Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 1

Development of a precision immunovirotherapy expressing a bispecific immune cell engager for treatment of glioblastoma

RJ Bayliss[1], C Stewart[1], EA Bates[1], AL Parker[1]

[1]School of Medicine, Cancer and Genetics Building, University Hospital Wales, Heath Park, Cardiff University, Cardiff CF14 4XN

Glioblastoma multiforme (GBM) is the most common and aggressive brain tumour in adults. Its high heterogeneity and ability to rapidly invade healthy cells only 5% of patients will survive more than 5 years with the average life expectancy being 12-18 months after diagnosis. Existing treatment includes surgery, radiotherapy, and chemotherapy however, complete removal of the tumour is difficult due the complexity of the disease.In this study we use an Ad5 based viral vector ablated of native tropism ($Ad5_{NULL}$) and re-targeted to αvβ3/5 integrins, known to be overexpressed in GBM, through incorporation of and RGD4C motif into the fibre region ($Ad5_{NULL}$-RGD). We utilise this virotherapy to express a bispecific immune cell engager (CD3xEGFR) targeting T cells via CD3 and Epidermal growth factor receptor (EGFR), over-expressed on tumour cells to induce a T-cell response at tumour sites and regress tumour growth.

The efficacy of the newly developed virus was evaluated in vitro in Glioma stem cells (GSC). Expression of the bispecific construct was assessed via western blotting in various GSC, and co-culture assays were used to determine T-cell activation in the presence of the bispecific molecule in conjunction with cell viability assays to determine immune cell mediated cancer cell killing.

GSC transduced with $Ad5_{NULL}$-RGD.αCD3xEGFRscfv and co-cultured with CD3+ T-cells show a significant increase in T-cell activation across the three lines tested. Cell viability assays showed more than 50% decrease in Glioma stem cells survival following virus transduction in the presence of T-cells

Our results indicate $Ad5_{NULL}$-RGD delivering an αCD3XEGFR bispecific molecule leads to T-cell activation and immune mediated Glioma killing in vitro. This novel approach has the potential to become a much-needed alternative treatment option for patients with treatment resistant Glioblastoma.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 2

WISTERIAN - WIndow STudy of ExpeRimental Interventional Approaches in Neuro-oncology

Matthew Williams[1], Angela Casbard[2], Elena Brogden[2], Nelofer Syed[1], Gerben Borst[4], Iain McNeish[1], Lillie Pakzad-Shahabi[1], Sophie Camp[3], David Gardner, Claire Cherrington, Kevin O'Neill[3], Eslam Maher[1]

1: Imperial College London; 2: Cardiff University; 3: Imperial College Healthcare NHS Trust; 4: The Christie NHS Foundation Trust

Aims

WISTERIAN is a randomised phase 1 window study, currently in development, assessing the biological effect of radiotherapy and arginine deprivation in newly diagnosed glioblastoma.

Methods

Standard therapy for glioblastoma (GBM) comprises maximally safe surgical resection followed by chemoradiotherapy and further chemotherapy. However, even with this, median survival is 15 months.
Development of new treatments has been very slow, in part because animal models of GBM are so poor; because of that, there is increasing interest in window studies to measure the biological impact of new treatment in human GBM tissue samples.
ADI-PEG20 (pegylated arginine deiminase) depletes serum arginine and has a well established safety profile. The POBIG study has shown that a single-fraction of pre-operative radiotherapy is safe for newly diagnosed glioblastoma patients.
ADI-PEG20 and radiotherapy has been shown to be safe in the post-operative setting in a phase 1 trial in patients with newly diagnosed glioblastoma. Pre-clinical work has demonstrated that delivery of a single-fraction of radiotherapy and ADI-PEG20 led to a complete response, and significant changes in T-cell activation.
The WISTERIAN trial is currently in development and is a multi-centre, CTIMP for adult newly diagnosed patients with glioblastoma. It has two parts:

1. A safety run of 8 patients that will evaluate the biological effect of ADI-PEG20 as a single agent and check the safety of preoperative ADIPEG-20. Participants will be given two doses of ADI-PEG20, followed by neurosurgical resection and standard of care (SOC).

2. A phase 1 window RCT to explore the impact of combining arginine deprivation and radiotherapy on CD8+ T-cell infiltrate. 30 patients will be randomised to either:
- radiotherapy, followed by neurosurgical resection and SOC.
- radiotherapy and 2 doses of ADI-PEG20, followed by neurosurgical resection and SOC.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 3

UK radiotherapy practice in volume delineation – data from the APPROACH trial (ISRCTN:1339049) radiotherapy quality assurance (RTQA) programme benchmark outlining case

Dr. Jenny Golten 1, Prof Emiliano Spezi 1, Ms. Anna Bruce 2, Mr. Daniel Egleston 2, Ms. Elizabeth Miles 3, Dr. James Powell 1, Dr. Louise Murray 4

1. Velindre University NHS Trust, Cardiff University; 2. National Radiotherapy Trials QA (RTTQA) Group, The Clatterbridge Cancer Centre NHS Foundation Trust, Liverpool; 3. National Radiotherapy Trials QA (RTTQA) Group, Mount Vernon Cancer Centre; 4. Leeds Cancer Centre, Leeds Teaching Hospitals NHS Trust; University of Leeds

Aims

Interobserver variation in the contouring of radiotherapy target volumes is recognised as an important factor affecting the robustness of results of clinical trials involving radiotherapy treatment.

A comprehensive RTQA programme for the APPROACH trial (Analysis of Proton vs Photon Radiotherapy in Oligodendroglioma and Assessments of Cognitive Health) includes a pre-accrual benchmark outlining case to assess the quality of contouring of tumour target volumes and organs-at-risk (OARs).

Methods

Between Dec 2022 and Nov 2024 prior to centre activation a benchmark outlining case was sent to all centres. The results of these were retrospectively assessed against gold standards (GS) using conformity indices (CIs) on an overall volume and slice by slice basis. These measures include Jaccard conformity index (JCI) which is widely used in literature for multiple tumour sites.

Results

Structures showed high variability in overall conformity with JCI ranging between 0.18-0.91 (1 representing perfect conformity).

There was good (>0.7) intra centre conformity for the target volumes (GTV-FLAIR 0.87, CTV 0.91), eyes (JCI 0.82-0.84), brainstem (0.79) and left lens (0.70).

