



British Neuro-Oncology Society

Rare Brain and CNS Tumours Guidelines

In collaboration with the

National Cancer Action Team

Guidelines on the diagnosis and management of Optic Pathway Glioma (OPG)

Officers of the British Neuro-Oncology Society:

- President:** Professor Geoff Pilkington
Professor of Cellular & Molecular Neuro-oncology
Director of Research, School of Pharmacy & Biomedical Sciences
University of Portsmouth
- Vice President:** Professor David Walker
Professor of Paediatric Oncology
Queen's Medical Centre
Nottingham
- Secretary:** Mr David Jellinek
Consultant Neurosurgeon
Royal Hallamshire Hospital
Sheffield
- Treasurer:** Dr Jeremy Rees
Consultant Neurologist
National Hospital for Neurology and Neurosurgery
London

Optic Pathway Glioma (OPG) Guidelines

Contents

Section	Page
Introduction.....	1
Summary of key recommendations	1
Background	2
UK Clinical Trials in Low Grade Glioma (LGG1 and LGG2 1997-2010).....	2
Epidemiology	4
Clinical Presentation.....	4
Imaging Characteristics	5
NF1 related OPG.....	6
OPG Staging Systems.....	7
Histology.....	9
Data items for future audit	10
Treatment	10
Clinical Approach: Organisation of services	10
Surgery	12
Radiotherapy Protocol	13
Chemotherapy / Drug therapy	15
Rehabilitation.....	15
Clinical assessment of NF cases.....	16
Supportive care, Rehabilitation and General palliative care.....	16
Core Members of Supportive Care services	17
Extended members of Supportive Care services	17
Specialist palliative care	20
Survivorship / Living with cancer	23
Appendix 1: Information Principles for Visually Impaired individuals.....	25
Appendix 2: Endocrinology.....	26
Clinical assessment and diagnostic tools	28
Table: Diagnosis of Hypopituitarism	31
Minimal requirements for endocrine follow-up.....	32
Appendix 3: Additional support for brain tumour patients and carers.....	33
Appendix 4: Table: Symptom related referral pathway to supportive care services for patients with Optic Glioma tumours.....	35
Appendix 5: Optic pathway imaging guidelines	35

Guidelines on the diagnosis and management of Optic Pathway Glioma (OPG)

Introduction

The brain tumour IOG recommended that national tumour groups for rare CNS tumours should be established to coordinate the approach to care; this should include developing protocols for the investigation, management, registration and clinical research into rare tumours. It was also advised that they should also maintain a national register of all these cases.

The purpose of this report is to provide a schema for the management of adults with optic pathway glioma (OPG), which can be applied nationally, leading to standardised management.

In writing these guidelines, it is acknowledged that since OPG arise almost exclusively during childhood and adolescence, the principles of management have been adapted where it is appropriate from guidelines for their management of children taking into account the anticipated consequences of their management within national clinical trials that have been active since the late 1990s recruiting over 80% of incident cases nationally.

OPGs are benign tumours and as such the cancer paradigm cannot be directly applied. They constitute a chronic disorder subject to periods of quiescence and progression during childhood and adolescence. Their anatomical involvement of supratentorial mid line brain structures involved in visual mechanisms. Up to 50% are associated with Neurofibromatosis type (NF1).

Summary of Recommendations

- 1. Brain tumour services in adulthood should incorporate special arrangements for transition and following up of survivors of low grade astrocytomas generally, and OPG in particular, which we estimate to account for ~50% of patients under long term follow up by paediatric neuro-oncology teams. This transition service should include strong links to endocrine, ophthalmic and neuro-rehabilitative services.**
- 2. These services should be developed for people aged <24 years in conjunction with the Teenage and Young Adult Multi-disciplinary Team (TYA MDT)**
- 3. As many of these patients will have previously been treated in international clinical trials and be part of childhood cancer registers adult neuro-oncology MDTs caring for these patients should seek to collaborate with late follow up data collection where at all possible.**
- 4. When patients with OPGs are associated with NF1, access to specialty support services linked to NF1 should be identified by the neuro-oncology MDT and offered in appropriately complex cases (see section 7).**

5. When OPGs are associated with visual impairment, access to special support services for visual handicap should be provided by the neuro-oncology MDT.
6. Special arrangements should be in place for creating and maintaining suitable information sources suitable for people with visual impairment.
7. Each case should be assessed and an individualised strategy be developed in conjunction with representatives of both children and adult neuro-oncology MDTs.
8. Timely referral to rehabilitation and supportive care services is imperative and is dependent on rapid, comprehensive communication between medical and AHP staff.

Background

Optic Pathway Gliomas (OPG) are histologically benign tumours that typically develop during early childhood arising within optic nervous tissues or in adjacent structures to the optic tract, most commonly hypothalamus, temporal and occipital lobes. They have the greatest tendency to grow in the first 3-5 years of life; rarely they metastasise to leptomeninges (<5%) although this does not appear to confer a poorer prognosis for survival in childhood. Clinically they can be classified into sporadic tumours arising in individuals with or without a pre-disposing condition.

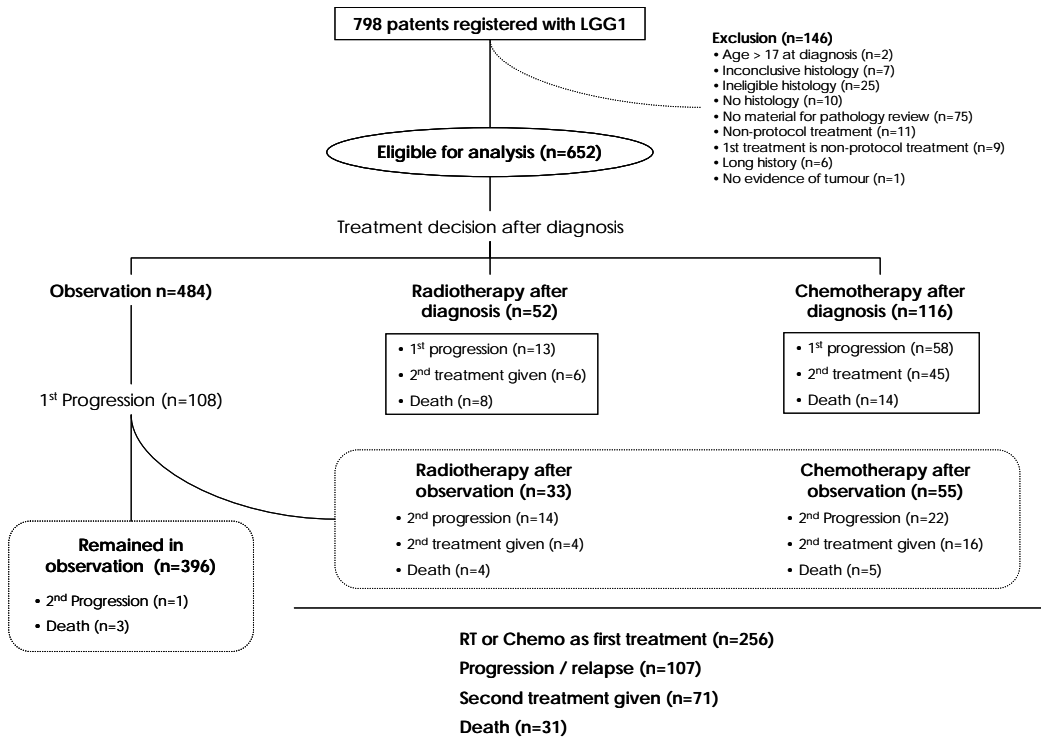
Sporadic tumours typically arise within the chiasmatic-hypothalamic region or in other brain structures adjacent to, or involving the optic tract; they do not typically involve the optic nerves.

