

NCRI Brain Group

Annual Report 2020 - 2021



NCRI Partners

NCRI is a UK-wide partnership between research funders working together to maximise the value and benefits of cancer research for the benefit of patients and the public. A key strength of the NCRI is our broad membership with representation across both charity and government funders as well as across all four nations in the United Kingdom.



List of Appendices

Appendix 1	Membership of the Group, Subgroups and their specialty & location
Appendix 2	Group and Subgroup strategies
Appendix 3	Top 5 publications in reporting year
Appendix 4	Recruitment to the NIHR portfolio
Appendix 5	Annual report feedback 2019-20
Appendix 6	Quinquennial Review (QQR) feedback

NCRI Brain Group

Annual Report 2020-21

1. Top achievements in the reporting year (up to three)

Achievement 1

Three new studies funded by NIHR and charities (see section 5 for details). APPROACH is a multi-centre study comparing proton and photon radiotherapy in oligodendrogliomas. PROSPER will investigate the role of progesterone as a steroid-sparing agent in patients with brain metastases. COBRA will develop core outcome sets and patient reported outcomes for gliomas.

Achievement 2

We have completed the Cochrane reviews for brain tumours led by Robin Grant (<https://gnoc.cochrane.org/neuro-oncology-reviews>) which provide a benchmark for developing new studies and these will be used to develop the forthcoming strategy 2021-2026. We have also published two position statements on imaging and repeat surgery in gliomas that will help develop future studies in these areas.

2. Structure of the Group

- Existing structure maintained with main Group and Subgroups – some changes to Subgroups including Gary Doherty (medical oncologist) to provide brain metastases expert input.
- We are transitioning to the new structure in 2021 with a core Executive Group and a series of strategy directed Working Groups (pending strategy day in July 2021)
- Excellent and invaluable contributions from our Consumers and we have fantastic engagement with charities.
- Representation on the Group from The Brain Tumour Charity has stopped as they are not paid up members of NCRI – however we continue to engage with them on specific studies.
- Input from trainees has been mixed. One has engaged well and is running the non-portfolio BRITER study. One has found participating in Group activities educational and interesting but was too early in her training to fully engage and was also undertaking a PhD. One has had limited engagement.

3. Brain Group & Subgroup strategies

Brain Group

Key strategic aims are:

1. Portfolio development

Three studies funded in last 12 months:

- APPROACH (proton versus photons in oligodendrogliomas). NIHR HTA (pending revisions). CI: Louise Murray, Susan Short, James Powell. Multi-centre.
- COBRA (Core outcome sets in brain tumours). The Brain Tumour Charity. CI: Anthony Byrne. Multi-centre.
- PROSSPER (Progesterone as a steroid-sparing agent in metastases). NIHR EME. CI: Paul Chumas. Multi-centre.

2. Raising group profile

- We continue to be aligned with professional societies including British Neuro-Oncology Society and Society of British Neurological Surgeons. These links provide opportunities to align research activities across multiple disciplines for brain tumour patients.

3. Strengthen UK wide and international working

- The Group is actively engaged with the BRAIN MATRIX study in Birmingham to look for opportunities to add new investigational agents (e.g., Prof Susan Short is developing a Canabinoid trial that will use BRAIN MATRIX as the platform to deliver the study). *For the review committee please note that BRAIN MATRIX was developed by the Group when Colin Watts was still Chair (contrary to the panel's comment to the 2020 report).*
- We continue to engage with international partners, e.g., the Brain Tumour Charity funded COSMIC study (Core Outcome Sets in Meningiomas) [CI Jenkinson] has international collaborators from Europe (EORTC, EANO), North America (SNO, ICOM) and others (SBNS, BNOS, IBTA).

4. Research group structure and function

- The restructure in 2016 has delivered three active Subgroups – each producing new clinical trials onto the portfolio (as detailed in the QQR report). Planned changes to NCRI Group structures for 2021 will facilitate wider national engagement with clinicians, AHPs and scientists, e.g. by leveraging expertise from former Group members as well as newer researchers.

5. PPI and impact

- We have excellent PPI involvement and engagement on the Group. Since most brain tumour trials take many years to complete and report, we have had few 'high impact factor' publications from UK-developed and led trials. There are several completed studies that have not reported (e.g. GALA-5 and GALA-BIDD are under peer-review at present). There are several trials on the portfolio that will report within the next few years (e.g. PARADIGM) but many will not report for at least 5 years (e.g. ROAM, FUTURE-GB, SPRING, BRAIN MATRIX). The next Brain Group Chair (due 2023) will reap the rewards from all the studies developed over the last 5 years.