Structures with JCI < 0.7 include Pituitary fossa (0.67) right lens (0.66), right hippocampus (0.62) left hippocampus (0.59), right and left optic nerves (0.58 and 0.57 respectively), right and left hypothalamus (both 0.51) right and left cochlea (0.47 and 0.44 respectively), Optic chiasm (0.37) and left and right lacrimal glands (0.25 and 0.18 respectively).

Conclusion

Within the APPROACH trial benchmark outlining case the contoured volumes showed a range of conformity compared to gold standard. GTV-FLAIR and CTV showed good conformity overall, however the contouring of OARs showed poorer concordance.

Reasons for poor conformity identified from examination of the contours include over and under contouring especially at the superior and inferior of the structures. Misidentification of anatomical structures, and different local contouring practice.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 4

Stereotactic radiosurgery (SRS) for brain metastases: re-audit of a single cancer centre experience of toxicities and outcomes.

Ali Hussnain[1], Nicholas Gomez[1], Sara Walters[1], Jason Griffiths[1], Jillian MacLean[1], Najmus Sahar Iqbal[1] and James Powell[1]

1. Velindre Cancer Centre, Cardiff

Aim

To measure overall survival (OS) following SRS and assess tolerance and toxicities experienced by patients in Velindre Cancer Centre

Methods

Data was collected on all patients undergoing SRS at VCC between September 2020 and December 2024. Toxicity data was collected prospectively and patient demographics, performance status (PS), outcome and primary disease data were collected retrospectively.

Results

245 SRS treatments were given to 197 patients. 190 (77.5%) were first treatments and 43 (17.5%) were second treatments.

165 (67.3%) of the treatments were directed at a single metastasis, 46 (18.7%) at 2 metastases, 26 (10.6%) at 3 metastases, 7 (3%) at 4 metastases and only one treatment was aimed at 5 metastases, during the same course.

The most commonly treated tumour site was lung with 111 treatments (45.3%), followed by breast with 44 (17.9%) and then melanoma with 39 (15.9%) treatments.

Median overall survival (OS) of this cohort was 13.54 months compared to 11.2 months for the previous cohort, audited between 2015 to 2020. Median OS for patients with a single metastasis treated was 14.32 months, 2 metastases was 12.9 months, 3 metastasis was 5.5 months.

Most of the toxicities experienced were mainly grade 1, with a small proportion experiencing grade 2. The most commonly experienced toxicities were fatigue and headache. No grade 4 toxicities were reported.

Conclusion

SRS continues to be well tolerated providing improved intracranial disease control, although this declines for patients with increasing number of metastases treated, as expected. The improved OS for this cohort could be attributed to evolving systemic treatment options, increasing surveillance for intracranial disease and better patient selection.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster
5

Polymer-Templated Microcylinders for Sustained Co-Delivery of Acriflavine and Doxorubicin in Glioblastoma Therapy

Sophie.K. Hill [1], Benjamin Newland [1, ,2]

[1] School of Pharmacy and Pharmaceutical Sciences, Cardiff University, King Edward VII Avenue, Cardiff, CF10 3NB, United Kingdom
[2] Leibniz Institute of Polymer Research Dresden, Max Bergmann Center of Biomaterials Dresden, Hohe Str. 6, 01069 Dresden, Germany

Biomaterials with well-defined elongated morphologies, such as microcylinders, are attractive candidates for local drug delivery due to their high surface-area-to-volume ratio and capacity for sustained therapeutic release. In this study, polymer-templated microcylinders were fabricated using 3-sulfopropyl acrylate and poly(ethylene glycol) diacrylate (PEGDA), forming uniform cylindrical structures via UV-photopolymerisation. The incorporation of sulfonate groups enabled electrostatic affinity binding of cationic drugs with distinct mechanisms of action—acriflavine and doxorubicin. Acriflavine has recently gained significant interest as a HIF-1α inhibitor, showing promising results for in vivo glioma models, while doxorubicin remains a widely used and effective anticancer agent. Localised administration of drug cargo can overcome the limitations of systemic therapies by achieving high drug concentrations in the critical days following surgery. This delivery system is designed for direct injection into the post-resection glioblastoma cavity, offering a minimally invasive alternative to the commonly used gliadel wafers, which can cause side effects such as seizures, headaches, and cerebral edema due to their large size and mechanical stiffness.

Following synthesis and material characterisation, the microcylinders achieved drug loadings of approximately 13 wt% for acriflavine and 20 wt% for doxorubicin, exhibiting 70% release over 7 days, demonstrating the ability to deliver therapeutics over an extended time frame. This delivery platform has the potential to provide continuous exposure of glioma cells to both agents while minimizing systemic toxicity. In vitro testing on U87 and patient-derived L0 glioma cell lines confirmed the effective cytotoxicity of the released drugs and demonstrated their sustained activity, whilst biocompatibility assays with human astrocytes confirmed a favourable safety profile.

By combining acriflavine and doxorubicin, the system aims to target multiple pathways and tackle key mechanisms underlying glioma resistance and heterogeneity. Further studies will investigate the synergistic potential of this combination, optimizing dosing and release profiles to enhance efficacy. This work seeks to establish a flexible, minimally invasive platform capable of delivering multiple drugs locally, laying the groundwork for a personalized, post-resection glioblastoma therapy with the potential to improve patient outcomes.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 6

Impact of Covid-19 on decision making in patients with Glioblastoma, what have we learnt?

Harriet Hebbes[1,2], Sara Walter[3], James Powell[2,3], Jillian Maclean[3], and Najmus Sahar Iqbal[3]

[1]Torbay and South Devon NHS Foundation Trust, Torquay; [2]School of Medicine, Cardiff University; [3]Velindre University NHS Trust, Cardiff.

Background:
Glioblastoma multiforme (GBM) is the most common primary brain tumour in adults, associated with poor prognosis despite multimodal therapy. This retrospective study evaluates the impact of and the COVID-19 pandemic in patients with GBM.

Methods:
A retrospective review of 231 patients diagnosed with GBM at Velindre Cancer Centre between 2018 and June 2023 was conducted. Data were collected on demographics, performance status (PS), treatment modalities, molecular markers, and survival. Survival analyses were performed using Kaplan–Meier curves, with statistical significance assessed by log-rank test.

Results:
The median overall survival was 8.8 months. One and five year survival was 40% and 2.3% respective. Factors associated with improved survival were total surgical resection, and long course chemoradiotherapy. Performance status was a significant predictor of survival; patients with PS 3–4 were less likely to receive aggressive therapy and had poorer outcomes. The COVID-19 pandemic led to reduced biopsy rates: prior to the pandemic, 57% patients with WHO PS 3-4 underwent biopsy, compared to 36% during and 5% after the pandemic period. In patients who underwent biopsy, MGMT promoter methylation status was associated with improved survival: those with methylated MGMT had a median survival of 16 months, vs. 12 months in the unmethylated cohort.

