Clinical Priorities & Clinical Research Agenda

Dr. Robin Grant
Consultant Neurologist
Whose Priority?

A 1-cm cancer has about 100 million cells

“GBM cell-line or patients derived xenografts can’t reflect the true biological nature of GBM”

Stem Cells

Therapy

Animal models

QoL
Which Pie?

Competition - lower

Local Brain Tumour Charities

National Brain Tumour Charities (e.g. BTR, brainstrust, TBTC others)

UK Cancer Charities (e.g. CRUK, Macmillan, Marie Curie)

Complexity - Lower

Local Hosp. / Univ. Funds

National Funds (£1b/yr) NIHR & MRC
- Project Grant
- Programme Grant
- Fellowships

International Funds
- e.g. European Union, NIH (US) - Partners

Competition high

Complexity - V High
NIHR Aims include

• Establish the **NHS** as an *internationally recognised centre of research excellence*

• Attract, develop best research professionals to **conduct people-based research**

• **Commission research** focused on improving health and social care

• **Drive faster translation of scientific discoveries** into benefits for patients

• **Funding Research (Research Projects £250m/year)**
  
  • **Research Programmes** with support of **Research Design Service**
  
  • **Research Delivery in NHS through Clinical Research Networks (CTUs)**
  
  • **Research to Determine Evidence Reviews** (eg Cochrane Systematic Review)
  
  • **Support the James Lind Alliance Priority Setting Partnerships**
James Lind Alliance PSP

- Brings patients/carers & clinicians together in partnerships to ensure that researchers, and funders of health research, are aware of what matters to both patients/families and clinicians.

- To identify/prioritise “treatment uncertainties” which they agree are important for clinical research.
Established JLA Neuro-Oncology Group

- **James Lind Alliance – Neuro-Oncology Meeting –**
  July 2013 Cochrane Editorial Unit, Kings Fund, London
  - Scope of work – Adult brain & spine tumours
  - Developed Stakeholder Group (50:50 split)
  - Secured funding for the group (Charities, Cochrane, ELHF)
  - Obtaining JLA agreement – to provide facilitator / facilitation
  - Development of JLA Neuro-Oncology Website
  - Survey of the brain tumour community – what questions?
    - > 600 questions – identified the top 10 questions
Top 10 uncertainties

1. Do lifestyle factors (e.g. sleep, stress, diet) influence tumour growth in people with a brain or spinal cord tumour?

2. What is the effect on prognosis of interval scanning to detect tumour recurrence, compared with scanning on symptomatic recurrence, in people with a brain tumour?

3. Does earlier diagnosis improve outcomes, compared to standard diagnosis times, in people with a brain or spinal cord tumour?

4. In second recurrence glioblastoma, what is the effect of further treatment on survival and quality of life, compared with best supportive care?

5. Does earlier referral to specialist palliative care services at diagnosis improve quality of life and survival in people with a brain or spinal cord tumours?

6. Do molecular subtyping techniques improve treatment selection, prediction and prognostication in people with a brain or spinal cord tumour?

7. What are the long-term physical and cognitive effects of surgery and/or radiotherapy when treating people with a brain or spinal cord tumour?

8. What is the effect of interventions to help carers cope with changes that occur in people with a brain or spinal cord tumour, compared with standard care?

9. What is the effect of additional strategies for managing fatigue, compared with standard care, in people with a brain or spinal cord tumour?

10. What is the effect of extent of resection on survival in people with a suspected glioma of the brain or spinal cord?

*Uncertainties relate to any age.
Top 10 questions fed back to NIHR
Commissioned Calls or Researcher Led
‘Develop UK Strategy’ to support Clinical Neuro-Oncology Research Applications

Funders of the JLA Neuro-Oncology project 2013-15
26th June 2015 (Centre for Clinical Practice, NICE Offices, London)

Also Present: Prof Mark Baker – Director CCP, NICE; Prof Luke Vale Chair Health Economics; Ms. Laura Macdonald JLA Neuro-Onc Group Manager
Best People ( >3 Centres ) & Clinical Priority Studies ( JLA )
Systematically Reviewed – Cochrane Neuro-Oncology

Best Design       Best Clinical Research       Best Evidence       Best Practice

Research Design Service

NCRI National Cancer Research Institute

SCRN

Cochrane

NHS National Institute for Health Research

CaCTUS Clinical Research Network Cancer

NICRN Clinical Research Network

MRC Hubs for Trials Methodology Research

NISCHR

HSC Public Health Agency

Funding from Government (NIHR), Large Research Charities, Cancer Charities (CRUK, MC) Brain Tumour Charities
National Cancer Research Institute (NCRI)

