gillian Whitfield	DP	Diane Playford
LF	Lorna Fern	IV	Igor Vivanco	JL	Joanne Lewis	FB	Florian Boele
MM	Martin McCabe	JP	James Powell	JP	Jonathan Pollock	HB	Helen Bulbeck
OH	Oliver Hanemann	LC-H	Laura Clifton-Hadley	KK	Kathreena Kurian	KO	Kathy Oliver
PH	Phil Hexley	NC	Natalie Cook	OH	Oliver Hanemann	WH	Willie Hamilton
PH	Paul Sanghera	PB	Paul Brennan	RB	Richard Baird		
SE	Sara Erridge	SE	Sara Erridge	RZ	Rasheed Zakaria		
SJ	Sarah Jefferies	SM	Silvia Marino	SJM	Samantha Mills		
SJM	Samantha Mills	SS	Stuart Smith				
SM	Silvia Marino						
SS	Stuart Smith						
RG	Robin Grant						
WQ	Wendy Qian						
TB	Thomas Booth						

Strategic objective	Action	CSG Lead	Date	Outcomes
1a. Portfolio development (general)	Create a large portfolio of studies for patients with brain tumours	All	On going	Increased access to clinical studies for patients
	Review study proposal before submission to funding bodies to improve grantsmanship	All	On going	
1b. Portfolio development (glioma subgroup)	Increase trials for patients with gliomas  Studies in development: <ul style="list-style-type: none"> <li>• Repurposing Itraconazole</li> <li>• Adaptive glioma clinical trial</li> <li>• Role of revision surgery in glioblastoma</li> <li>• Role of intraoperative ultrasound and MRI in paediatric and TYA tumours (MERIT)</li> </ul>	All subgroup members	Ongoing	Ongoing
		SJ/SE	Nov 2017	Submitted to CRUK
		All	August 2018	Submit to TBTC
		PB/SS/SJ/SE	April 2019	Workshop planned
1c. Portfolio development (meningioma & metastases subgroup)	Increase trials for patients with meningioma, metastasis & others  Studies in development: <ul style="list-style-type: none"> <li>• Management of incidental meningioma</li> <li>• Epilepsy in meningioma: NIHR HTA</li> <li>• Surgical resection of brain metastases</li> <li>• Imaging markers of PCNSL</li> </ul>	All subgroup members		
		JP/MDJ/TS	Oct 2019	
		MDJ	Oct 2018	Submit to NIHR HTA
		RZ/MDJ	Oct 2018	Present at NCRI brain mets workshop 2/3/18
		SJM/MDJ	Oct 2018	Present to main CSG and develop submission for NIHR RfPB

Strategic objective	Action	CSG Lead	Date	Outcomes
1d. Portfolio developments (supportive & palliative care)	Increase trials for patients with brain tumours addressing symptom burden	All	On going	NIHR HTA funded TBTC funded  Funded by Vitaflow
	Cochrane Complex Reviews (interval scanning, earlier diagnosis, earlier referral to palliative care, molecular subtyping, long term effects or surgery and/or RT).	RG	August 2017	
	Funded studies:	RG	April 2018	
	• SPRING trial (Seizure prophylaxis in glioma)	AR/RG	Oct 2017	
	• BTLife (brain tumours; lifestyle intervention and fatigue evaluation)	MDJ	Sept 2018	
• The KEATING Trial – a randomised study of the ketogenic diet				
Studies in development:	KO	2019		
• Effect of ketogenic diet on tumour growth	FB	2019		
• Palliative care supportive care master protocol				
• Improving support for family caregivers				
• Early diagnosis of primary brain tumours	RG	2019		
• Posterior Fossa				
2. Raising profile	Routine dissemination of results from studies through speciality meetings e.g. SBNS, BNOS, CNS Bootcamp	Study Chief Investigators	On going	Continued engagement of investigators to recruit to studies
	Presentation of NCRI CSG role and portfolio at specialty meetings:	•MDJ/SS/SJ/SE/SM	Annual presentations from March 2018	Raise awareness, identify new chief investigators, encourage CSG review of proposals before submission to funders
	•British Neuro-Oncology Society (BNOS)	•MDJ/SS		
	•Society of British Neurological Surgeons (SBNS)	•SJ		
	•CNS bootcamp	•MDJ		
	•British Neurosurgical Research Group (BNRG)	•KK		
	•British Neuropathology Society (BNS)	•SM		
	•Glioma Club	•RG/MDJ		
	•Joint ABN / SBNS meeting		Sept 2018	

## B – Glioma

The formation of the Glioma Subgroup is to improve the access and entry of patients with a diagnosis of a glioma into clinical trials throughout the United Kingdom. The Subgroup has been selected to have representation from centres in England, Scotland, Wales and Northern Ireland.