Conclusion:
Performance status influences treatment decisions and survival outcomes in GBM. Aggressive multimodal treatment confers survival benefit but is predominantly offered to patients with good functional status. Despite a reduction in surgical interventions during the COVID-19 pandemic, survival outcomes were maintained, highlighting the potential for greater flexibility in diagnostic and treatment approaches in GBM management. Whilst histological diagnosis is important and allows patients to enter clinical trials, it is evident that biopsy alone does not improve survival, therefore it should only be offered to patients with good performance status who may be fit enough to undergo oncological treatments.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster 7

Can perfusion be a predictive biomarker for treatment response in patients undergoing stereotactic radiosurgery?

Najmus S Iqbal[1,2], Richard Wise[3], Maeve Williams[4], John N Staffurth[1,5], James R Powell[1,5]

[1]Velindre University Hospital NHS Trust, Clinical Oncology, Cardiff; [2]Cardiff University Brain Research Imaging Centre, Department of Psychology, Cardiff; [3]G. D'Annunzio University, Institute for Advanced Biomedical Technologies & Department of Neuroscience, Imaging and Clinical Sciences, Chieti, Italy; [4]Velindre University Hospital NHS Trust, Medical Physics, Cardiff; [5]Cardiff University, School of Medicine

Aim:
The aim of this study was to examine if tumour perfusion can predict response to treatment in patients with brain metastases.

Methods:
Patients receiving stereotactic radiosurgery (SRS) underwent arterial spin labelling (ASL) MRI scans at baseline, 1- and 3-months after SRS treatment, utilising the 3T Siemens MRI scanner at the Cardiff University Brain Research Imaging Centre (CUBRIC). Cerebral blood flow (CBF) was measured. Mann-Whitney U Test was performed to test the statistical significance. 20 patients had MRI imaging at baseline, 15 at 1 month and 8 at 3 months including T1-and T2-weighted images. MRI data of 26 metastases in 20 patients who had MRI scans at CUBRIC were analysed. Response assessment in Neuro-Oncology in brain metastases (RANO-BM) was used to assess progression (2).

Results:
Of the 26 metastases, 6 metastases has progressed at 3 months. Three of these were surgically resected and histology was consistent with malignancy. The remaining 3 metastases were in patients died at 3-, 4-, and 5-months following SRS, all of which were neurological deaths. Median CBF was 26.35, 31.18, 34.93 ml/100g/min at baseline, 1- and 3-months respectively. Baseline CBF in the metastases was significantly lower in patients who demonstrated evidence of stable disease or partial response at their first standard post treatment MRI at 3 months compared to patients who had progressive disease, (20 vs 104 ml/100g/min, p-value=0.03).

Conclusion:
Perfusion of brain metastases can be performed routinely using standard MRI scanners using the ASL technique. It is increasingly being performed after SRS treatment to assess response, however, at baseline it may be a predictive biomarker. Increased CBF may signify presence of hypoxia (3). Hypoxia is an important factor in radioresistant disease (4). For patients where surgery and SRS may have equivalent outcomes, e.g. accessible location, anaesthetic fitness and good prognosis, CBF may guide treatment decision-making.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 8

Evaluating the effects of rurality and patient opinion on virtual consultations in neuro-oncology in West Wales: using creativity and innovation to challenge and change practice.

Janet Bower[1], Ms Linsey Jones[1], Dr Prashanth Bhat[2], Dr Jennifer Kahan[2]

1. Hywel Dda University Health Board; 2. South West Wales Cancer Centre, Singleton Hospital.

Aims:

Within Hywel Dda Health Board (HDD) 38 patients a year (average) are diagnosed with CNS tumours. Patients experience changes in physical and cognitive health and require long-term follow-up.
Rurality and geography can hamper the provision and accessibility of health care for patients, 65% (248,000 people) live rurally in West Wales.
Our aim was to assess patients experience of rurality and evaluate acceptability of virtual consultations to adapt to the patient's needs, while developing the unique role of the cancer specialist nurse supporting rural patients.

Methods:

A patient survey assessed rurality and perception of virtual consultations. The initial survey of 20 questions was sent to patients reviewed in the previous 12 months. We planned an adaptive approach to follow up, dependant on outcomes.

Results:

The survey was returned by 7 patients, aged 18-64. All patients took more than 30 minutes to travel to the hospital, and the majority (57%) took 1-2 hours, 87% depended on others to travel.
87% had previously had a telemed consultation, 71% had a video consultation and all found the virtual appointments easy or very easy for convenience and understanding.
87% reported they would want virtual appointments, 14% said they did not want virtual appointments.
More than half had a previous home visit, and all said it was easy or very easy for convenience and understanding.
In response to these outcomes the clinic adapted a hybrid style, offering in-person or virtual consultations.

Conclusions:

This project demonstrates patients welcome non-traditional consultation delivery, which can deliver equitable healthcare in rural settings. Streamlined virtual working can also increase efficiency of the team.
This audit is due to be repeated. Ongoing evaluation of patient opinion in such a service will allow us to continue to tailor a service appropriate to the healthcare needs of the patients.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 9

Uncovering the gene regulatory networks controlled by the transcription factor ZEB1 in Glioblastoma

Suresh Kaushik[1], Aimee Jones[1], Niharika Singh[1], Dorit Siebzehnrubl[1] and Florian Siebzehnrubl[1]

[1]European Cancer Stem Cell Research Institute, School of Biosciences, Cardiff University

Glioblastoma (GBM) is the most aggressive cancer of the brain with a median survival rate of fifteen months. Treatment options include tumour resection followed by adjuvant radiotherapy and chemotherapy. The E-box binding transcription factor ZEB1 is a multi-faceted gene that plays a key role in both astrogliogenesis and GBM. Previously, our lab has demonstrated that ZEB1 has a regulatory role in GBM tumour invasion, chemoresistance and re-initiation of tumorigenic potential in residual cells post resection surgery. While ZEB1 is a promising candidate for targeting of GBM, transcription factors are notoriously hard to target due to their pleiotropic nature. Hence, it is opportune to target downstream candidate genes that function as effectors of ZEB1 controlled regulatory gene networks in GBM.