Glioma Subgroup (Chair, Dr Sara Erridge)

There are 3 key strategic aims for the Glioma Subgroup:

1. Develop new trials within the Subgroup for glioma and ensure areas of unmet need included

In 2019/20 the Glioma Subgroup had a change in some of the members to provide opportunities to newer investigators from neuro-surgery and oncology. New studies which members have been involved in include:

- FUTURE GB (opened 2021)
- BRAIN MATRIX (opened 2021)
- SPRING (opened 2020)
- Improving treatment of glioblastoma: distinguishing progression from pseudoprogression (opened 2020)
- iWOT (EORTC trial opened 2021)
- Ways ahead (qualitative study in low grade gliomas [LGG] opened 2021)
- APPROACH: protons v photons for oligodendroglioma (NIHR HTA funded pending revisions)

Two position papers have been published on imaging:

- (<https://pubmed.ncbi.nlm.nih.gov/33634034/>) (and second surgery)
- (<https://pubmed.ncbi.nlm.nih.gov/33791952/>) to assist with design of future studies of recurrent gliomas.

Group members are currently in the process of developing trials looking at novel imaging methods, drug-radiation combinations, re-irradiation, phase I studies of new agents, and a keto-genic diet.

2. Provide feedback for non-Subgroup member studies
 - In 2020-2021 we reviewed the six study proposals providing expert guidance on feasibility, eligibility, imaging and follow-up protocols, and endpoints.
3. Widen the access to trials throughout the UK through a neuro-oncology network
 - Due to the COVID-19 pandemic, opportunities to reach out to colleagues have been curtailed but the work undertaken over previous years has obviously been of benefit as many investigators have reached out to the group for advice on studies.

Meningioma, Metastases & Other Tumours Subgroup (Chair, Professor Oliver Hanemann)

Mr Tom Santarius (TS) stood down as Chair of the Meningioma, Metastasis & Other Tumours Subgroup and Professor C Oliver Hanemann (COH) was elected as the new Chair. The membership of the Subgroup also changed slightly to better represent different disciplines and become a bit smaller. We planned to recruit 1-2 Early Career Researcher (ECR) candidates however recruitment of new members was put on hold.

Key strategic aims:

1. Support and develop new clinical trials for patients with meningioma
 - The ROAM study (CI: Jenkinson) which was developed by the Brain Group in 2012 closed to recruitment and will report in 2026.
 - The Subgroup developed a biomarker study for meningioma called PROGRAM-BIO which has been submitted to NIHR EME (outline). CI: Oliver Hanemman.
 - The Subgroup supported STRATIFY EM (Stratifying epilepsy risk in meningioma surgery). Submitted to NIHR EME (outline). CI: Adel Helmy
 - The members Michael Jenkinson (MDJ), TS and COH successfully represent the UK in the International Meningioma Consortium (ICOM) contributing to several review articles in Neuro-oncology.
2. Support and develop new clinical trials for patients with metastases
 - EDAM-BRAIN (screening lung cancer patients for brain metastases) was submitted to NIHR RfPB March 2020 – Not funded.
 - PROSSPER (Progesterone as a steroid sparing agent in brain metastases) has been funded by NIHR EME and is in set up (CI: Paul Chumas).
 - We also reviewed how we can best contribute to brain metastasis studies where the primary tumour site oncologist is leading CI. This has been achieved by working with the Lung, Skin and Breast Research Groups and to ensure that brain metastases don't necessarily have to be an exclusion criterion in study design.
 - We started to stimulate research idea submissions by ECRs.

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

The key strategic aims of the Subgroup were to:

- Promote grantsmanship (advising on how to strengthen proposals by improving clinical reported outcome assessment and QoL components).
- Encourage and develop research studies.
- Increase collaboration and reach of research findings.

In 2020-21, the S&PC Subgroup have promoted grantsmanship on:

- BRAINpower: Brain Patient Outcomes With Enhanced Radiotherapy: (PI: N Burnett);
- Neurotoxic-Oncology SALT Rehabilitation: (PI: S Andrew)
- PREPARED – Providing resources to Engage Patient and Relative in End of Life care Decisions – (PI: Dr Boele);
- Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour (SCARF-BT): a Feasibility Study (NIHR RfPB funded NIHR200495 Feb 2021-Jan 2024)
- SHIPPING - Scanning Headache to Identify Positive Predictive factors for use IN Guidelines (PI: T Ham / R Grant) NIHR HS&DR submission June 2021).