The Subgroup has neurosurgical representation to build on the successful current platform of neurosurgical trials. A medical oncologist with phase I experience has been appointed as it is recognised that this is an area that needs improvement in the current trial portfolio. A scientist with a dedicated interest in translational science has been appointed to help with this aspect within trial design. A radiologist and neuropathologist have been appointed for specialist advice in clinical trial development. It is planned to advertise for two trainees to join the Subgroup from any of the contributing disciplines to foster links with developing expertise for those working in neuro-oncology in the future.

The Subgroup will act as platform to provide support for the development of UK-led clinical trials, including commercial and academic studies. Plans are in place to provide a quick guide to apply for adoption to the portfolio for commercial studies.

We will also provide direct or targeted support for one-two grant applications per year for studies in glioma. Work is already underway for the development of a re-irradiation protocol which will be able to be utilised in multiple studies. The Subgroup also aims to develop a network for UK clinical oncologists who treat glioma.

There is a well-established Group for neurosurgeons in the British Society of Neurosurgical Oncology and similarly there is a forum for basic research at the glioma club meeting. The infrastructure for an annual neuro-oncology meeting has been established at the CNS Bootcamp which aims to optimise information about current clinical trials and protocols that are in development to optimise trial entry across the UK. The ultimate aim will be to combine these three meetings to optimise clinical trial design and execution from the UK neuro-oncology community.

### Strategic Aims:

1. Develop new trials within the Group for glioma and ensure areas of unmet need included
2. Provide feedback for non-Group member studies
3. Widen the access to trials throughout the UK through a neuro-oncology network

Strategic Components	Action	Group Lead	Date	Outcome
<b>1b. Portfolio Development (Glioma Subgroup)</b>	Increase trials for patients with glioma	All	On going	On going
	Itraconazole Trial in glioblastoma	All Subgroup	Submitted to CRUK Early Phase and	June 2018

			Feasibility December 2017	
	Standard ChemoRT+/- Ipilumimab in newly diagnosed GBM (Mulholland)	All Subgroup	Submitted for funding 2017	Funded – aim to start recruitment in 7 UK centres Q4
	ATOMIC G	Presented CNS Bootcamp CM, NC	Submission to EME – input requested from sub-Group	Resubmission later in 2018
	Role of revision surgery in recurrent glioblastoma	All Subgroup	July 2018 – workshop to formalise trial design	Trial application to NIHR HTA November 2018
	Platform for radiology studies - MIMICING	GT, JP, IV	Meeting planned for 30.10.2018	Unified research platform for radiology studies
	Long-term survivor of GBM study (Brodbelt)	PB, EH, SS	All UK sites identified for data collection Pathology data set agreed April 2018	On going
<b>2. Raising Profile</b>	CNS Bootcamp	SJ	Meeting Planned for September 2018 2019 – joint meeting with Glioma Club at start of BNOS 2020 - EANO	Raise awareness, identify new investigators, increase clinical trial entry
<b>3. Strengthen UK wide and international working</b>	Engage with EORTC	SE	On going	EORTC studies on portfolio

### **C – Meningioma, Metastases & Other Tumours Subgroup**

Strategic objective that have been achieved by the Subgroup are in **bold and underlined**

#### **Vision**

To create a large portfolio of clinical trials for patients with meningioma and metastases.

#### **Mission statement**

It is our goal to build on the existing portfolio and to develop new clinical trials for patients with meningioma and metastases. We will accomplish this by focusing on clinical priorities for patients, identifying research-active clinicians and providing a forum to advise on study

applications. Our success will be measured by the number of successful grant applications and new studies adopted onto the portfolio.

### Strengths

Two of the Subgroup members (Professor Jenkinson and Dr Santarious) are part of the founding committee of BIMS (<https://britishirishmeningiomasociety.wordpress.com>) and have good links to the EORTC meningioma research committee (Professor Jenkinson is a member) and the Society for Neuro-Oncology International Meningioma Consortium (Professor Jenkinson, Dr Santarious, Professor Hanemann & Dr Samantha Mills). These networks will be essential for developing UK trials and interGroup trials with EORTC. The Group also draws on expertise in metastasis trials (Dr Gillian Whitfield, Dr Richard Baird & Dr Paul Sanghera).