We aim to identify both the protein-protein and protein-DNA interactomes of ZEB1 in GBM. To this end, we have generated novel genetically engineered human GBM cells to monitor ZEB1 promoter activation and gene expression and identify its DNA binding targets and protein-protein interactome, by generating a multi-functional ZEB1 allele using state of the art genome editing. We will uncover the interactome of ZEB1 using a combination of chromatin immunoprecipitation followed by Next Generation Sequencing (ChIP-Seq) and affinity purification followed by mass spectrometry (AP-MS). Additionally, we will also identify ZEB1 binding motifs in different GBM stem cell compartments.

We envisage our study will uncover ZEB1 binding preferences in the genome of human GBM cells and help identify several candidate druggable targets for GBM. The results of this project will help to lay the foundations for the development of next generation drugs to treat GBM.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 10

A qualitative evaluation of a Clinical Nurse Specialist and Allied Health Professional joint clinic for neuro-oncology

Cathryn Lewis, Rhian Burke, Charlotte John, Magdalena Kwiatkowska, Sarah Cordeaux, Rebecca Davies, Rebekah Trapnell, Carmen Reed, Helen Tate, Dr J Powell, Dr J Maclean, Dr S Iqbal

Velindre Cancer Centre, Cardiff

Background:

Neuro-Oncology patients often face complex and evolving needs that are best addressed through a coordinated, cohesive multidisciplinary approach. At Velindre Cancer Centre, the Clinical Nurse Specialist (CNS) and Allied Health Professional (AHP) joint clinic was established in December 2019, to provide holistic, integrated care and address gaps such as unmet needs, duplicated efforts, and fragmented pathways.

The clinic has gained strong support from the wider teams, and Velindre executive board. It has also received recognition from the Tessa Jowell Foundation and earned multiple awards, including Macmillan accreditation, Advancing Health (AHP) recognition, and local Employee Excellence Awards, highlighting its innovation and service improvement for patients.

The clinic is attended by the patient, and their family members, alongside the CNS, Physiotherapist, Occupational Therapist and Speech and Language Therapist, which provides the opportunity to identify and manage specialist holistic needs at several points throughout the patient journey.

Methods:

This qualitative evaluation draws on data collected through clinic activity, including patient-reported outcome measures (PROMs) assessing quality of life before and after clinic attendance, clinical assessments, interventions, referrals, and the provision of supportive information and advice. Patient and family feedback was also gathered to evaluate the perceived impact of the clinic.

Central to this evaluation is a detailed patient case study, used to illustrate the practical application of the clinic model. The case study highlights the CNS and AHP collaborative roles in assessment, planning, and delivery of care, along with reflections from the patient and their family.

Results:

The data will build on the resounding success of collaborative working between CNS and AHPs within the Neuro-Oncology MDT clinic. Pre- and post-clinic analysis demonstrates the positive impact of this integrated and proactive model, enabling timely access to specialist support across the treatment pathway.

The case study brings to life how holistic needs were identified and addressed in a coordinated manner, showing how patient-centred care can be effectively delivered in a virtual format.

Patient and family feedback reinforces the value of the clinic in improving overall experience and support.

Conclusion:

The CNS and AHP joint clinic model have proven to be a valuable, award-winning innovation in Neuro-Oncology care. The use of a case study helps to demonstrate the clinics model's and positive impact. Continued development of the clinic will further enhance the delivery of high-quality, personalised care for patients and families navigating the Neuro-Oncology Pathway.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 11

Microstructural imaging of Glioblastoma tumours using ultra-strong gradient diffusion MRI

Michael Law, Jennifer Golten, Elise Gwyther, Najmus Sahar Iqbal, George Eralil, Harpreet Hyare, Hannah Khirwadkar, Kathy Seddon, Florien Siebzehnrubl, James Powell, Derek Jones, Marco Palombo.

Aims

Glioblastoma (GBM) is the most common and aggressive CNS tumour in adults. Treatment involves maximum resection followed by radiotherapy and Temozolomide chemotherapy. Recurrence almost always occurs, and median survival is 12-18 months. Repeat biopsies of brain tumours are challenging, and there is a need for sensitive non-invasive tools to monitor disease progression and treatment efficacy. Standard MRI lacks the resolution to detect microstructural changes characteristic of early stage GBM recurrence. However, diffusion MRI (dMRI) can detect these changes and could be used to define biomarkers of treatment response and progression. We present rich dMRI datasets from four participants and aim to collect 40 datasets at three timepoints using a state-of-the-art ultra-strong gradient dMRI scanner.

Method

dMRI datasets of suspected glioblastoma patients were acquired with a 3T Siemens Connectome scanner equipped with an ultra-strong gradient system (300mT/m) using a pulsed-gradient spin-echo echo-planar imaging (PGSE-EPI) sequence with voxel resolution 2mm^3 isotropic and full brain coverage; SENSE=2; six b-values (maximum b-value=8000s/mm^2) in three orthogonal directions; TE=[40-125]ms and TR=[3000-5000]ms. For each b-value and TE/TR combination, three diffusion encoding schemes were employed: Δ=[18–90]ms, δ=7ms; Δ=[25–90]ms, δ=12ms; and Δ=[31–90]ms, δ=20ms. Total acquisition time=1h:10m.

Results

We show unique dMRI measurements with ultra-high diffusion weighting and multiple TE/TR, enabling unprecedented characterisation of the GBM microenvironment. Excellent data quality (SNR>35) has enabled the estimation of whole-brain parametric maps of T1 relaxation time, compartmental (intracellular, extracellular, intra-neurite) T2 relaxation times and diffusion properties (cellular density, size).

Conclusion

The ultra-strong gradient scanner and novel dMRI acquisition shows promise for monitoring the GBM microenvironment. We aim to predict treatment response with follow-up scans.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster 12

Repurposing acriflavine for local delivery to glioblastoma via a soft implantable microcarrier drug delivery system

Pakiza Mammadsalahova, Sophie Hill, Ben Newland

School of Pharmacy and Pharmaceutical Sciences, Cardiff University, King Edward VII Avenue, Cardiff, CF10 3NB

Acriflavine, a hypoxia-inducible factor (HIF) inhibitor, has shown promising pre-clinical efficacy in the models of glioblastoma (GBM). However, to take full advantage of small-molecule therapies using acriflavine, a highly effective local drug delivery system is needed to bypass many of the challenges associated with the treatment of GBM, such as the blood-brain barrier (BBB) and dose-limiting systemic side effects.

Herein, this work shows the synthesis of a novel drug delivery platform comprised of negatively charged cryogel microcarriers to load positively charged acriflavine via electrostatic interactions. This study aims to evaluate whether heparin-methacrylate (HEP-MA) cryogel microcarriers can be synthesized to effectively deliver acriflavine slowly with a view for future use in the resection cavity to help prevent tumour recurrence.