In 2020-21, the S&PC Subgroup have developed research studies within the group on clinical priorities:

- SPRING (Seizure PRophylaxis IN Glioma) – a RCT of prophylactic Levetiracetam vs no anti-epileptic prior to surgery – NIHR 16/31/136 HTA funded 2018-23- suspended due to covid for 6-9 months (CI: Dr Grant)
- BT LIFE - Brain Tumours, Lifestyle Interventions, and Fatigue Evaluation: a multi-centre phase II RCT – TBTC funded (CI: Dr Rooney)
- FuTuRE-GB - non-randomised multicentre Phase IIB study followed by phase III, multicentre RCT using “standard techniques” versus “new techniques for maximum safe tumour resection. NIHR127930 EME Nov 2020-2024 (PI: Mr Plaha / PPI Dr H Bulbeck)
- SCARF-BT - Social Cognition Assessment and Rehabilitation for Families living with Brain Tumour: a Feasibility Study. NIHR200495 RfPB Feb 2021 - 2024(PI: Mr S Price)
- COBra - Core Outcome in Brain Tumour Trials - Patient Reported Outcomes TBTC 2020-2023 (CI: Prof Byrne).

In 2020-21 the S&PC has increased collaboration and increased reach by:

- Collaborating between Brain Group members and Cochrane by publishing eight complex systematic reviews from which to base further funding proposals. This was achieved through a NIHR Cochrane Systematic Review Programme Grant (SRPG). The SRPG teams became familiar with the evidence around the 8 topic areas and strengths and weaknesses of previous research. This led to a Cochrane Special Collection <https://www.cochrane.org/news/special-collection-brain-tumour-diagnosis-and-management>
- This has been promoted widely around the world in several languages. The topic areas of: “*Diagnosing brain tumours quickly, safely, and accurately*”, “*Risk-sharing in decision making for brain tumours*” and “*Best treatment when decisions are difficult*” will be a focus of NCRI research studies going forward and a “position paper” has already been published on one topic in Feb 2021 (reference <https://www.frontiersin.org/articles/10.3389/fonc.2021.620070/full>) and a second position paper on early diagnosis is in development. Other “position papers” and research studies will be developed through “incubator days”.

Going forward the key Supportive and Palliative Care Subgroup members will continue to promote grantsmanship, develop multi-disciplinary and multi-centre research in the clinical priority areas, extend collaboration between groups and specialties and promote e-learning through Programme Grants funding for Applied Research and Research for Patient Benefit to embed clinical improvements into practice.

4. Cross-cutting research

We have started a cross-trial group collaboration between SPRING, FUTURE-GB and BRAIN-MATRIX to discuss co-enrolment possibilities and potentially how to minimise duplication of data collection / data sharing between gliomas trials. This is still at an early stage but will be essential to formalise for any trials in the future.

A specialty group encompassing those involved in prompt diagnosis of glioma has been established, led by R Grant (neurology), but including lead Cancer GP in England and Scotland, Ophthalmology Leads in England, Optometry Leads in England and Scotland and Neuro-Radiology in England and Scotland to produce a position paper on prompt diagnosis based on the recent Cochrane Systematic Review (Grant R et al. Interventions to reduce the time to diagnosis of brain tumours. Cochrane Database of Systematic Reviews 2020, Issue 9. Art. No: CD013564. DOI: 10.1002/14651858.CD013564.pub2) and to consider other NIHR and other funding streams that may be involved.

There are no task and finish groups within the Brain Group.

There have been no formal cross-research group meetings in this reporting year.

5. Funding applications in last year

Table 1 Funding submissions in the reporting year

Other committees**					
Study	Committee & application type	CI	Outcome	Level of Group input	Funding amount
PROGRAM BIO	NIHR EME (outline)	Oliver Hanemann	Under review	Developed by group	£400K
STRATIFY EM (Stratifying seizure risk in meningioma surgery)	NIHR EME (outline)	Adel Helmy	Under review	Supported by group	£1.0M
APPROACH (Proton versus photon radiotherapy for oligodendroglioma)	NIHR EME (full)	Louise Murray, Susan Short, James Powell	Funded, pending revisions	Developed by group	£1.5M
COBRA	TBTC	Anthony Byrne	Funded	Developed by group	£153K
MERIT (Maximising Extent of Research in Tumours)	NIHR HTA (outline)	Conor Mallucci	Not funded	Supported by group	£1.0
EREPIO (Early re-operation and biobanking in low grade gliomas)	NIHR HTA (outline)	George Samandouras	Not funded	Supported by group	£1.4
PROSPER (Progesterone as a steroid sparing agent in brain metastases)	NIHR EME (full)	Paul Chumas	Funded	Supported by group	£570K

**Other applications in the table to be completed by Group Chair

6. Consumer involvement

Zoe Faulkner

My Consumer involvement includes attending all the NCRI Brain Group meetings and I am also on the Glioma Subgroup. I ask questions, make comments and provide written feedback when appropriate. I also have an interest in the Supportive and Palliative Care Subgroup and will be attending my first meeting in July 2021. In addition, I have participated in NCRI Consumer Forum meetings and attended the NCRI Conference in November 2020.