### Weaknesses

New Subgroups members (Mr Jonathan Pollock and Dr Joanne Lewis) do not have experience of submitting grant applications. Current links with other Groups is poor and many primary cancer trials specifically exclude patients with brain metastases.

### Strategy for success

#### Meningioma

- Establish a network of research active clinicians (surgeons, oncologists, pathologist, radiologist) working on meningioma (via the British-Irish Meningioma Society) – in progress, expected May 2018. **Network established 2019 = objective achieved.**
- Define SOPs that will harmonise data collection for meningioma studies covering tumour tissue, blood samples and imaging (MRI) - in progress, expected May 2018. **SOPs for brain imaging published 2019. SOPs for tissue defined by ROAM trial = objective achieved**

#### Metastases

- Establish links with other Groups (e.g. Lung, Breast, Skin) to develop new trials for metastases patient Groups, with reference to study design / methodology / tissue sampling for brain metastases trials. **Two cross Group workshops held (2018 & 2020) with trials funded (RADIANT BC & BRITEMENT) or in development = objective achieved.**

### Clinical studies under consideration/development by Subgroup

Strategic Components	Action	Group Lead	Date	Outcome
1c. Portfolio Development (Meningioma & metastases)	Increase trials for patients	All	On going	On going
	Epilepsy in meningioma	MDJ	Nov 2018	<b><u>NIHR HTA funded April 2020 - £1.64M</u></b>

	Incidental meningioma management	JP/TS/MDJ/OH	2019 / 2020	<u>A large trainee project is due to start July 2020 to validate the IMPACT calculator. This included international sites.</u>
	Supramarginal resection of metastasis (SUPARMAN)	RZ/MJD/PS/TS/JL	2018 / 2019	NIHR HTA application planned
	Imaging markers and treatment pathway in PCNSL	SM/MDJ/TS	Nov 2018	RfPB application planned

### **D – Supportive & Palliative Care Subgroup**

#### **Membership (2019-20)**

Dr Robin Grant (Neurologist, Edinburgh)

Dr Ann Arber (Oncology Nursing Research, Surrey)

Professor Anthony Byrne (Professor Palliative Care, Cardiff)

Dr Catherine McBain (Clinical Oncologist, Manchester)

Dr Florian Boele (Research Psychologist, Leeds)

Dr Helen Bulbeck (NCRI brain S&PC Secretariat; Patient Involvement)

Mrs Kathy Oliver (Patient Advocate, Surrey)

Professor Jon Evans (Professor Applied Neuropsychology, Glasgow)

Dr Ally Rooney (Sen Lecturer Neuro-Psychiatry, Edinburgh)

Mr Stephen Price (Consultant Neurosurgeon, Cambridge)

Dr Cressida Lorimer (Oncology Trainee)

(Thanks to Professor Richard Neal (Primary Care, Leeds); Professor Robert Hills (Statistics, Oxford) for their recent previous involvement)

**The NCRI Supportive & Palliative Care (S&PC) Subgroup strategy is aligned with the main NCRI brain strategy**

Key themes for the S&PC Subgroup include:

#### **Grantsmanship**

- NCRI Brain S&PC Subgroup will advise on applications in JLA priority areas by providing brief expert peer review via the Subgroup on submissions at outline proposal stage.
- External review by the Subgroup twice a year will follow the CTRad model.
- PPI on submissions review will be done through the S&PC PPI representatives.
- The breadth of experience on the S&PC Subgroup will provide feedback on JLA studies ranging from Primary care and early diagnosis to Palliative Care and End of Life studies

### **Research Studies & Trials**

- To promote and support the development of clinical trials for patients with all types of brain tumours in JLA Priority areas
- To promote research into survivorship, quality of life and patient reported outcomes.
- To support, promote and advocate on behalf of brain tumour patients and their carers

### **Collaborations & Increasing reach**

- Collaborate with linked organisations that can assist with trial development in some way either in the trial development stage e.g. Cochrane Systematic Reviews in Priority Areas or Professional bodies that can improve visibility of the NCRI brain S&PC Subgroup aims to promote and support clinical research (e.g. Professional Organisations: ABN, SBNS, RCR, BNOS).
- NOCTURN (Neuro-Oncology Clinical Trials UK Research Network) website development to improve visibility of clinical trial development, funding and training.
- Building relationships to promoting NCRI trials and improve quality of trials.
- NCRI Brain S&PC Newsletter produced annually and distributed electronically.