OPG associated with *Neurofibromatosis type 1 (NF1)* characteristically involve optic nerve, chiasm and optic radiation, including the geniculate ganglion.

UK Clinical Trials in Low Grade Glioma (LGG1 and LGG2 1997-2010)

Two large multi-centre, international clinical studies have been conducted involving the UK childhood population since 1997.

LGG1: The first of these was a registry study using an agreed multi-disciplinary clinical strategy for selection of patients for observation or treatment. It recruited patients with low grade astrocytomas at all sites of which 225 were OPGs. The treatment schema is shown with recruitment numbers for all sites shown.



This study was closed in 2004 having recruited 80-86% of incident cases of LGG in UK childhood population through the UK Childrens Cancer and Leukaemia Group network of treatment centres. These patients have been followed until 2010. Further research is planned to evaluate their late effects.

Chemotherapy (Vincristine and Carboplatin for up to 1 year) was used to delay the use of radiotherapy in very young children (<5 years), the majority of the children receiving chemotherapy were OPG cases. Radiotherapy was used in a minority the radiotherapy guidance in this document is based upon this and the consequent LGG2 study protocols.

LGG2: This study was opened in 2005 as part of an international consortium of 14 countries. As we write, it is ongoing and is anticipated to recruit patients until 2012. OPG patients are a special focus for this study as there is a new visual assessment protocol. There is a randomisation for patients with unresectable progressive or symptomatic sporadic tumours, the majority of which are OPGs, which is investigating the addition of Etoposide to the previously used Vincristine Carboplatin regimen in sporadic tumours. LGG including OPGs associated with NF1 are treated with Vincristine and Carboplatin alone. The duration of therapy has been extended to 18 months.

In both these studies maximal surgical resection is recommended at diagnosis where neurological risks are acceptable, this is clearly a rare event in OPG. Radiation therapy is recommended if there is threat to vision and/or symptomatic or tumour progression. The evidence for the effectiveness of radiotherapy in OPG has been reviewed and is extensive. The use of the technique needs careful consideration of the consequences. These are very high for children and presumed to be lower for adults although they are not negligible.

Radiotherapy is not recommended except in extreme circumstances for patients with NF1, due to high risks of high grade second primary tumours and vascular complications (Sharif et al 2006).

Epidemiology

Based upon childhood studies about 40-50% of OPG that present clinically are sporadic, the remainder are associated with NF-1 (Singhal et al 2002; Stokland et al). Sexes are equally affected, the median age at presentation in childhood is about 5 years. Data concerning OPGs usually registered on a regional children's tumour registry has been extrapolated to estimate a population incidence of 0.3 per million annually.

Symptomatic OPG occur in about 5% of clinical cases of NF1 identified in childhood (Singhal et al 2002; McGaughan et al 1999), however, if such NF1 children are screened with MRI this rises to 15%. Based upon historical data up to 25% of NF1 patients may be diagnosed initially with an OPG during adulthood. Greater awareness coupled with vision screening and MR scanning of NF-1 population during childhood may reduce this percentage.

We are not aware of sporadic cases of OPG presenting in adulthood.

References

Singhal S, Kerr B, Birch J, Lashford L, Evans DGR. Clinical characteristics of symptomatic sporadic and NF1 related optic gliomata: implications for management. *Archives Dis Child* 2002; 87:65-70.

Tore Stokland, Jo-Fen Liu, James W Ironside, David W Ellison, Roger Taylor, Kathryn J Robinson, Susan V Picton, and David A Walker. A multivariate analysis of factors determining tumor progression in childhood low-grade glioma: a population-based cohort study (CCLG CNS 9702) *Neuro-Oncology* Submitted for Publication.

McGaughan J, Harris DI, Donnai D, Teare D, McLeod R, Kingston H, Super M, Harris R, Evans DGR. A clinical study of type 1 neurofibromatosis in North West England. *J Med Genet* 1999; 36: 197-203

Robert Listernick, MD,¹ Rosalie E. Ferner, MD,² Grant T. Liu, MD,^{3,4} and David H. Gutmann, MD, PhD⁵. Optic Pathway Gliomas in Neurofibromatosis-1: Controversies and Recommendations *Ann Neurol* 2007;61:189–198

Sharif S, Ferner R, Birch J, R Gattamaneni, Gillespie J, Evans DGR. Second primary tumours in Neurofibromatosis 1 (NF1) patients treated for optic glioma: substantial risks post radiotherapy. *J Clin Oncol* 2006; 24(16):2570-5

Clinical Presentation

The commonest presentation is the patient who has been previously diagnosed with sporadic or NF-1 associated OPG who was previously observed or treated during

childhood and adolescence. Thus the clinical presentation in adulthood may be as a result of a transition referral from paediatric neuro-oncology team or be associated with new visual symptoms / signs, symptoms of raised intracranial pressure, or as an incidental finding on brain scanning for other reasons such as investigation of endocrine disturbances or infertility.

Previous clinical management may have led to late consequences of the tumour or its treatment including:

- visual impairment: reduced visual acuity, and / or visual fields, the presence of optic atrophy, nystagmus and proptosis
- cognitive impairment due to: prior cranial radiation therapy in early life, tumour related brain injury post surgery, NF1 associated cognitive impairment
- endocrine deficits: TRH deficiency, growth hormone deficiency, LH / FSH impairment, diabetes insipidus or ACTH deficiency
- focal neurological deficit e.g. internal capsule or pyramidal damage
- behavioural disturbance e.g. hypothalamic syndrome of rage, appetite disturbance and obesity

Rarely OPG could present with symptoms of raised intracranial pressure e.g. headaches, vomiting and 6th nerve palsy. New tumour-related symptoms may be due to tumour re-growth or second tumour development i.e. radiation induced meningioma or more rarely high grade glioma. Risks of other primary and second tumours are considerably higher in NF1 especially if radiotherapy has been used. Malignant Peripheral Nerve Sheath tumours associated with NF1 classically occurring within radiation fields. In NF1 cases a de novo presentation in adulthood can only be truly confirmed if a prior brain scan was unaffected, a situation that was not recalled by the guidance group to have taken place. Similarly the guideline group could not recall a case where sporadic OPG presented de novo in the adult practice.