I actively participated in the NCRI Brain Proposal Guidance Meeting, on 27th May in Session 1: Brain metastasis, Session 2: Meningioma and Session 3: Gliomas, providing comments directly to the researchers and also providing written feedback.

I maintain links with the brain tumour charities via social media, participating in several closed Facebook groups, though my engagement varies.

The impact of my work may be best highlighted by how I have been consistently present and visible in providing the Consumer perspective whenever possible.

So far, I have not consulted my scientific mentor, though intend to when needed. I have been conscious of the impact of COVID-19 on people's working and personal lives and as such it has been a challenging time as a Consumer representative.

I have been almost the only active Consumer representative during this period, and I would be pleased to see another active Consumer, both to have a colleague and a team approach to ensure representation on all the brain tumour Subgroups and brain tumour types. There is considerable variation in primary Brain tumours, and the treatment prognosis varies considerably, adding to that is the secondary brain tumours. Whilst I have really tried, it is hard for one Consumer to cover all these areas adequately. I also look forward to some face-to-face meetings, as the remote work whilst offering some advantages has not facilitated informal discussion and working relationship development that is more possible during in-person meetings.

7. Collaborative partnership studies with industry

FUTURE-GB trial continues to work with Brainlab and Medtronic commercial partners. Pharma generally have limited interest in brain tumour trials due to the overall small number of patients, challenges delivering trials and experience of several negative trials in the past decade. These factors impact on our partnerships with Pharma. Nevertheless, Juanita Lopez (medical oncology) continues to work with Pharma and provides vital link for potential drug trials for brain tumour patients.

8. Priorities and challenges for the forthcoming year

Priority

The Brain Group strategy (2016-2021) has been delivered effectively with a raft of new trials on the portfolio for all tumour types at most stages of their treatment pathway. We have also raised awareness of the role of NCRI Brain Group with increased engagement with other professional bodies and charities. Priority for 2021 is to hold a productive strategy meeting (2/7/21), adopt the new NCRI Group structure and develop a series of time-limited working groups to develop more clinical trials. Integral to our future success will be engaging with the wide brain tumour community to make good use of key opinion leaders and experienced researchers, as well as finding those future trial leaders.

Challenge

Adapting to the new Group structure and identifying leaders for each working group. Most members of the NCRI Brain Group and Subgroups are full-time NHS clinicians with no research time in their job plans. Most of the activity takes place in individual's own time, therefore setting deadlines to complete working group activity is unlikely to be feasible.

Professor Michael Jenkinson (Brain Group Chair)

Appendix 1

Membership of the Brain Group

Name	Specialism	Location
Dr Juliet Brock	Clinical Oncologist	Brighton
Dr Sara Erridge	Clinical Oncologist	Edinburgh
Dr Juanita Lopez	Clinical Oncologist	London
Dr Jillian Maclean	Clinical Oncologist	Bristol
Professor Susan Short	Clinical Oncologist	Leeds
Dr Meera Nandhabalan	Clinical Oncologist	Oxford
Dr Cressida Lorimer*	Clinical Research Fellow	Brighton
Dr Paul Miller*	Clinical Research Fellow	Oxford
Dr Faye Robertson*	Clinical Research Fellow	Edinburgh
Dr Sarah Jefferies	Clinical Oncologist	Cambridge
Ms Zoe Faulkner	Consumer	Brighton
Dr Gary Doherty	Medical Oncologist	Cambridge
Dr Robin Grant	Neurologist	Edinburgh
Professor Oliver Hanemann	Neurologist	Plymouth
Professor Sebastian Brandner	Neuropathologist	London
Dr Thomas Booth	Radiologist	London
Dr Samantha Mills	Radiologist	Liverpool
Dr Igor Vivanco	Scientist	London
Professor Michael Jenkinson (Chair)	Surgeon	Liverpool
Mr Thomas Santarius	Surgeon	Cambridge
Mr Puneet Plaha	Surgeon	Oxford
Mr Stuart Smith	Surgeon	Nottingham

Consumer Representation

Name	Location
Ms Zoe Faulkner	Brighton

Trainee Members

Name	Specialism	Location
Dr Cressida Lorimer	Clinical Research Fellow	Brighton
Dr Paul Miller	Clinical Research Fellow	Oxford
Dr Faye Robertson	Clinical Research Fellow	Edinburgh