### **Clinical studies funded or under consideration**

- NCRI Brain S&PC continues to support SPRING (Seizure PRophylaxis IN Glioma) which is recruiting and encouraging centre involvement. (CI: Dr Grant). NIHR HTA funded.
- NCRI Brain S&PC supported BT Life, developed through NCRI Incubator days. This has finished and results are being analysed. (CI Dr Rooney). Brain Tumour Charity funded.
- NCRI Brain S&PC fed back comments on SCARF BT Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour. (PI: Mr Price) NIHR RfPB funded.
- NCRI brain S&PC fed back comments on FuTuRE-GB is a non-randomised multicentre learning and evaluation phase Phase IIB study) followed by prospective, phase III, multicentre randomised controlled trial using “standard techniques” versus “new techniques (DTI and Intra-operative Ultrasound. (PI: Mr Plaha). NIHR EME funded.
- NCRI brain S&PC fed back comments on Core Outcome Measures. (PI Professor Byrne) Submitted to TBTC (Under consideration).
- NCRI brain S&PC fed back comments on PREPARED – Providing resources to Engage Patient and Relative in End of Life care Decisions – (PI: Dr Boele: (under consideration).
- NCRI brain S&PC fed back comments on SHIPPING study. Scanning Headache to Identify Positive Predictive factors for use IN Guidelines. (Co-PIs: Mr Ham/Dr Grant). NIHR HSDR (Being Developed).

## Studies previously submitted– for further work and re-submission

NCRI brain S&PC Subgroup have advised on submissions from outwith the Group.

- Comments on: CaPaBLE - a small, multi-centre non-randomised study exploring the use of better tools for QoL measures in patients with HGG. (PI: Dr M Williams).
- Comments on: LGG surgical trial – (PI: Dr Samandouras)
- Comments on: BRAINpower: Brain Patient Outcomes With Enhanced Radiotherapy: (PI: N Burnett).
- Comments on: SCAN-LGG - Symptom correlates and neuroimaging in low-grade glioma. (PI: G Thompson).
- Comments on: Neurotoxic-Oncology SALT Rehabilitation: (PI: S Andrew)

## Collaborations & Increasing reach

- Cochrane systematic review programme grant funded (Cochrane Neuro-Oncology Group & NCRI Brain CSG) (Dec 2017- Nov 2020) –to jointly evaluate evidence for future studies in 7 JLA topic areas for future possible brain trials and guidelines.  
Four of the Cochrane Reviews have now been published:
  1. Lawrie TA, Gillespie D, Dowswell T, Evans J, Erridge S, Vale L, Kernohan A, Grant R. Long-term neurocognitive and other side effects of radiotherapy, with or without chemotherapy, for glioma. Cochrane Database of Systematic Reviews 2019, Issue 8. Art. No.: CD013047. DOI: 10.1002/14651858.CD013047.pub2.
  2. Thompson G, Lawrie TA, Kernohan A, Jenkinson MD. Interval brain imaging for adults with cerebral glioma. Cochrane Database of Systematic Reviews 2019, Issue 12. Art. No.: CD013137. DOI: 10.1002/14651858.CD013137.pub2.
  3. Hanna C, Lawrie TA, Rogozińska E, Kernohan A, Jefferies S, Bulbeck H, Ali UM, Robinson T, Grant R. Treatment of newly diagnosed glioblastoma in the elderly: a network meta-analysis. Cochrane Database of Systematic Reviews 2020, Issue 3. Art. No.: CD013261. DOI: 10.1002/14651858.CD013261.pub2.
  4. Jenkinson MD, Barone DG, Bryant A, Vale L, Bulbeck H, Lawrie TA, Hart MG, Watts C. Intraoperative imaging technology to maximise extent of resection for glioma. Cochrane Database of Systematic Reviews 2018, Issue 1. Art. No.: CD012788. DOI: 10.1002/14651858.CD012788.pub2.
- NOCTURN (Neuro-Oncology Clinical Trials UK Research Network) website developed as an informational resource about developing trials. Under expansion to allow pages for NCRI brain glioma Group.
- Building relationships to explore ways of promoting NCRI and trials and expand the Group and link with the NCRI Living With and Beyond Cancer Group and other NCRI Groups. NCRI brain S&PC Group have been liaising with “Living with and Beyond “Group members (Professor Sara Faithful) on Neurotoxic –Oncology Rehabilitation (NIHR funding application).