**NCRI Partners** include: DoH, CRUK, CSO, MRC, Wellcome Trust, Children with Cancer UK, Macmillan Cancer Support, Marie Curie

- Each NCRI Clinical Studies Group (CSG) has a UK-wide strategic remit to:
  - **Develop** a national portfolio of **clinical trials and well-designed studies:**
  - including, but not limited to, **large-scale pragmatic trials**, and studies in **health service research**
  - encompassing both **academic and industry** sponsored trials
  - **proposed by CSG members** and individuals outside the CSG membership
- **Liaise with funding bodies in order to:**
  - **Develop the questions in collaboration** (Lay Reps/Funders/CTUs/NCRI Brain CTG/Cochrane) – **“Incubator days”**
  - Provide written comments on application submissions
NCRI brain CSG Supportive & Pall Care subgroup

- Dr Robin Grant (Chair)  Cons. Neurologist
- Dr Helen Bulbeck (Sec)  Patient Advocate
- Dr Anne Arber  Sen Lect Cancer and Palliative Care
- Dr Florien Boele  Acad. Fellow in Neuro-Psychology
- Dr Anthony Byrne  Cons. Palliative Care
- Prof Jon Evans  Prof Neuro-Cognition
- Prof Robert Hills  Prof Clinical Cancer Res Methodology
- Dr Catherine McBain  Cons. Clinical Oncology
- Prof Richard Neal  Prof Primary Care Oncology
- Kathy Oliver  Consumer/charity - Director IBTA
- Dr Ally Rooney  Acad PSYStar Fellow in Psychiatry
Do Lifestyle Factors (diet) influence tumour growth?

“Does addition of the KD in GBM, undergoing Chemo-Rad lead to improved response, survival and QoL?”

• NCRI brain CSG link – Kathy Oliver (IBTA)
• Cochrane Review Underway
• Which type of KD? – Liverpool (Keating)
• Incubator Day Jan 2017
• Charity Partners (Matthews Friends, BTR, Astrofund)
• Trials Unit – Imperial, London & Liverpool
• Lead - Dr Matt Williams (Oncologist)
• Research Grant – Brain Tumour Research
• NIHR – HTA / EME in future?
What is the effect on prognosis of interval scanning to detect recurrence?

- NCRI brain CSG – G Thomson
- Cochrane Rev – (G Thomson/M Jenkinson / L Vale)
- Incubator Day - planned 2018
- Charity Partners (TBA)
- Trials Unit (TBA)
- Health Economist (Luke Vale)
- Lead - (Gerry Thomson)
- NIHR – HTA or MRC

**scanxiety**
noun. [skan-zi-etee] the uneasiness associated with waiting for the results of cancer scans

*Pseudoprogression Example*

Before RT

4 weeks after RT (TMZ begun)

8 weeks after RT

6 months later
Does Early Diagnosis Improve Outcomes compared to standard diagnosis times in brain & spinal cord tumour?

- NCRI brain CSG link – R Neal (GP)
- Cochrane Review – NIHR SRPG
- Incubator Day - 2016/Dec 2017
- Charity Partners (TBTC)
- Health Econ. (Prof Hollingworth)
- Research Grant (2 TBTC grants)
- NIHR – 2018 proposals
- HA+ New Optometry Pathway
- HA + Risk factor assessment
In second recurrence GBM what is the effect of further treatment on survival and quality of life compared with best supportive care?

- NCRI brain CSG – C McBain (Manchester)
- Cochrane Review – CNOG priority review
- Incubator Day - (---) 2018
- Charity Partners (brainstrust)
- Trials Unit (---)
- Health Economist (---)
- Lead - (C McBain / A Byrne)
- Research Grant – (---)
- NIHR – HTA / MRC / Marie Curie?
Does earlier referral to specialist Palliative Care services at diagnosis improve quality of life and survival?

- NCRI brain CSG link – A Byrne (PC)
- Cochrane Review – CNOG priority
- Incubator Day - 2017 (Cardiff)
- Charity Partners (brainstrust +/- MC)
- Trials Unit (Cardiff CTU)
- Health Econ (Cardiff/Newcastle)
- Lead - (A Byrne / C McBain)
- Research Grant – (---)
- NIHR – HTA / MRC / Marie Curie
Do molecular subtyping techniques improve treatment selection, prediction and prognostication?