Membership of the Subgroups

Glioma Subgroup		
Name	Specialism	Location
Dr Paul Miller*	Clinical Research Fellow	Oxford
Dr Faye Robertson*	Clinical Research Fellow	Edinburgh
Dr Sara Erridge (Chair)	Clinical Oncologist	Edinburgh
Dr Dusan Milanovic	Clinical Oncologist	London
Dr Sarah Jefferies	Clinical Oncologist	Cambridge
Dr Matt Williams**	Clinical Oncologist	London
Dr James Powell	Clinical Oncologist	Cardiff
Dr Juanita Lopez	Medical Oncologist	London
Dr Igor Vivanco	Medical Oncologist	London
Dr Thomas Booth	Radiologist	London
Dr Gerard Thompson	Radiologist	Edinburgh
Mr Stuart Smith	Surgeon	Nottingham
Dr Ryan Mathew	Surgeon	Leeds
Dr Laura Clifton-Hadley	Trial Manager	London

Meningioma, Metastases & Other Tumours Subgroup		
Name	Specialism	Location
Dr Joanne Lewis	Clinical Oncologist	Newcastle
Dr Jillian MacLean	Clinical Oncologist	Cardiff
Dr Juliet Brock	Clinical Oncologist	Brighton
Dr Gary Doherty	Medical Oncologist	Cambridge
Professor Oliver Hanemann (Chair)	Neurologist	Plymouth
Dr Samantha Mills	Neuro-radiologist	Liverpool
Dr Kathreena Kurian	Neuropathologist	Bristol
Mr Usama Ali	Patient	Oxford
Prof Michael Jenkinson	Surgeon	Liverpool
Mr Rasheed Zakaria*	Surgeon	Liverpool
Mr Thomas Santarius	Surgeon	Cambridge

Supportive & Palliative Care Subgroup		
Name	Specialism	Location
Dr Louise Murray	Clinical Oncologist	Leeds
Dr Cressida Lorimer*	Clinical Research Fellow	Sussex
Dr Catherine McBain	Clinical Oncologist	Manchester
Dr Helen Bulbeck	Consumer	Isle of Wight
Mrs Kathy Oliver	Consumer	Surrey
Dr Anthony Byrne	Director, Marie Curie Palliative Care Research Centre	Cardiff
Dr Robin Grant (Chair)	Neurologist	Edinburgh
Mr Stephen Price	Neurosurgeon	Cambridge
Dr Ally Rooney	Neuropsychiatry	Edinburgh
Prof Jon Evans	Neuropsychologist	Glasgow

Ms Rose Marshall	Occupational Therapist	London
Dr Florian Boele	Research Neuropsychologist	Leeds

* denotes trainee member

**denotes non-core member

Appendix 2

Brain Group & 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

B – Glioma Subgroup

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
1b. Portfolio Development (Glioma Subgroup)	Increase trials for patients with glioma	All	On going	Several new trials funded and opened 2018-2021 including: FUTURE-GB BRIOCHE APPROACH
	Itraconazole Trial in glioblastoma	All Subgroup	Submitted to CRUK Early Phase and Feasibility December 2017	June 2018
	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
2. Raising Profile	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
3. Strengthen UK wide and international working	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

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) and European Association of Neuro-oncology (EANO, Professor Hanemann is on SMAB). These networks will be essential for developing UK trials and interGroup trials with EORTC. The Group also draws on expertise in metastasis trials via clinical and medical oncologists on the group.

Weaknesses

There was a significant drop in research nurse support during the COVID pandemic, which affected recruitment as well as opening of new studies. 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	<u>NIHR HTA funded April 2020 - £1.64M</u>
	Incidental meningioma management	JP/TS/MDJ/OH	2019 / 2020	<u>A large trainee project opened in 2021 to validate the IMPACT calculator. This includes international sites.</u>
	Supramarginal resection of metastasis (SUPARMAN)	RZ/MJD/PS/TS/JL	2018 / 2019	This study has been through multiple iterations due to the rapidly changing clinical landscape for brain metastases. A grant will be submitted to NIHR HTA in 2021/2022
	Imaging markers and treatment pathway in PCNSL	SM/MDJ/TS	Nov 2018	MRC Carp application not supported for this study (2019).
	PragramBIO	COH, MDJ	April 2021	Stage 1 EME application

	NOTCH	JL	unfunded	On agenda for next subgroup meeting
	Meningioma phase II study form D Milanovic	JL, MDJ	2021	In discussion with Pharma
	Coordinating participation of meningioma in CRUK Determine	GD	2021	Waiting for it to get portfolio adopted