Potential research planned speech therapy in Intra-operative language testing in awake craniotomy.

- NCRI Brain S&PC Group led an “Incubator Day “with NCRI Living with and Beyond Group led by Professor Anne Marie Nelson. Further collaborative work planned to refine joint submissions.
- NCRI S&PC subgroup have also been in discussion with Professor Hawkins, NCRI TYA Quality of Life and Survivorship Subgroup to work to develop a joint proposal on later effects of CNS treatment Incubator Day which was to be held in Glasgow on 28th April 2020.
- NCRI subgroup continue to work with Cochrane Neuro-Oncology on the NIHR Systematic Review Programme Grant.
- The “Incubator Day on Quality of Life MDM” led by NCRI Brain S&PC Subgroup and NCRI Living with and Beyond Group included representatives from the Tessa Jowell Brain Cancer Mission on 28th January 2020 to plan research and development of Quality of Life MDM in Neuro-Oncology.

**NCRI Brain S&PC Newsletter was produced in March 2019 distributed electronically**

## Appendix 2

### Top 5 publications in the reporting year

The Group have published several Cochrane Complex Systematic Reviews (details in the SP&C section). These reviews are invaluable in supporting trial submissions in development and to aid future trial submissions, but they are not relevant to existing NCRI trials. The review on Intra-operative Imaging Technology was used in the NICE Guideline NG99 published in July 2018.

Trial name & publication reference	Impact of the trial	Group involvement in the trial
<p>ROAM / 1308 trial (Radiation versus observation following surgical resection of atypical meningioma.</p> <p>Challenges Conveying Clinical Equipose and Exploring Patient Treatment Preferences in an Oncology Trial Comparing Active Monitoring with Radiotherapy (ROAM/EORTC 1308). Sherratt FC, Brown SL, Haylock BJ, Francis P, Hickey H, Gamble C, Jenkinson MD, Young B. <i>Oncologist</i>. 2020 Apr;25(4):e691-e700. doi: 10.1634/theoncologist.2019-0571.</p>	<p>This has identified the key challenges in conveying equipose in trials comparing adjuvant radiotherapy versus monitoring after surgical resection of meningioma. Strategies to improve recruitment are described and the results are generalisable across other brain tumours trials and will have an impact on future study design.</p>	<p>Developed by Group. (CI: Professor Jenkinson)</p>
<p>KEATING study (Ketogenic diet as an adjuvant therapy for glioblastoma).</p> <p>Ketogenic diets as an adjuvant therapy for glioblastoma (KEATING): a randomized, mixed methods, feasibility study. Martin-McGill KJ, Marson AG, Tudur Smith C, Young B, Mills SJ, Cherry MG, Jenkinson MD.</p>	<p>Trial established that patient selection is a key part of establishing those suitable for diet therapy. Patients are able to stay on diet for around 6 weeks. This will inform future trial design for phase 3 studies.</p>	<p>Developed by Group. (CI: Professor Jenkinson)</p>

J Neurooncol. 2020 Mar;147(1):213-227. Doi: 10.1007/s11060-020-03417-8. Epub 2020 Feb 8.		
PRaM-GBM (Predicting sites of tumour progression in the invasive margin of glioblastoma).  Semi-automated construction of patient individualised clinical target volumes for radiotherapy treatment of glioblastoma utilising diffusion tensor decomposition maps. <i>Br J Radiol</i> 2020; <b>93</b> : 20190441.	Output from PRaM-GBM study. The has the potential to impact on radiotherapy planning for glioblastoma.	Developed by Group. (CI: Mr Price)

### Group involvement with NICE appraisals

NICE appraisal	Appraisal outcome	Group involvement with NICE appraisal
Depatuzumab mafodotin in combination for untreated EGFR-amplified glioblastoma multiforme [ID1466]	Pending	Brain Group responded with comments. NICE appraisal submission was premature and results of main trial publications were pending.
Nivolumab with radiation therapy for previously untreated glioblastoma multiforme [ID1562]	Pending	Brain Group responded with comments. Since Checkmate 143 trial was negative there was no role for Nivolumab in recurrent GBM.