Imaging Characteristics

Sporadic OPG:

The most common (70-90%) location for these tumours is the optic chiasm/hypothalamic region. In a minority of cases (approx 30%) the tumour may be isolated to the intraorbital optic nerve. Tumour related cysts are common, as is extension beyond optic pathway structures. In a small proportion of cases 'arachnoid' cysts may be encountered in the middle cranial fossa adjacent to the tumour. These tumours tend to be larger than NF1 related tumours at presentation and show more evidence of progression over time.

CT scanning: CT scanning should be avoided as the characterization and full assessment of optic pathway tumours is inferior to MRI. In addition patients harbouring these tumours

usually require serial scanning, for which interstudy comparability is essential. The use of CT for follow up studies suffers not only from lower inherent diagnostic accuracy but also the not insignificant risks associated with a cumulative radiation burden

MRI assessment demonstrates smaller tumours that may respect their anatomical origin – the chiasm may be expanded but identifiable. Larger tumours make identification of the site of origin (chiasm v hypothalamus) impossible.

T1 imaging: the tumour is hypo- to iso-intense; cysts tend to be markedly hypointense.

T2 and FLAIR imaging: the lesions appear hyperintense.

Enhancement: this is variable but often intense, highlighting cystic foci. Leptomeningeal enhancement may be identified in both the intracranial and intraspinal compartments in a small proportion of cases (5%).

Diffusion weighted imaging (DWI): the tumours are usually hyperintense on DWI and ADC maps, reflecting their relatively hypocellular characteristics, however this is variable.

Perfusion MR imaging may demonstrate variably elevated rCBVs.

Magnetic Resonance Spectroscopy (MRS): Choline is generally elevated, NAA low. There is variable mild to moderate myo-Inositol elevation. Paradoxically for a low grade tumour, a prominent lipid/macromolecular complex is not infrequently present.

See appendix 5 for advisory imaging guidelines for optic pathway gliomas, adapted from the CCLG brain tumour imaging protocol.

NF1 related OPG

Neurofibromatosis Bright Objects (NBO) / T2 hyperintensities are common radiological features seen in brain scans of children and young people with NF1, which need to be differentiated from tumours. These lesions co-exist with and are hallmark findings in patients with NF1 related optic pathway gliomas. They occur most commonly in the globus pallidi, but are also frequently encountered in the thalami, hippocampi, geniculate ganglia, brainstem and deep cerebellar white matter/dentate nuclei. They are T2 and FLAIR hyperintense, mildly T1 hypointense, show little mass effect, do not in general enhance following contrast administration and show increased diffusivity on DWI. MR spectroscopy may show mild choline elevation and NAA reduction but the findings are often non-specific. There is frequently overlap with the diffuse tumours associated with NF1, with which they may merge. These lesions gradually involute with age. The natural history is for these to disappear by adulthood, where they have not disappeared specialist follow up may occur in the context of a specialist NF clinic.

OPGs with NF1 occur at more variable sites along the anterior and posterior visual pathways. There is frequent involvement of the optic nerves (65%), which may be unilateral or bilateral and frequently asymmetric, the chiasm is involved in 60%. Retro-orbital optic nerve involvement frequently merges with tumour centred on the optic chiasm/hypothalamus, with asymmetric involvement of these structures and the optic

tracts. Posterior extension may involve adjacent brain tissue in the mesial temporal lobes, striatal structures, thalami. However there is considerable overlap with the vacuolated non-neoplastic NF1 related lesions occurring at these sites.

As with the sporadic form, 'arachnoid' like cysts may be present in the middle cranial fossa adjacent to the tumour mass. In approximately 50% of cases the tumour remains stable on serial scanning. Tumour related cysts are less common than the sporadic form.

MRI assessment: the optic nerve disease is best visualized on axial and coronal imaging employing T1 and T2 fat saturated sequences and contrast enhancement. Optic nerve involvement may vary from subtle slight expansion of part of the nerve to gross involvement of the entire intra-orbital extent, with or without retro-orbital extension.

T1 imaging: both the intra- and retro-orbital components are T1 hypo- to iso-hypointense.

T2 and FLAIR imaging: there is corresponding hyperintensity, which is often markedly heterogeneous, however there is frequently heterogeneity. The optic nerve component may appear of lower signal intensity to the retro-orbital disease.

Enhancement: the enhancement pattern is usually variable in both the intra-orbital and retro-orbital tumour, with foci of strong enhancement but not infrequently this is absent or minimal. Enhancement may vary with the natural history of the tumour or as a consequence of tumour modulating therapy. In some cases the enhancement may disappear, but may return at a later date, and fluctuate intermittently.

Diffusion weighted imaging (DWI): the lesions are generally hyperintense on DWI and ADC maps.

Perfusion MRI: perfusion indices are generally low but may show variable moderately elevated rCBVs associated with foci of enhancement.

Magnetic Resonance Spectroscopy (MRS): a pattern similar to the sporadic OPGs is generally encountered, however the more diffuse confluent NF1-related lesions may show a more non-specific pattern.

OPG Staging Systems

Anatomical definition of optic pathway tumours is required for optimal surgical planning in those cases where surgical intervention is deemed necessary and for prognostication, with tumours centred on the chiasm having the poorest outcome for vision.

A classification system was first published by Dodge et al in 1958 (1). This system was based upon the localisation of the tumour in relation to the optic nerves (stage A), optic chiasm, with or without optic nerve involvement, (stage B), and hypothalamic or other adjacent structure (stage C).

PLAN classification (Modified Dodge Classification).

The advent of sophisticated and anatomically accurate imaging provided by MRI has led to a modification of the Dodge classification, which takes into account optic fibre tract localisation required for the prediction of visual outcome and surgical access (2). A four point classification system is employed with sub-classifiers to provide detailed tumour evaluation, coupled with NF and tumour dissemination status, as follows:

Stage 1.

- 1a. Single optic nerve (L/R)
- 1b. Bilateral optic nerve (L>R, R>L)
- 1c. Cisternal segment of optic nerve (L, R, bilateral, L>R, R>L)

Stage 2.

- 2a. Central chiasm
- 2b. Asymmetric chiasm (L>R, R>L)
- H+. Hypothalamus involved
- H-. Hypothalamus not involved

Stage 3.