D – Supportive & Palliative Care Subgroup

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

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 (from 2018-21)

NCRI Brain S&PC helped develop and support:

- The KEATING Trial – a randomised study of the ketogenic diet. – **completed** – (CI Mr Jenkinson). **Vitaflow funded.**
- SPRING (Seizure PRophylaxis IN Glioma) – a randomised controlled trial of prophylactic Levetiracetam vs no anti-epileptic prior to surgery – **active** - (CI: Dr Grant). **NIHR HTA funded.**

- **BT LIFE** - Brain Tumours, Lifestyle Interventions, and Fatigue Evaluation: a multi-centre phase II randomised controlled Trial – **completed** - (CI Dr Rooney). **The 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. – **active** - (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. – **active** - (PI: Mr Plaha). **NIHR EME funded.**
- NCRI brain S&PC *fed back comments on* COBra: Core Outcome in Brain Tumour Trials - Patient Reported Outcomes - **active** - (PI Professor Byrne). **TBTC Funded.**
- 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: (unsuccessful).
- 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 (Submitting to NIHR HS&DR 4th June 2021).

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.

Several Cochrane Reviews have now been published including NCRI members to set the evidence base for future submissions for research study funding:

1. Byrne A, Sivell S, Moraes FY, Bulbeck H, Torrens-Burton A, Bernstein M, Nelson A, Fielding H. Early palliative interventions for improving outcomes in people with a primary malignant brain tumour and their carers. Cochrane Database of Systematic Reviews 2019, Issue 9. Art. No.: CD013440. DOI: 10.1002/14651858.CD013440. Accessed 08 April 2021.
2. 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.
3. 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.
4. 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.

5. 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.
6. Grant R, Dowswell T, Tomlinson E, Brennan PM, Walter FM, Ben-Shlomo Y, Hunt DWilliam, Bulbeck H, Kernohan A, Robinson T, Lawrie TA. Interventions to reduce the time to diagnosis of brain tumours. Cochrane Database of Systematic Reviews 2020, Issue 9. Art. No.: CD013564. DOI: 10.1002/14651858.CD013564.pub2
7. McBain C, Lawrie TA, Rogozińska E, Kernohan A, Robinson T, Jefferies S. Treatment options for progression or recurrence of glioblastoma: a network meta-analysis. Cochrane Database of Systematic Reviews 2021, Issue 1. Art. No.: CD013579. DOI: 10.1002/14651858.CD013579.pub2.
8. McAleenan A, Kelly C, Spiga F, Kernohan A, Cheng H-Y, Dawson S, Schmidt L, Robinson T, Brandner S, Faulkner CL, Wragg C, Jefferies S, Howell A, Vale L, Higgins JP T, Kurian KM. Prognostic value of test(s) for O6-methylguanine–DNA methyltransferase (MGMT) promoter methylation for predicting overall survival in people with glioblastoma treated with temozolomide. Cochrane Database of Systematic Reviews 2021, Issue 3. Art. No.: CD013316. DOI: 10.1002/14651858.CD013316.pub2.
9. McAleenan A, Jones HE, Kernohan A, Faulkner CL, Palmer A, Dawson S, Wragg C, Jefferies S, Brandner S, Vale L, Higgins JPT, Kurian KM. Diagnostic test accuracy and cost-effectiveness of tests for codeletion of chromosomal arms 1p and 19q in people with glioma. Cochrane Database of Systematic Reviews 2019, Issue 8. Art. No.: CD013387. DOI: 10.1002/14651858.CD013387.
10. 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 (Covid casualty).
 - 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.

Appendix 3

Top 5 publications in the reporting year

There are no trial-related publications in the last 12 months. The Group has published two position statements (see below) and completed the Cochrane Review project (led by Robin Grant; <https://gnoc.cochrane.org/neuro-oncology-reviews>).

A Position Statement on the Utility of Interval Imaging in Standard of Care Brain Tumour Management: Defining the Evidence Gap and Opportunities for Future Research. Thomas C Booth^{1,2}, Gerard Thompson³, Helen Bulbeck⁴, Florian Boele^{5,6}, Craig Buckley⁷, Jorge Cardoso¹, Liane Dos Santos Canas¹, David Jenkinson⁸, Keyoumars Ashkan⁹, Jack Kreindler¹⁰, Nicky Huskens¹¹, Aysha Luis^{1,12}, Catherine McBain¹³, Samantha J Mills¹⁴, Marc Modat¹, Nick Morley¹⁵, Caroline Murphy¹⁶, Sebastian Ourselin¹, Mark Pennington¹⁷, James Powell¹⁸, David Summers¹⁹, Adam D Waldman³, Colin Watts^{20,21}, Matthew Williams²², Robin Grant³, Michael D Jenkinson^{23,24} PMID: 33634034 PMCID: PMC7900557 DOI: 10.3389/fonc.2021.620070