HEP-MA cryogel microcarriers were synthesised using a microfluidic droplet system and polymerised under subzero temperature. The mechanical properties of HEP-MA cryogel were analysed by uniaxial compression. The microcarriers were then loaded with acriflavine by simple mixing of the drug and delivery system, and the HEP-MA cryogel s drug loading ability and drug release characteristics were analysed.

Soft and compressible cryogel microcarriers were successfully produced with near monodispersity. They exhibited high acriflavine loading efficiency (>50% drug removed from solution to the carrier), effectively loading 124 µg to 0.1mg of cryogel. The drug was released from the cryogels under physiological conditions that mimic the brain parenchyma, demonstrating a sustained release profile over 24 days with no initial burst release.

These early findings suggest that HEP-MA cryogel microcarriers could be an effective way to deliver drugs locally whilst minimising systemic side effects.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster
13

Validation of ASAH1 as a novel target for glioblastoma

Dr Saul Michue-Seijas, Loren Waters, Gabrielle Evans, Dr Heulyn Jones, Dr Helen Waller-Evans, Dr Florian Siebzehnrubl, Prof Emyr Lloyd-Evans and Prof Simon Ward.

Medicines Discovery Institute, Cardiff University

Glioblastoma is the most common form of malignant brain cancer, with a poor prognosis for survival of less than 15 months from diagnosis. Currently, patients undergo tumour resection followed by combination radiotherapy and chemotherapy. Regardless of this multimodal approach, the aggressive and heterogeneous nature of the tumour limits success and tumour recurrence is frequent. Emerging evidence of a small population of cells named glioblastoma stem-like cells (GSCs), possess a regenerating capacity that contributes to the aggressiveness and recurrence of the tumour. Despite the significant advances in our understanding of tumour pathology, a safe, effective, brain permeable drug treatment for glioblastoma remains elusive, highlighting an unmet clinical need. As our understanding of tumour biology and mechanisms driving cancer progression and resistance advances, new potential targets are identified.

Studies have shown significantly higher expression of ASAH1 in glioblastoma cells, particularly in GSC populations, which correlates with poor patient survival. Ceramide, a potent tumour suppressor lipid, is metabolised by ASAH1 to sphingosine, which is further metabolised to sphingosine 1-phosphate (S1P), which was found at elevated levels in glioblastoma cells. Carmofur is a potent ASAH1 inhibitor but is majorly limited by its selectivity and toxicity. This prodrug metabolises intracellularly to fluorouracil (5-FU), a clinical chemotherapy known to induce cell apoptosis via DNA alkylation. However, lack of selectivity means healthy cells are also targeted leading to adverse effects ranging from nausea to severe neurotoxicity. Furthermore, overexpression of ASAH1 has been reported to reduce the sensitivity of glioblastoma cells to radiotherapy. Consequently, selective ASAH1 inhibition offers a promising opportunity for safer and more effective treatments for glioblastoma patients. Our aim is to use an in-house synthesised small molecule ASAH1 inhibitor that has demonstrated sub-μM IC50 potency in vitro across different glioblastoma cell lines, showing the highest ASAH1 inhibition in the patient-derived GSCs (IC50 = 266 nM). The in vivo ADME profile in a rat model showed low metabolic clearance (22 ml/mg/kg) and evidence of blood-brain barrier penetration. This promising compound will be further evaluated in cell viability and apoptosis assays to assess growth and survival ability following treatment and investigate the combination therapy potential with temozolomide, the standard-of-care chemotherapy for glioblastoma.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference
19th September 2025 Sophia Gardens Cricket Ground

Poster 14

Evaluation of HyperArc for intracranial stereotactic radiosurgery at Velindre Cancer Service

Jonathan Mohajer[1], Matthew Williams[1], James Fergusson[1], Jon Gilchrist[1], Rhydian Maggs[1], Michael Chu[1], Tony Millin[1]

1. *Medical Physics, Velindre Cancer Centre, Velindre Rd, Cardiff CF14 2TL*

Aims

Work has been undertaken at Velindre Cancer Service to support the clinical introduction of Varian's 'HyperArc', a linear accelerator radiotherapy technique for the simultaneous treatment of multiple intracranial targets using non-coplanar, mono-isocentric volumetric modulated arcs. The existing radiosurgery approach at our centre consists of dynamic conformal arcs (DCA), with one treatment isocentre per target volume treated. The introduction of HyperArc aims to reduce patient treatment duration and improve treatment plan generation efficiency while delivering equivalent or better treatment plan quality and delivery accuracy compared to DCA.

Methods

Selection of the optimal clinical beam energy for HyperArc was performed based on a literature review. A retrospective treatment planning study comparing HyperArc and DCA via several plan quality metrics (Paddick's conformity index, normal brain D10cc, brainstem Dmax) was performed for previously treated cases: 12 patients with single brain metastases, 20 patients with multiple brain metastases, 11 patients with vestibular schwannoma. Investigations of the influence of HyperArc treatment plan optimisation parameters on plan complexity and dose modelling accuracy were conducted. Treatment plan verifications to establish the accuracy of HyperArc planned dose distributions were performed with a range of measurement devices.

Results

Linac flattening-filter-free beam energy 6 MV was selected for clinical use. In the planning study, HyperArc generally performed better than DCA for all indications and across all plan quality metrics (see Table 1). Recommendations for several plan optimisation parameters to reduce the complexity and improve the verification accuracy were made. Treatment plan verifications confirmed clinically acceptable planned dose accuracy, with the mean single point dose difference across nine plans measured as –1.7% (range –3.8% to 1.1%).

Treatment site	HyperArc favourability per plan quality metric		
	Paddick's conformity index	Normal brain D10cc	Brainstem Dmax
Single brain mets	83%	100%	75%
Multiple brain mets	97%	95%	80%
Vestibular Schwannoma	100%	100%	91%

Table 1. Proportion of plans for the treatment site for which the plan quality metric was favourable for HyperArc in comparison to the pre-existing DCA approach

Conclusions

The experimental work undertaken at Velindre Cancer Service has shown that HyperArc performed as well or better than our existing radiosurgery solution for a range of clinical cases.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster
15

Heparin-derived nanocarriers as a precision medicine drug for therapeutic reprogramming of glioblastoma phenotypic states

Vadim Le Joncour,[1] Austin D. Evans,[2] Oommen P. Oommen*[2,3]

[1]Translational Cancer Medicine Research Program, Faculty of Medicine, University of Helsinki, Finland; [2]Bioengineering and Nanomedicine Lab, Faculty of Medicine and Health Technology, Tampere University, Finland; [3]School of Pharmacy and Pharmaceutical Sciences, Cardiff University

Among primary malignant brain tumours, glioblastoma (GB) has the highest incidence and worst prognosis due to infiltrative growth and poor response to current therapy (including surgery, chemotherapy, and radiation). This resistance is largely attributed to the immunosuppressive tumour microenvironment and dynamic phenotypic switching of GB cells, which enables them to adopt drug-resistant mesenchymal-like characteristics that survive therapeutic intervention.