- 3a. Symmetric optic tract involvement
- 3b. Asymmetric optic tract involvement. (L>R, R>L)

Stage 4

- 4a. Diffuse posterior tracts
- 4b. Asymmetric posterior tracts (L>R, R>L)

Neurofibromatosis type 1 status:

NF1+

NF1-

Metastatic status:

M0 (no leptomeningeal dissemination)

M1 (leptomeningeal dissemination)

References

1. Dodge HW, Lowe JG, Craigh WM et al. Glioma of the optic nerves. Arch Neurol Psychiatr 1958;79:607-621
2. Taylor T, Jaspan T, Walker D. et al. Radiological classification of optic pathway gliomas: experience of a modified functional classification system. Br J Radiol 2008;81:761-76.
3. Kornreich L, Blaser S, Schwarz M et al. Optic pathway glioma: correlation of imaging findings with the presence of neurofibromatosis. Am J Neuroradiol 2001;22:1963-69
4. Parsa C, Hoyt CS, Lesser RL et al. Spontaneous regression of optic gliomas. Arch Ophthalmol 2001;119:516-29
5. Parazzini C, Triulzi F, Bianchini et al. Spontaneous involution of optic pathway lesions in Neurofibromatosis Type 1: serial contrast MR evaluation. Am J Neuroradiol 1995;16:1711-18

Histology

Histological assessment and diagnosis of OPG should be performed by an accredited pathologist who is registered as Neuropathologist or Histopathologist, has specialised expertise in Neuro-oncology and takes part in the national External Quality Assurance scheme for Neuropathology organised by the British Neuropathological Society.

OPG are predominantly benign pilocytic astrocytomas. Because of their typical clinical presentation and classical imaging characteristics, biopsy is not routine practice at presentation, particularly in “imaging-typical” tumours associated with NF1. Imaging-typical *sporadic* tumours may also be treated without biopsy.

Pilocytic astrocytoma are WHO Grade I tumours, and generally do not transform to more malignant tumour phenotypes, although rare examples of pilocytic astrocytomas undergoing malignant transformation have been reported. Pilocytic astrocytomas have a characteristic biphasic histological appearance, with solid areas often containing Rosenthal fibres and cystic areas with granular eosinophilic bodies. However, a wide spectrum of pathological appearances can occur, and care should be taken to distinguish a predominantly solid pilocytic astrocytoma from a diffuse fibrillary astrocytoma WHO grade II.

Leptomeningeal infiltration is particularly common in pilocytic astrocytomas of the optic nerve, and may result in deposition of reticulin around the area of infiltration. Involvement of the subarachnoid space is not indicative of aggressive behaviour, although distant spread may rarely occur.

Pilomyxoid astrocytomas are related to pilocytic astrocytomas, and occur most often in the hypothalamic/chiasmatic region in young children, but has been reported in adults. These tumours are characterised by a monomorphous bipolar cells in a perivascular arrangement within a mucoid matrix. Pilomyxoid astrocytomas behave in a more aggressive fashion

than pilocytic astrocytoma, with local recurrence and dissemination occurring more frequently.

Diffuse astrocytomas WHO grade II involving the hypothalamus / chiasmatic structures can occur; these usually have a fibrillary morphology and behave more aggressively than pilocytic astrocytomas. In adults, these tumours have the capacity to transform to more malignant phenotype (anaplastic astrocytoma WHO grade 3 or glioblastoma WHO grade 4). Rare examples of the primary occurrence of anaplastic astrocytomas and glioblastomas in the optic pathway in adults have been reported.

Mixed neuronal-glial tumours (ganglioglioma) involving the optic pathway have also been reported in young adults, most of which are WHO grade I lesions.

Reference:

Louis D, Ohkagi H, Wiestler O, Cavenee WK (eds). *WHO Classification of Tumours of the Central Nervous System*. IRAC, Lyon, 2007.

Data items for future audit

- Vision outcome studies correlating PLAN score and treatment with visual outcome
- Audit access to specialist rehabilitation resources those affected by visual impairment and NF1.
- Comparative survivorship outcomes in people with sporadic versus NF1 OPGs.
- Late Effects and Tumour Surveillance: The value of surveillance for late effects after any treatment but radiotherapy in particular and the risk of recurrent or second tumours in sporadic versus NF1 associated OPGs.

Treatment

It can be anticipated that there are a number of scenarios where people with OPG may present in adulthood. They include OPGs arising and diagnosed in childhood or adolescence, and presenting with either:

- new progressive symptoms after prior observation alone
- new progressive symptoms after prior chemotherapy
- new progressive symptoms after prior radiotherapy
- new progressive symptoms and radiological evidence of high grade transformation (We believe this is very rare)
- symptoms and / or radiological evidence of second malignancy

Investigational evidence of long-term effects of therapy alone or (more commonly) combined with the effects of the tumour itself such as:

- Endocrine Syndromes: Hypothalamic syndrome, Pan Hypopituitarism, Infertility
- Visual handicap with change in visual function
- Neuropsychological or psychiatric symptoms e.g. learning difficulties, organic psychiatric disorder, affective disorder
- New or persisting neurological symptoms or deficit
- Rehabilitation, social and survivorship issues

Clinical Approach: Organisation of services

The IOG for Children and Young People defines standards for service delivery for teenager and young adults (TYA, up to age 24) with cancer. Therefore TYA with brain tumours need to be managed in a setting which complies with these generic standards.

Key principles include the following:

Planning, commissioning and funding for all aspects of care TYA with cancer, across the whole healthcare system, should be coordinated to ensure that there is an appropriate balance of service provision and allocation of resources. The principle that underpins the guidance is that of age-appropriate, safe and effective services as locally as possible, not local services as safely as possible. Commissioners should ensure, through cancer networks in partnership with services for TYA, that:

- there is a clear organisational structure for these services, including a cancer network lead for TYA with cancer – all aspects of care for TYA with cancer should be undertaken by appropriately trained staff
- principal treatment centres for each cancer type are identified for TYA, with associated referral pathways, including to centres outside the network of residence when necessary
- principal treatment centres are able to provide a sustainable range of services, with defined minimum levels of staffing, as outlined in the guidance
- shared care arrangements are established, which identify a lead clinician and lead nurse and have approved clinical protocols for treatment and care, and defined areas of responsibility with the principal treatment centres
- all sites delivering cancer therapy in this age group should be subject to peer review
- all relevant national guidance is followed

Care should be delivered throughout the patient pathway by multidisciplinary teams (MDTs), including all relevant specialist staff. Membership and governance of these teams should be explicit and include clearly defined responsibility for clinical and managerial leadership.

Appropriately skilled, professional key workers should be identified to support individual children and young people, and their families, by:

- coordinating their care across the whole system and at all stages of the patient pathway providing information in an appropriate format for people with learning difficulties or visual impairment typical of OPGs
- assessing and meeting their needs for support.

All care for young people of 19 years and older should also have unhindered access to age-appropriate facilities and support when needed. All TYA must have access to tumour-specific or treatment-specific clinical expertise as required.

Theatre and anaesthetic sessional time should be adequately resourced for all surgical procedures, including diagnostic and supportive procedures, in addition to other definitive tumour surgery. Anaesthetic sessional time should also be assured for radiotherapy and painful procedures. The surgeon with a commitment to oncology should have access to emergency theatre sessions during routine working hours.

All TYA with cancer should be offered entry to any clinical research trial for which they are eligible and adequate resources should be provided to support such trials. Participation in trials must be an informed choice.