- NCRI brain CSG link – R Kurian (NP)
- Cochrane Review–NIHR SRPG grant
- Incubator Day - (--- - 2018)
- Charity Partners (---)
- Trials Unit (---)
- Health Economist (---)
- Lead - (Reena Kurian & Sarah Jeffries)
- Research Grant (---)
- NIHR – HTA or MRC?
What are the long term physical and cognitive effects of surgery +/- RT in brain tumours?

- NCRI brain CSG link – J Evans (N-P)
- Cochrane Review – NIHR SRPG
- Incubator Day - 2018
- Charity Partners (brainstrust)
- Trials Unit (SCRTU)
- Health Economist (Prof Vale (Newcastle)
- Lead - (to be decided)
- Research Grant – (---)
- NIHR – HTA or MRC
What is the effect of interventions to help carers cope with changes that occur in people with brain tumours?

- NCRI brain CSG link – F Boele (N-Psy)
- Cochrane Review – GNOC Priority
- Incubator Day - 2017
- Charity Partners (brainstrust)
- Trials Unit (---)
- Health Economist (Leeds)
- Lead - (Florien Boele, Leeds)
- NIHR – ?Research for Patient Benefit
What is the effect of additional strategies to manage fatigue?

- NCRI CSG link H Bulbeck
- Cochrane Review – Complete
- Incubator Day - 2017
- Charity Partners (brainstrust)
- Trials Unit (SCRTU)
- Health Economist (Glasgow)
- Lead - (Ally Rooney)
- Research Grant – TBTC
- Trial - Edinburgh/Glasgow/Manchester
What is the effect of extent of resection on survival in people with a brain tumour?

“Technology to maximise extent of resection in glioma”

- NCRI CSG link – C Watts
- Cochrane Review – NIHR SRPG
- Incubator Day - 2017 / 2018
- Charity Partners (brainstrust)
- Trials Unit (---)
- Health Economist (---)
- Lead - (Colin Watts, B’Ham)
- Research Grant – planned
- NIHR – HTA or MRC
“Umbrella Protocol”

- “Brain Matrix” - Joint working of UK Centres
- “Basket trials/flexible design/multiple options”
- Supportive care studies sitting over therapy trials

Supportive care master protocol

Agree appropriate Patient Reported Outcome Measures (PROMs)
Have Core Outcome Measures for Evaluation of Trials (COMET)
Involve Routinely Collected Datasets – with patient consent – e.g. CPRD / NCRN / CPES
Last 6 months

- **NIHR HTA 16/31/136 - SPRING-Seizure Prophylaxis IN Glioma**
  In patients with seizure-naïve newly diagnosed glioma undergoing surgery, does prophylactic AED reduce the risk of developing seizures? (Multi-centre RCT) **CI R Grant – Trial Unit SCRTU**

- **NIHR SRPG 16/114/18 Cochrane SR Programme Grant**
  (NCRI/Cochrane) 8 Complex Systematic Reviews on JLA topics **CI R Grant – Cochrane Neuro-Oncology Section**

- **TBTC QoL Grant – BT LIFE: CI A Rooney—** Lifestyle Intervention and Fatigue Evaluation – a multi-centre feasibility randomised controlled trial”, **CI A Rooney— Trial Unit SCRTU**
Funding Boost over next 5 years

Department of Health & Social care – “Brain cancer research to receive £45 million funding”

Tessa Jowell

- National Institute for Health Research - £20 million in funding will be invested through the NIHR over the next 5 years.

- Cancer Research UK will invest £25 million in research into brain tumours over the next 5 years. This is on top of £13 million each year on the research and development of cancer treatments.

Future for Research is brighter – if > 70% goes into Clinical Research!
Summary

• NCRI are aligned to JLA clinical priorities
• Shift the agenda towards clinical research
  • **Funding Bodies** - More clinicians/patients on committees
  • **Applied research** – Neuro-Path/Imaging/Clinical/S&PC
    – Clinical Scientist Fellows and Advanced Clinical Scientist Fellows
  • **Establish a Network of Clinical Trials Units**
    – Drug & Supportive & Palliative Care Trials
    – Umbrella protocol with flexible trial design
    – “Basket of treatments” & “Pick a winner design”
  • **Fund linking of routinely collected data (CPRD; NCRN; CPES)** “consent patients at diagnosis”
  • Meta-analysis of available studies – “open trials”.
  • Realistic Goals - more patients into trials –10% in 10 years.