We have discovered a novel precision medicine drug employing heparin-based nanoparticles (HP-NPs) designed to cross the blood-brain barrier and target mesenchymal-like glioma stem cells (MES GSCs). The HP-NPs were designed by conjugating fluorescein molecules to the heparin backbone, facilitating self-assembly into 140 nm nanoparticles. We encapsulated doxorubicin (DOX) within HP-NPs (HP-DOX-NPs) to enhance the therapeutic efficacy of the nanocarrier. Encapsulation of DOX reduced drug-mediated complement and coagulation cascade and enhanced hemocompatibility in human whole blood. In vitro, HP-NPs showed efficient cellular uptake across various patient-derived GB cell lines with varying EGFR expression levels. In vivo administration of HP-NPs and HP-DOX-NPs in patient-derived xenograft (PDX) models revealed that HP-NPs alone were more effective in suppressing GB progression than their DOX-loaded counterpart. We discovered that HP-NPs homed to the mesenchymal-like glioma stem cells (MES GSCs) expressing heparin-binding epidermal growth factor (HBEGF). HP-NPs targeting MES-like GSCs and downregulating HBEGF lead to differentiation of these drug-resistant cells to more vulnerable astrocyte (AC)-like cells, and oligodendrocyte precursor cell (OPC)-like phenotypic states inducing tumour suppression.

Thus, HP-NPs as a promising precision medicine platform to combat GB recurrence and improve patient outcomes by reprogramming GB into treatment-sensitive phenotypes.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference
19th September 2025 Sophia Gardens Cricket Ground

Poster 16

Outcome of patients with brain metastases who underwent surgical resection in South Wales

Laura Palles-Clark[1], Lauren Best[2], Sara Walters[3], James Powell[3], Jillian Maclean[3] and Najmus Sahar Iqbal[3]

[1]Aneurin Bevan University Health Board,; [2]Cardiff and Vale University Health Board; [3]Velindre University NHS Trust, Cardiff

Aims

Surgical resection of brain metastases offers the advantage of reduced local recurrence, better functional independence, and improved overall survival (1). NICE does not recommend adjuvant stereotactic radiosurgery (SRS) to patients who have undergone complete surgical resection of brain metastasis (2). We aim to look at outcomes of patients who underwent neurosurgical resection for brain metastasis.

Methods

153 patients were identified from the South Wales Neuro-Oncology MDT between 2018 and 2023. Patient demographics, tumour type, presence of residual disease, and adjuvant treatments were recorded using electronic patient records. Radiological progression following surgery was assessed, including the date and location of recurrence, and subsequent management. The primary outcomes were overall survival (OS) and time to progression. Survival outcomes were analysed using Kaplan-Meier curves on SPSS. Log rank test was used for statistical significance.

Results

The mean age was 57.70 (range 28-81) years; 59% were female. The most common primary tumours were lung (39.90%), melanoma (20.92%) and breast (16.40%). 55 patients had radiologically confirmed residual disease, 39 had no residual disease, and unknown in the remaining cases. 41 patients received adjuvant SRS to the surgical cavity, 13 underwent Whole brain radiotherapy (WBRT), 17 were unknown, and 82 patients had no adjuvant radiotherapy.

The median overall OS for all the patients was 8.459 (95%CI:5.8-12.1) months. The median OS was significantly higher in patients who had SRS, vs. WBRT or no adjuvant radiotherapy; 24.9, 8.5, and 7.2 months respectively (p-value=0.005). Recurrence at the surgical site occurred in 78 patients. Of these, 12 received SRS, 1 received partial radiotherapy, and 14 underwent WBRT.

Conclusion/ Discussions

Adjuvant SRS has demonstrated a significantly improved survival in this patient cohort. Limitation of this study includes retrospective analysis and potential patient selection bias when deciding on adjuvant therapies. This finding needs to be tested in a prospective randomised trial.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference
19th September 2025 Sophia Gardens Cricket Ground

Poster 17

Development of Precision Virotherapies for Diffuse Midline Gliomas

Mariana Varela Pereira 1, Emily A. Bates 1, Florian Siebzehnrubl 2, Chris Jones 3, William Gray 4 and Alan L. Parker 1

1 Division of Cancer and Genetics, School of Medicine, Cardiff University; 2 European Cancer Stem Cell Research Institute, School of Biosciences, Cardiff University; 3 The Glioma Group, Institute of Cancer Research, London; 4 Neuroscience and Mental Health Innovation Institute, School of Medicine, Cardiff University

Introduction

Diffuse Midline Gliomas (DMGs) are highly infiltrative and aggressive paediatric brain tumours located within the brainstem. With a median overall survival of just 9-11 months - a figure that has remained unchanged for over four decades - there is an urgent need for novel, targeted therapeutic strategies. The VITAL lab has developed an engineered adenovirus, modified to eliminate native receptor usage and retargeted with an RGD4C motif to enhance tumour-specific uptake while minimising off-target effects.

Aims

This project aims to evaluate Ad5NULL-RGD as a therapeutic agent for diffuse midline glioma (DMG) and to characterise the receptor profile of these tumours. Given the infiltrative nature of DMG, we also seek to incorporate molecular switches that enhance the specificity and controllability of viral activity. These include tetracycline-inducible systems, toehold switches, and synthetic super enhancers, each providing an added layer of tumour-selective regulation. Together, these strategies aim to optimise the safety and efficacy of virotherapy for DMG, ultimately advancing the development of a targeted and controllable therapeutic platform.

Methods

Surface receptor profiling of DMG cell lines was performed using immunostaining followed by flow cytometry, assessing the expression levels of αvβ3 and αvβ5 integrins as well as the Coxsackievirus and Adenovirus Receptor (CAR). Transduction efficiency was evaluated through luciferase-based reporter assays following infection with the unmodified Ad5 vector and the modified Ad5NULL-RGD4C vectors, providing a quantitative measure of transduction across DMG cell lines.