Second surgery for progressive glioblastoma: a multi-centre questionnaire and cohort-based review of clinical decision-making and patient outcomes in current practice. P M Brennan¹, R Borchert², C Coulter³, G R Critchley⁴, B Hall^{5,6}, D Holliman³, I Phang⁷, S J Jefferies², S Keni⁸, L Lee⁸, I Liaquat⁹, H J Marcus¹⁰, S Thomson¹¹, L Thorne¹², M Vintu⁴, A N Wiggins⁹, M D Jenkinson^{5,6}, S Erridge⁹ PMID: **33791952** DOI: 10.1007/s11060-021-03748-0

Appendix 4

Recruitment to the NIHR portfolio

Summary of patient recruitment by Interventional/Non-interventional and number of studies opened/closed

Year	All participants		Cancer patients only*		Number of studies	
	Non-interventional	Interventional	Non-interventional	Interventional	Opened	Closed
2016/17	280	149	280	149	10	8
2017/18	214	273	199	273	11	7
2018/19	342	335	342	335	11	4
2019/20	480	341	480	341	11	8
2020/21	618	179	618	179	12	5

*This data is based on a proxy from CPMS (the NIHR database used to collect patient recruitment data) and includes diagnostics, screening and prevention patients.

Appendix 5

Annual report feedback 2019-20

06 November 2020

Dear Michael

Re: NCRI Brain Group Annual Report 2019-20

Thank you for submitting an annual report for the Brain Group for 2019/20, especially given the challenges with the ongoing COVID-19 pandemic which will have impacted on both the Group and the report itself.

All the Group's annual reports were reviewed at a two-day meeting on the 12th and 13th October 2020 by a panel consisting of some former NCRI Group Chairs, NCRI CPath Chair, former NCRI CTRad and the current NCRI Strategic Advisory Group (SAG) Chair, NCRI Head of Research Groups and representatives from the NIHR Cancer Coordinator Centre, NHS Cancer Alliances, epidemiology, CTU/basic science, allied health profession, NCRI Consumer Forum and the Canadian Cancer Clinical Trials Network.

We are writing to you now with a summary of the feedback which is based on the information provided in the report. It was noted that there is likely to be more activity taking place within the Group than is documented.

Please share the contents of this letter with your members for discussion at the next Group meeting.

Generic feedback for all the Groups

Strategic objectives and the impact of COVID 19

- Due to the research funding challenges and restrictions on NHS resources resulting from COVID 19, the Panel recommended the Groups evaluate their strategic objectives and focus on the most important priorities or questions that need to be answered as it would not be feasible for the Groups to be doing everything they planned or continue to "plug in the gaps." Additionally, the Panel suggested looking for more cost-efficient methods of working where they can.
- The Panel felt that the strategic objectives for most Groups were too broad especially in the current climate. The Groups were asked to provide specific, measurable aims for their strategic objective and attach timelines/metrics to them.

Multidisciplinary approach to research and membership

- The Panel noted the importance of collaborative and multidisciplinary working, especially in the current climate, and would encourage all Groups to continue to reach out to other relevant NCRI Groups and consider the NCRI strategic priorities where appropriate.

National Cancer Research Institute, 2 Redman Place, London, E20 1JQ

T: +44 (0)20 3469 8798 **W:** www.ncri.org.uk

NCRI is a Charitable incorporated Organisation registered in England and Wales (charity number 1160609)

Linking with the wider research community

- The Groups were asked to link with the wider research community and engage with relevant networks, in particular, with researchers who are developing or are running large national platform studies when there is one available in the disease site e.g. PrecisionPanc (Upper GI Group) and TRACERx (Lung Group). The NCRI recognised that there is a role for them to play in promoting collaboration and will be working with the partners to encourage greater interaction between the Groups and the networks in future.

Funding opportunities

- Given the potential decrease in funding opportunities, the Groups are encouraged to explore alternative funding sources and collaborations e.g. with industry, government funders, NHS Cancer Alliances etc.

Consumers involvement

- The Panel encouraged Groups to integrate public and patient involvement (PPI) in all aspects of the Group's activities e.g. study design, proposal development, prioritisation of strategic areas etc.
- The Panel wanted to ensure that the consumer activity was captured throughout the report and not just in the consumer section, especially where the consumer reports are missing.