TYAs with cancer who are not participating in a clinical trial should be treated according to agreed treatment and care protocols based on expert advice, and resources provided to monitor and evaluate outcomes.

The issues related to the registration of cancers in 15–24-year-olds and the potential value of a dedicated register within the structures of the National Cancer Registries should be addressed urgently.

The need for trained specialist staff across all disciplines, able to work with TYA with cancer, should be included in workforce development plans by cancer networks, to ensure the provision of a sustainable service.

Specific attention is required to address the shortage of allied health professional expertise in this area and the evaluation of the contribution of such services.

Agencies that can be of help for patients with visual impairment and NF1 are listed in Appendix 1.

Surgery

By definition, due to their location, surgery of any sort for one of these tumours results in almost inevitable damage to the optic nerve or pathway and where imaging characteristics are classical biopsy cannot usually be justified. Similarly where useful vision is maintained on the side of the tumour it is hard to argue for debulking or resective surgery. The risks of surgery are not just to the optic pathway itself but to the vascular supply to adjacent structures such as the hypothalamus and pituitary.

On the other hand these are generally benign tumours with an expansile nature and are not necessarily infiltrative and in the context of failing or useless vision on one side the argument is increasingly made for debulking or resective surgery to protect vision on the good side, potentially controlling hydrocephalus and delaying radiotherapy in what is often a young patient group.

Simplistic historical statements that “surgery is not an option for optic pathway tumours due to their location” are unhelpful and it is probably better to have a strategy of managing these patients on an individualised basis.

Where biopsy is sought due to atypical imaging appearances this may be carried out either under direct vision using an open craniotomy approach for tumours around the optic nerve and chiasm or via a burr hole using an image guidance system for very large or more posteriorly situated lesions.

Large tumours can result in hydrocephalus of an obstructive nature while very proteinaceous CSF may lead to an element of communicating hydrocephalus. CSF shunting and surgery to decompress tumour related cysts will have a role in some patients. Debulking of large tumours is most likely to be valuable where continued growth is threatening or causing neurological deterioration. Radical or complete resections will be unusual especially in the region of the hypothalamus where the surgeon should be wary of the risks of causing post operative hypothalamic syndrome which is not compatible with good quality life.

Radiotherapy Protocol

Best evidence for vision sparing effect in older children and adulthood, contra-indicated to NF1 due to high risk of 2nd tumours, exceptions occur if complication considered life threatening.

Indications for RT

Treatment at diagnosis: severe neurological symptoms, severe ophthalmic symptoms.

Treatment after observation: progressive neurological symptoms, progressive ophthalmic symptoms, neuroradiological progression.

Timing of Radiotherapy

Treatment should commence within six weeks of surgery for patients receiving postoperative RT, or within four weeks of decision to treat for patients deemed not suitable for surgery.

Diagnostic Imaging for Target Volume Definition

In order to assess the precise extent of tumour growth MR scanning including contrast enhanced T1, T2 weighted or 'flair' imaging is necessary. For treatment planning preoperative and postoperative imaging is necessary.

Treatment technique

It is necessary to minimise the volume of normal tissue exposed to a high RT dose. Three-dimensional conformal RT (3D-CRT) is therefore mandatory. Conformal techniques should be used to minimise irradiation of normal tissue. In addition, the dose to Organs at Risk (OARs) should be recorded. Whenever feasible image fusion of diagnostic MRI and planning CT-scans should be used to determine the target volume. The use of Intensity Modulated radiotherapy (IMRT) may be considered appropriate for individual patients.

Target volumes

Target volumes will be defined according to the ICRU 50/62.

The GTV encompasses the visible tumour as seen on MR (T2 weighted or flair images). If surgery was performed, postoperative delineation of residual disease will be used for treatment planning. In the case of postoperative treatment the GTV should include the surgical excision site. The preoperative scans are used to identify regions of possible tumour infiltration. It is not necessary to entirely encompass areas of cerebral oedema.

For the CTV an additional margin of 0.5 cm should be added along areas of potential tumour infiltration. When defining CTV anatomical boundaries (e.g. skull) should be taken into account.

The PTV encompasses the CTV with an additional margin according to the precision of treatment technique (e.g. 0.2 - 0.5 cm if rigid head fixation and 0.5 - 1.0 cm if a conventional face masks/head shell is used) depending on departmental policy.

Dose specification

RT dose is specified according to the ICRU 50/62 report. The ICRU reference point by definition is located in the centre of the target volume. Dose inhomogeneity within the target volume should not exceed the tolerance limits of between 95% and 107%.

Dose prescription

The RT dose of 54.0 Gy should be administered in a fractionated dose of 1.8 Gy daily, 5 days per week. All fields should be treated daily.

Patient positioning

It is recommended that an individualised face mask (head shell) is used. An alternative would be a rigid head fixation device (e.g. GTC frame etc).

Craniospinal Radiotherapy (CSRT)

CSRT should be considered for the very rare patients who present with leptomeningeal metastatic disease.

For recommended CSRT target volume definition and treatment techniques please refer to the protocol for medulloblastoma/PNET or for intracranial germ-cell tumours.

Radiotherapy Dose for CSRT

Brain: 35.0 Gy in 21 fractions of 1.67 Gy.

Spine: 35.0 Gy in 21 fractions of 1.67 Gy.

Boost to intracranial metastatic deposits or primary site: 20.0 Gy in 12 fractions of 1.67 Gy.

Boost to spinal metastatic deposits: 15.0 Gy in 9 fractions of 1.67 Gy.

Acute treatment related toxicity

Routine steroid prophylaxis of cerebral oedema is not mandatory during radiotherapy. If cerebral oedema occurs dexamethasone should be given orally or iv, if necessary.

Chemotherapy / Drug therapy

Indications for chemotherapy

- Heavily pre-treated patients who have had prior Radiotherapy in whom repeat radiotherapy, by whatever technique (gamma knife, conformal or Proton Beam techniques) is considered to be associated with unacceptable risks.
- Contemporaneous evidence of low grade histology (grade 1 / 2), progressive disease on imaging and evidence of symptomatic progression.

Drug selection

The selection of drugs is problematic. The evidence for the benefit of chemotherapy comes from its use in young children where the aim of treatment is to delay radiotherapy until after 5-8 years of age. In phase 2 studies in this age group, response has been defined as static disease, partial response and complete response. Nearly all drugs and combinations of drugs show similar response rates of 50% -70% response rates. There is no current evidence that tumours become resistant to chemotherapy. Recent consensus has identified that future studies should be stratified by age so as to ensure that results are not confounded by age at the time of treatment.

There are no studies of the use of chemotherapy in adult OPGs whether they are associated NF, or are sporadic.

The drugs used and their associated toxicities are therefore strongly influenced by the age of the patients.

The mechanism of action of these chemotherapy drugs in these benign tumours is not understood. It is not clear whether they are acting by arresting cell division or acting as anti-angiogenic agents.