Results

Our findings indicate that DMG cell lines consistently overexpress αvβ3 and/or αvβ5 integrins, supporting their use as viable entry receptors for retargeted Ad5NULL-RGD4C vectors. CAR expression was found to be variable within the cell line range studied. Transduction assays demonstrated that Ad5 and Ad5NULL-RGD4C vectors are capable of efficiently infecting DMG cells, however there is a preferentiality for the glioma-specific targeted vector (Ad5NULL-RGD4C).

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster
18

Hippocampal dosimetry and implication for treatment planning in patients undergoing stereotactic radiosurgery for limited brain metastases

Iqbal NS[1,2], Williams MC[2], Williams MGJ[2], Doherty C[2], Bryant A[2], Chu M[2], Maclean J[2], Millin A[2], Palaniappan N[2], Staffurth J[1,2] & Powell JR[1,2]

[1]School of Medicine, Cardiff University; [2]Velindre University NHS Trust, Cardiff.

Introduction

Stereotactic radiosurgery (SRS) is recommended for patients with limited brain metastases, offering survival benefits while minimising neurocognitive function (NCF) decline compared to whole brain radiotherapy. However, despite its precision, SRS can still cause hippocampal radiation exposure, with the potential to adversely impact NCF.

Methods

This study retrospectively examined hippocampal dosimetry in 30 patients with 1 - 3 brain metastases treated using linear accelerator-based SRS using a dynamic conformal arc (DCA) technique. We then conducted a planning study in 10 patients who received the highest hippocampal doses to assess the feasibility of hippocampal-sparing SRS planning. Two hippocampal sparing SRS techniques were evaluated and compared to the standard technique, namely hippocampal-sparing DCA and hippocampal-sparing volumetric modulated arc therapy (VMAT).

Results

Retrospective hippocampal dosimetric analysis revealed inter-individual variation in hippocampal dose received: 25% of patients received >5 Gy and 50% received >2 Gy to 0.1cc of the closest hippocampus. Proximity of planning target volume (PTV) to the hippocampus, brainstem, and optic chiasm, as well as PTV volume and metastasis location in the temporal lobe and cerebellum significantly influenced hippocampal dose. The number of metastases did not correlate with increased hippocampal exposure. Both hippocampal sparing techniques significantly reduced hippocampal dose without compromising PTV coverage or organ at risk (OAR) constraints. Hippocampal-sparing DCA achieved the lowest doses to the hippocampus, while VMAT plans delivered slightly higher low-dose volumes (e.g., V1Gy) to the brain.

Conclusion

This study demonstrates that SRS can result in significant hippocampal irradiation, particularly for metastases within 2 cm of the hippocampus. Delineating the hippocampus during planning enables meaningful dose reductions without affecting plan quality. These findings support incorporating hippocampal delineation into standard SRS planning for patients with limited brain metastases. Further prospective studies are needed to establish clinical dose constraints and correlate hippocampal dose with NCF outcomes to refine radiotherapy strategies and reduce cognitive toxicity.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster 19

Long term release of charged small molecules from a polymer implant for local delivery in glioblastoma resection cavity

Sabarni Sarker[1], Sophie K. Hill[1], Hannah Gagg[2], Greg Wells[2], Benjamin Newland[1,3]

1. School of Pharmacy and Pharmaceutical Sciences, Cardiff University; 2. School of Medicine and Population Health, University of Sheffield; 3. Leibniz-Institut für Polymerforschung Dresden e.V., Dresden, Germany

Glioblastoma is a highly aggressive brain tumour with poor prognosis and frequent recurrence despite standard treatments. As most patients undergo surgical resection, localized drug delivery into the resection cavity offers a promising strategy to enhance therapeutic efficacy while minimizing systemic toxicity. Additionally, drug repurposing provides an opportunity to explore a wide range of therapeutic agents for local delivery. This study investigates the affinity-based delivery of repurposed, positively charged small-molecule drugs from a negatively charged polymer implant, aiming to achieve sustained local release and improve treatment outcomes.

A library of 2222 small-molecule drugs with repurposing potential were screened in silico using Chemicalize software to identify compounds with a net positive charge at physiological pH, yielding 1312 candidates. From these, 45 drugs were selected based on literature evidence and evaluated for in vitro cytotoxicity against glioblastoma cell lines. Negatively charged polymer implants were synthesized via free radical polymerization and characterized using light microscopy and Fourier Transform Infrared Spectroscopy (FTIR). Eight positively charged drugs—doxorubicin, mitoxantrone, pixantrone, tilorone, sertindole, ribociclib, vinblastine, and memantine—were selected for loading optimization and long-term release studies.

The negatively charged implants successfully loaded all selected drugs across various buffer systems, except memantine. Sustained release was achieved for several candidates, with doxorubicin and mitoxantrone releasing over 99 days, pixantrone over 75 days, and sertindole, ribociclib and tilorone over 7–15 days. Future work will involve evaluating the cytotoxicity of the release samples in glioma and normal astrocyte cell lines.

This study demonstrates the feasibility of using affinity-based polymer implants for the sustained local delivery of repurposed, positively charged small-molecule drugs, offering a promising strategy to enhance glioblastoma treatment post-surgery.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 20

Cell plasticity of host astrocytes drives glioblastoma progression via cell-cell interactions

Ayesha Begum* (1), Mathew Clement* (2), Alex Gibbs* (1,3), Vasileios Eftychidis (1), Suresh Kaushik (1), Florian A Siebzehnrubl (1)

(1) European Cancer Stem Cell Research Institute, School of Biosciences, Cardiff University; (2) Division of Infection and Immunity, School of Medicine, Cardiff University; (3) Wales Cancer Research Centre
** equal contribution*

Glioblastoma (GBM) is the most frequent and most lethal type of brain cancer in adults, with poor survival rates of 15-20 months with therapy. GBM tumor heterogeneity and therapy resistance are key factors affecting poor survival, and crosstalk between GBM and host cells in the tumor microenvironment (TME) promotes GBM progression, heterogeneity, and therapy resistance. We have previously shown that host astrocytes can positively or negatively affect brain tumor invasion into the surrounding parenchyma, depending on the status of astroglial reactivity.