Specific feedback for the Brain Group

Areas of strength:

- The Panel enjoyed reading about how the Group were utilising previous study outputs and learnings to feed into new study designs.
- The Panel was impressed that trials included QoL and a focus on neurosurgery. Several of the trials are high impact and the Panel commented on the strength of the Group to develop trials that recruit well.
- The Panel encouraged the Group to continue to reach out to the wider community more and strengthen links to benefit collaboration and future studies the Group develops.
- The Panel commended the brain metastasis workshops that have been held over the past couple of years, noting the strength of collaboration with other NCRI Groups to deliver these.
- The Panel noted that the Group has a Subgroup specifically for supportive and palliative care activity. It was evident from the report that this Subgroup is consulted with.

Areas which the Group need to consider:

- The Panel advised the Group to leverage support from NCRI in selling themselves when writing reports in the future. The Panel felt that the report undersold the Groups achievements, although recognised the influence of COVID 19 on this.
- The Panel recommended that the Group identifies areas within their activity that may benefit from AHP or nursing members and recruit these to the Group to support future study development.
- The Panel felt that the Group should be more involved with big data, imaging and molecular precision medicine and this should be more detailed in their strategy. The Panel would also like to see the Group leverage collaboration and support more from CTRad to help meet their aims.

National Cancer Research Institute, 2 Redman Place, London, E20 1JQ

T: +44 (0)20 3469 8798 **W:** www.ncri.org.uk

NCRI is a Charitable incorporated Organisation registered in England and Wales (charity number 1160609)

- The Panel encouraged the Group to work with the NCRI to ensure that they can be influential with trials/initiatives that do not originate from the Group. There was a lack of evidence in the report that the Group are linking with other initiatives such as Brain Matrix, which will soon be starting, running from Birmingham CTU.
- The Group was encouraged to link with the NIHR Research Delivery Manager for help with site selection for trials if needed.

Congratulations to you and your members for all your hard work and achievements in 2019/20.

If you have any comments on this year's process, please send them to Nanita Dalal (Nanita.Dalal@ncri.org.uk) for collation.

Best wishes,



Professor Meriel Jenney
Annual Reports Review Committee Chair, NCRI
Consultant Paediatric Oncologist,
University Hospital of Wales



Dr Gillian Rosenberg
Head of Research Groups,
NCRI

National Cancer Research Institute, 2 Redman Place, London, E20 1JQ

T: +44 (0)20 3469 8798 **W:** www.ncri.org.uk

NCRI is a Charitable incorporated Organisation registered in England and Wales (charity number 1160609)

Appendix 6

Quinquennial review feedback - 2021

Areas of strength:

- The panel congratulated the productivity of the Group and noted their vibrant portfolio with interesting designs covering a broad range of topics.
- The panel praised the diversity of the Group, noting a good gender balance and a wide geographical representation.
- The panel noted that this is a well assembled, multi-disciplinary Group of well-respected experts.
- Efforts to link up with other Research Groups were applauded.
- The panel commended excellent patient recruitment to clinical trials and high-quality trial applications to Cancer Research UK.
- The panel highlighted valuable work on clinical outcomes assessments and patient reported outcomes.
- The panel acknowledged that although little has been published as yet, the current studies that are being performed will likely result in high quality publications.

Areas for consideration:

- The panel agreed that meningioma and metastases are both important and under-researched tumour types and questioned the rationale for them to be joined in the same subgroup.
- Recent investment in basic science was noted and the Group was encouraged to ensure translation of findings to allow studies to be more hypothesis driven.
- The panel commented that whilst study outputs from the Group are good, they lack originality and could take the opportunity to make transformative changes in clinical trials.
- The panel was keen to see the Group increasing the involvement of junior investigators.
- Brain cancer has been highlighted by Cancer Research UK as an area of unmet need. The Group was encouraged to think tactically about how best to access some of the allocated funding.
- The Group should consider how the trial portfolio can meet the needs of as diverse a range of patients as possible.
- The panel noted the lack of industry funded studies on the portfolio and, whilst acknowledging the challenges, encouraged development of a strategy for industry engagement.
- The Group members were encouraged to continue to build upon their international connections as international collaboration will strengthen the work of the Group, especially for rare cancers.

Issues for the NCRI to consider:

- The NCRI will support the Group in their upcoming strategy development to consider the issues raised at the QQR.
- The NCRI will support the involvement of more trainees with the Group.
- The NCRI will support the Group to develop practice changing trials



National Cancer Research Institute
2 Redman Place,
London, E20 1JQ

T: +44 (0)20 3469 8460
F: +44 (0)20 3014 7658

info@ncri.org.uk