Current biological research is identifying a whole new range of genetic mutations associated with these grade 1 and 2 tumours. There are now research based animal models of NF associated OPG. New biological agents are therefore in pre-clinical and phase 1 trial.

The evidence for conventional chemotherapy therefore is not directly applicable to the adult population. As a consequence chemotherapy or other drug therapy within this guideline can only be recommended within the context of a clinical trial. If one is not available, an individualised consultation with those working in the field within the Adult and Paediatric NCR Brain Tumour Clinical Study Groups is recommended.

Rehabilitation

Visual impairment:

People with OPG are almost always visually impaired and at least 50% are associated with NF1. Rehabilitation of someone acquiring visual impairment is highly specialised and dependent upon the combined support from local authorities, further education, employment advisors and the RNIB and other charitable support groups (see appendix 1)

Neurofibromatosis type 1:

NF1 population have low average IQs as a group although the range of IQ is the same as the normal population. There are well recognised specific learning problems including impaired spatial awareness, fine and gross motor inco-ordination, Attention Deficit Hyperactivity Disorder, reading and language difficulties. They may have delayed development throughout their childhood and adolescence. They may have serious concerns about their facial appearance. These serious problems when compounded by visual impairment may mean that affected individuals will be unable to live independently, they may be socially isolated from family and friends and unable to work. These psychosocial impacts can be significant and require careful attention. In making clinical decisions they may need special assessment and support within the Mental Capacity Act 2005.

Clinical assessment of NF cases

Patients presenting with OPGs associated with *NF1* should in addition be offered access to:

- Regional NF clinics in genetics units

- National Commissioning Group (NCG): Complex NF1 Service Sites:
 - Guys and St Thomas's NHS Foundation Trust
 - Central Manchester University NHS Foundation Trust referral should be made if their case is complex
- UK NF Association

Sporadic OPG

Family involvement in the detailed decision making surrounding the OPG will, in most cases have been extensive previously. It is entirely understandable that the family members previously involved may wish to be part of clinical discussions as their expertise may be considerable and also the implications of any clinical decisions may have profound consequences upon the family subsequently.

Supportive care, Rehabilitation and General palliative care

Any tertiary treatment centre has to demonstrate a robust pathway for accessing and providing the necessary support services.

When considering the supportive care for patients with primary CNS lymphoma, PNET, optic glioma, and pineal tumour, few centres and clinicians will gain wide experience in their management because of their rarity (NICE 2006). This means these patients present particular problems in management and service co-ordination. They may need long-term monitoring due to problems associated with their disease and/or its treatment e.g. physical and cognitive impairment.

Patients diagnosed with these tumours require input from a well co-ordinated multi-professional team (NICE 2006:Table 8 p37), to support their complex changing care needs throughout the patient pathway. This approach does not differ from other patient groups with disease affecting their CNS (RCP, NCP & BSRM 2008; NICE 2006; NSF 2005; NICE 2004).

“Supportive Care is an umbrella term encompassing the work of a broad range of healthcare professionals to address the changing needs of patients, their relatives and carers throughout the patient journey” (NICE 2006). This has been extensively described in previous national guidances (NICE 2004: Ch10; 2006: Ch8) in order to optimise patients' quality of life. Support services will include Allied Health Professionals (AHP) and other professionals within the multi professional team:

Core Members of Supportive Care services

- Physiotherapists
- Occupational Therapists
- Speech & Language Therapists

- Dietitians

Extended members of Supportive Care services

- Nurses
- Primary healthcare team
- Neuropsychology, neuropsychiatry and psychological therapy
- Social services and care managers/ continuing care manager
- Orthotic/appliance officer
- Wheelchair and other equipment services
- Chaplaincy and bereavement services
- Ophthalmologist services
- Complementary therapy services (NICE 2006:111)

Referral to supportive care services should not be dependent on diagnosis, but on patient need (CAT 2010, NICE 2006). Intervention may be required at any stage of the patient's disease trajectory dependent on presentation of their symptoms: pre – diagnosis, diagnosis, initial treatment, post treatment, disease progression and end of life care (CAT 2010, NICE 2006, NICE 2004) – see appendix 4 (Symptom related referral pathway to supportive care services for patients with CNS tumours).

Observational studies show patients with 1° CNS tumours can benefit from rehabilitation intervention (CAT 2010). This is predominantly identified in inpatient multi-professional units (Geler-Kulcu et al 2009, Tang et al 2008, Greenberg *et al.* 2006, Giordana & Clara 2006, Garrard et al 2004, Huang et al 1998, 2000, 2001 a & b, Mukand et al 2001, Marciniak et al 2000, Sliwa & Marciniak 1999, O'Dell et al 1998, Marciniak et al 1996) and some out patient settings (Giovagnoli et al 1999, Sherer et al 1997). All demonstrate the importance of rehabilitation to improve function and facilitate discharge to the community for these patients. Current evidence regarding timing of rehabilitation in relation to medical treatment e.g. radiotherapy treatment, is inconclusive (Marciniak 1996, Huang *et al.* 2001). However, based on theoretical evidence concerning neuroplasticity and brain tumours (Duffau 2006, 2008) and parallel literature concerning therapy intervention (DH 2007), rehabilitation intervention should begin as early as possible to optimise rehabilitation opportunities and functional participation in society (CAT 2010).

The importance of timely access to appropriate rehabilitation services is dependent on rapid, comprehensive communication between AHP's. This is discussed in NICE 2006 and echoed in other evidence based guidance for patients with long-term neuro-degenerative conditions (CAT 2010, RCP, NCPC & BSRM 2008; MSS 2008; MNDA 2004). These recommend early referral to specialist rehabilitation services when patients present with symptoms affecting their independence and/or participation in their current environment. They advocate ongoing, comprehensive assessment and provision of support according to

patient's changing needs. This may include integrated care planning by health, social services and the voluntary sector.

According to their individual diagnosis and treatment, the particular clinical features of these patients will fluctuate, change and ultimately deteriorate. These may be as a consequence of the patient's disease, prognosis and/or treatment related side effects.

To ensure a holistic approach, it is essential that local service provision provides specialist rehabilitation including: vocational/leisure interests, equipment, environmental adaptation, and psycho-social support (RCP, NCPC & BSRM 2008, DH & Macmillan Cancer Support 2009). Ongoing re-assessment at key stages of the patient pathway is recommended (CAT 2010, NICE 2006, NICE 2004). NICE 2004 also acknowledges the need for patients to obtain reliable information about complementary therapy services and empower them to make informed decisions regarding their use.

The need for psychological support services including neuropsychology and neuropsychiatry for patients with CNS disease is advocated in previous guidance (RCP, NCPC & BSRM 2008; MSS 2008, NICE 2006, NSF 2005, NICE 2004).