Here, we investigate cell-cell interactions between GBM and host astrocytes in patient-derived orthotopic xenografts and syngeneic in vivo models. We find that GBM-astrocyte crosstalk promotes the expression of the cell-plasticity associated transcription factor, ZEB1, both in GBM and in host astrocytes. Using a conditional-inducible transgenic mouse model for deletion of Zeb1 in murine astrocytes we find that loss of host astrocyte plasticity restricts tumor invasion in vivo and remarkably increases animal survival. Single cell transcriptional profiling of tumor-bearing control and Zeb1-deleted mice identifies key alterations of astrocyte states as well as immune cell activation which contribute to GBM tumor progression. Additionally, we identify ligand-receptor candidates that mediate GBM-astrocyte crosstalk, and which may constitute therapeutic targets for reprogramming the host TME to reduce GBM progression.

Our findings demonstrate that host astrocytes in the TME are powerful regulators of glioblastoma growth and that reprogramming host astrocytes can block brain tumor progression.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 21

The development of a dynamic 3D iPSC-derived brain organoid to evaluate patent-specific glioblastoma and immune interactions.

Julia Spagnolello, Catia Neto, Mark Gumbleton

School of Pharmacy & Pharmaceutical Sciences, Cardiff University

Glioblastoma (GBM) is an aggressive brain tumour, representing approximately 50% of all primary brain malignancies. The median survival for GBM patients is 20 months with less than 10% surviving beyond 5 years post-diagnosis, and currently there are no FDA-approved targeted therapies for GBM. Recent studies have highlighted the crucial role that microglia, the resident myeloid cells of the brain, play in supporting GBM progression and survival. However, the mechanistic interactions remain poorly understood due to the lack of an accurate model.

This project aims to generate a biologically relevant 3D patient – derived model to elucidate underlying mechanistic interactions between microglia and GBM which lead to tumour progression, with the opportunity of providing patient-specific immunological care. Using patient GBM tumour samples and matched blood specimens provided by King College London, GBM cells and peripheral blood mononuclear cells (PBMCs) are isolated and expanded in culture. Following this, PBMCs are reprogrammed into iPSC via Sendai virus-mediated transduction of the Yamanaka factors. Lastly, these iPSCs are then directed towards the neural induction pathways to generate brain organoids or the mesodermal pathway to generate microglia. The final model integrates both patient- derived GBM cells and iPSC-derived microglia into the brain organoid recreating a 3D system allowing tumour-microglia interactions to take place.

With this model, we aim to better understand the relationship between microglia and GBM which promotes tumour progression and treatment resistance. With this novel 3D immunocompetent model, previous challenges such as the lack of tumour micro-environment and the inability to study spatial relationships are overcome, allowing for a better understanding of the role of the immune system in the progression of GBM. Furthermore, the novelty of this model being patient specific can enable personalised immunotherapy.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales Brain Tumour Conference

19th September 2025 | Sophia Gardens Cricket Ground

Poster 22

Oncolytic Adenovirus 5 Mediated Prodrug Conversion Therapy for use in Glioblastoma

Wallace R[1], Bates EA[1], Parker AL[1]

1. *School of Medicine, Cardiff University*

Current treatments for glioblastoma are extremely limited. Consequently, the Viral Immunotherapies and Advanced Therapeutics Lab (VITAL) group is designing Adenovirus (Ad) based oncolytic viruses as the next generation of glioblastoma treatments.

We inserted the FCU1 transgene, which converts the harmless antifungal agent 5-flourocytosine (5-FC) into chemotherapy drug 5-flourouracil (5-FU), into our $Ad5_{NULL}$-RGD vector, which is both de-targeted from all natural Ad5 binding sites and re-targeted to glioblastoma. We hope to achieve a multimodal effect with this new therapy: The oncolytic virus infects cancer cells and, through oncolysis, releases both tumour and viral antigens into the tumour microenvironment, stimulating the immune system. Replication leads to the production of more virus within the tumour. At the same time, infected cells locally produce the encoded transgene and convert the prodrug to chemotherapy at the site of need. The viruses were produced using in-house recombineering techniques and tested in vitro using multiple human glioma stem-cell lines. Primary in vitro results are promising, as the vectors effectively kill glioma stem-cell lines. This effect is enhanced in the presence of 5-FC and can be observed in a dose dependent manner. Additionally, the “null” mutations introduced into the virus to reduce off-target effects and increase safety do not diminish infective capacity of tumour cells.

In conclusion, this presents an exciting possibility for the future of glioblastoma treatments and new hope to current and future patients.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative

Cancer Research Wales
Brain Tumour Conference

19th September 2025 Sophia Gardens Cricket Ground

Poster
23

A comparison of gas-free MRI methods for CMRO2 quantification in primary brain tumour

Stefano Zappalà 1, Eleonora Patitucci 1, James Powell 2, Sahar Iqbal 2, Fabian Küppers 3, Jon Shah 3, Richard Wise 4, Michael Germuska 5

1.Cardiff University Brain Research Imaging Centre (CUBRIC), Cardiff University; 2. Department of Oncology, Velindre University NHS Trust, Cardiff; 3. Institute of Neuroscience and Medicine 4, Forschungszentrum Jülich; 4. Department of Neurosciences, Imaging, and Clinical Sciences and Institute for Advanced Biomedical Technologies, University 'G. D'Annunzio' of Chieti-Pescara, Italy; 5. Department of Radiology, University of California Davis Medical Center, CA, USA

Recent interest in non-invasive alternatives to PET imaging has shown the development of MR techniques for the quantification of cerebral metabolic rate of oxygen consumption (CMRO2). Their relative performance in significantly altered pathology has not been previously assessed.

Two gas-free MR methodologies for mapping CMRO2 in gliomas were compared, namely: breath-hold calibrated functional MR imaging (bhc-fMRI) and quantitative blood oxygenation level dependent (qBOLD) imaging via relaxometry. Their accuracy in estimating oxygen extraction fraction (OEF) in grey matter (GM) was gauged against validated TRUST measurements at the superior-sagittal sinus.

Twenty-five participants with a diagnosis of low- and high-grade glioma were recruited to the study (44.4±8.5 years, 5 females). Maps of cerebral blood flow (CBF) as well as anatomical scans were acquired.

CMRO2 estimates of bhc-fMRI and qBOLD were in good agreement in healthy GM, with OEF values in good correspondence with TRUST measurements. For the bhc-fMRI method, significant differences between healthy and pathological tissues were found, in line with the expected altered physiology. Estimates from qBOLD suffered from its sensitivity to haemorrhage and iron deposits typical of more aggressive tumours.

In their current form, bhc-fMRI may be preferable to qBOLD imaging thanks to its selective sensitivity to oxygenated blood.

ymchwil canser cymru
cancer research wales

menter ymchwil tiwmorau'r ymennydd
brain tumour research initiative