The emotional and spiritual needs of the patient, family and carers must be recognised by the multi professional team throughout the patient pathway from pre-diagnosis to end of life care. Additionally, patients may substantially benefit from early contact (as soon after diagnosis as possible) with dedicated brain tumour-specific charities and not-for-profit organisations which offer face-to-face, telephone and online support opportunities as well as a wide range of comprehensive, practical information regarding brain tumours. Talking through the challenges of brain tumours with other patients and caregivers who are on the same journey can provide a unique level of emotional support and hope. Appropriate local spiritual support and bereavement care services support should be accessed (NICE 2004, NICE 2006). See appendix 3.

References

1. CAT (2010) Cancer and Palliative Care Rehabilitation Care Pathways (draft). Cancer Action Team. London
2. Cole, R.P. Scialla, S.J. Bednarz, L. (2000) Functional recovery in cancer rehabilitation. *Archives of Physical Medicine and Rehabilitation* 81(5) pp 623-7
3. DH (2007) National Stroke Strategy, Department of Health. London. available at http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_081062 [accessed online 28.7.09]
4. DH and Macmillan Cancer Support (2009) Vocational Rehabilitation Strategy Paper: A proposed model of vocational rehabilitation in cancer. National Cancer Survivorship Initiative Work and Finance Workstream, London November 2009
5. DH 2009 National Cancer survivorship initiative
6. Duffau H (2006) Brain plasticity: from pathophysiological mechanisms to therapeutic applications. *Journal of Clinical Neuroscience* 13:885-897

7. Duffau H (2008) Brain Plasticity and tumours. *Advances and Technical Standards in Neurosurgery* 330: 3-33 - DOI-10.1007/978-3-211-72283-1_1
8. Garrard, P et al (2004) Rehabilitation of the Cancer Patient: Experience on a Neurological Unit *Neurorehabilitation & Neural Repair* 18 (2) pp 76-79
9. Geler-Kulcu, D Gulsen, G Buyukbaba Ozkan, D (2009) Functional recovery of patients with brain tumour or active stroke after rehabilitation: a comparative study *Journal of Clinical Neuroscience* 16:74-78
10. Giordana, MT and Clara, E (2006) functional rehabilitation and brain tumours patients. A review of outcome. *Journal of Neurological Sciences* 27:240-244
11. Giovagnoli, AR (1999) Quality of life in patients with stable disease after surgery, radiotherapy, and chemotherapy for malignant brain tumour *Journal of Neurology, Neurosurgery and Psychiatry* 67 pp 358-363
12. Greenberg, E. Treger, I. Ring, H. (2006) Rehabilitation outcomes in patients with brain tumours and acute stroke. *American Journal of Physical Medicine and Rehabilitation* 85(7) pp 568-73
13. Huang, ME, Cifu DX, Marcus, LK (1998) Functional outcome following brain tumour and acute stroke: a comparative analysis *Physical Medicine & Rehabilitation* 79 pp1386-90
14. Huang, ME, Cifu DX, Ketser-Marcus, L (2000) Functional outcomes in patients with brain tumour after in-patient rehabilitation: Comparison with traumatic brain injury *Physical Medicine & Rehabilitation* 79 (4) pp 327-335
15. Huang, ME Wartella, J Kreutzer, J Broaddus, W Lyckholm, L (2001a) Functional outcomes and quality of life in patients with brain tumours: a review of the literature. *Brain Injury* 10 pp843-56
16. Huang, ME Wartella, JE Kreutze, JS (2001b) Functional outcomes and quality of life in patients with brain tumours: a preliminary report *Archives of Physical Medicine and Rehabilitation* 82 pp1560-6
17. Marciniak, C.M. Sliwa, J.A. Spill, G.E. Heinemann, A.W. Semik, P.E. (1996) Functional outcome following rehabilitation of the cancer patient. *Archives of Physical Medicine and Rehabilitation* 77 pp 54-7
18. MSS (2008) Translating the NICE and NSF guidance into practice: A guide for physiotherapists Second Edition. London Available online at <http://www.mssociety.org.uk> [accessed 3.8.09]
19. Mukand JA, Blackinton DD, Crincoli MG, Lee JJ, Santos BB (2001) Incidence of neurological deficits and rehabilitation of patients with brain tumours *American Journal of Rehabilitation Medicine* 80 pp346-50
20. NICE (2004) *Guidance on Cancer Services: Improving Supportive and Palliative Care for Adults with Cancer* chapter 10. National Institute for Clinical Excellence, London.

21. NICE (2006) *Guidance on Cancer Services: Improving outcomes for people with tumours of the brain and central nervous system*, National institute for Clinical Excellence, London
22. NSF (2005) *The National Service Framework for Long- term conditions*. Department of Health. London
23. O'Dell, MW Barr, K Spainer, D Warnick, RE (1998) Functional Outcome of inpatient rehabilitation in persons with brain tumours *Archives of Physical Medicine* 79 pp 1530-4
24. RCP, BSRM, NCPC (2008) *Long-term neurological conditions: management at the interface between neurology, rehabilitation and palliative care: concise guidance to good practice No 10*. Royal College of Physicians, British Society of rehabilitation Medicine, National Council for palliative Care Services. London
25. Sherer, M Meyers, CA Bergloff, P (1997) Efficacy of post acute brain injury rehabilitation for patients with primary malignant brain tumour *Cancer* 80(2) pp250-7
26. Sliwa, JA Marciniak, C (1999) Physical rehabilitation of the cancer patient *Cancer Treatment and Research* 100 pp 75-89
27. Tang V, Rathbone M, Dorsay JP, Jiang S, Harvey D (2008) Rehabilitation in primary and metastatic brain tumours. Impact of functional outcomes on survival. *J Neurol* 255: 820-827

Specialist palliative care

Progression of OPG threatening life is extremely rare however there are circumstances where large tumours often with a long history continue to progress locally and cause progressive neurological dysfunction, disturb CSF circulation which, coupled with the consequent physical disability can lead to death. Another scenario, perhaps more common, is the development of progressive malignant peripheral nerve sheath tumour in patients with NF1 who have had prior radiotherapy. Similarly other intracranial tumours such as meningioma or secondary high grade gliomas may present with the need for palliative care.

The World Health Organization (WHO) has defined palliative care as “an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual” [1]. Palliative care “is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications” [1]. This philosophy is endorsed in the NHS Cancer Plan [2], the Improving Supportive and Palliative Care for Adults with Cancer document [3], and the Improving Outcomes for People with Brain and Other Central Nervous System Tumours document [4].

Palliative care specialists have a particular role in the management of “difficult-to-control” symptoms, and in the planning and provision of end of life care. The remit of specialist palliative care services is discussed in detail in the Improving Supportive and Palliative Care for Adults with Cancer document [3], whilst the Department of Health’s guidance on end-of-life care is set out in detail in the End of Life Care Strategy document [5].

The management of difficult-to-control symptoms involves adequate assessment, appropriate treatment, and adequate re-assessment (i.e. review of the efficacy and tolerability of the treatment). The objective of assessment is to determine the aetiology of the symptom. Thus, many of the symptoms associated with PNETs are non-specific (e.g. headache, nausea and vomiting), and patients may also experience these symptoms as a consequence of the anticancer treatment, the supportive care treatment, or a co-existent medical condition [6,7]. Inadequate assessment may result in the initiation of inadequate or inappropriate treatment, which will inevitably result in continuation of the problem (and possibly loss of confidence in the ability of members of the MDT by the patient and their carers).

Headache due to tumour or raised intracranial pressure may be effectively managed in the short term by corticosteroids, and / or conventional analgesic drugs. However, corticosteroids are rarely effective in other causes of headache (e.g. migraine, “tension type headache” [6]), and although conventional analgesic drugs may be effective for many causes of headache, they may not be the most appropriate treatment for specific causes of headache [6]. It should be noted that there is almost no data on the management of specific symptoms in patients with adult PNETs, and so treatment strategies need to be extrapolated from patients with other CNS tumours (and indeed patients with other types of cancer).

In addition to providing advice and assessment of difficult-to-control physical symptoms throughout the disease trajectory, referral may be particularly beneficial in patients with advanced disease. In this situation, management of challenging physical symptoms (e.g. pain, sleep disturbance, seizures at the end of life) and any associated psychosocial or spiritual symptoms can be addressed. Planning for the future is imperative as patients with PNETs may undergo progressive cognitive impairment, personality changes and communication difficulties. Advance care planning – the voluntary process of discussing wishes and preferences for future care, should be offered early whilst the patient has the capacity to make those decisions. National guidance is available on how to manage advance care planning in clinical practice from the Royal College of Physicians [8] and Advanced Care Planning section of the National End of Life Care Programme [9].

When a patient has entered the terminal phase of their illness and it is recognised that a patient is actively dying, integrated pathways for the care of the dying, such as the Liverpool Care Pathway of the Dying Patient [10], should be considered. These can be used in any setting, and the use of such pathways has been recommended from the End of Life care programme and more recently in the End of Life Care Strategy [5]. There is a paucity of data specific to the management of patients with brain tumours and the end of life. Local palliative care teams can provide guidance on specific symptoms e.g. continuing regular opioid analgesia or anticonvulsant medication via the subcutaneous route when the oral route is not possible.

Patients with advanced OPGs who are approaching end of life may still be on long term maintenance doses of steroids. If they become unable to take oral medication, the decision needs to be taken whether or not the steroids should be discontinued abruptly, weaned or given parenterally. There is no evidence on the best practice and the decision needs to be made on an individual basis, although symptoms that might arise as a result of withdrawal can usually be dealt with by adjusting the patient's other medication (e.g. in a subcutaneous syringe driver), thus ensuring optimal symptom control continues.

References

- [1]. World Health Organization. National Cancer Control Programmes. Policies and Managerial Guidelines, 2nd edn. Geneva: WHO; 2002.
- [2]. Department of Health. The NHS Cancer Plan: A Plan for Investment, a Plan for Reform. London: DOH; 2000.
- [3]. National Institute for Clinical Excellence. Improving Supportive and Palliative Care for Adults with Cancer. London: NICE; 2004.
- [4]. National Institute for Health and Clinical Excellence. Improving Outcomes for People with Brain and Other Central Nervous System Tumours. London: NICE; 2006.
- [5]. Department of Health. End of Life Care Strategy. Promoting high quality care for all adults at the end of life. London: DOH, 2008.
- [6]. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders, 2nd edn. Oxford: Blackwell Publishing; 2004.
- [7]. Mannix KA. Palliation of nausea and vomiting. In: Doyle D, Hanks G, Cherny N, Calman K (eds). Oxford Textbook of Palliative Medicine, 3rd edn. Oxford: Oxford University Press; 2004. pp.459-68.
- [8]. Royal College of Physicians, National Council for Palliative Care, British Society of Rehabilitation Medicine, British Geriatrics Society, Alzheimer's Society, Royal College of Nursing, Royal College of Psychiatrists, Help the Aged, Royal College of General Practitioners. Advance Care Planning. Concise Guide to Good Practice, No12. London: RCP, 2009.
- [9] Advance Care Planning: A guide for Health and Social Care Staff. London: NHS End of Life Care Programme publication supported by NCCP. Updated August 2008. Gateway Reference: 7793. Accessed via: <http://www.endoflifecare.nhs.uk/eolc/acp.htm>.
- [10] Liverpool Care Pathway for the Dying Patient (LCP). Available from: <http://www.mcpcil.org.uk/liverpool-care-pathway/index.htm>

Survivorship / Living with cancer

The supportive care issues and recommendations outlined in the NICE guidance 'Supportive Care and Continuing Care of People with Brain and Other CNS Tumours' (NICE 2006) and 'Improving Supportive and Palliative Care for Adults with Cancer' (NICE 2004) should be referred to and followed for adults with Optic Pathway Glioma. Similarly, the Cancer and Palliative Care Rehabilitation Care Pathways (CAT 2010), due for publication, should be followed.

The Department of Health National Cancer Survivorship Initiative Vision document (2010) sets out that all cancer survivors should have:

- A personalised assessment and care plan;
- Support to self-manage their condition;
- Information on the long-term effects of living with and beyond cancer; and
- Access to specialist medical care for complications that occur after cancer.

The specialised requirements for treatment of this rare tumour type require a key worker to co-ordinate treatment across both local and potentially distant specialised treatment centres, in order to develop and deliver such a personalised approach to the care of the brain tumour patient. This role should be available throughout the patient pathway, and the patient and their family should be informed if their key worker changes.

Ongoing emotional support is required for these patient groups and their families/carers. In addition, well co-ordinated treatment and appointments are essential, especially if patients require treatment at different centres and departments. Patient hand-held records may clarify who is responsible for various aspects of their care, and identify who to contact if they have changes in symptoms or concerns of any kind.

To ease the general financial burden, proactive advice should include comprehensive and supportive information. If treatment is required at a non-local specialised centre, travel and accommodation costs warrant discussion with patients and their families.

The key worker role should provide support and signposting to appropriate services:

- local health authority,
- charitable institutions which may provide grants for such purposes.
- state benefits
- Disability employment advisors at local Job Centres, for those patients fit enough to return to work

The welfare and support of the patient's primary carer and immediate family need to be considered at key points throughout the patient pathway. This must include appropriate management of the point of diagnosis, the end of each round of treatment, disease recurrence, the terminal phase and bereavement care (ref NICE 2004).

References:

CAT (2010) Cancer and Palliative Care Rehabilitation Care Pathways (draft). Cancer Action Team. London

National Cancer Survivorship Initiative Vision (2010) Department of Health, Macmillan Cancer Support and NHS. Improvement available for download from http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_111230 or www.ncsi.org.uk.

National Institute for Clinical Excellence (2004) Improving supportive and palliative care for adults with cancer. *NICE cancer service guidance*. Available from: www.nice.org.uk/csgsp

National Institute for Clinical Excellence (2006) Improving Outcomes for People with Brain and Other CNS Tumours. *NICE cancer service guidance*. Available from: <http://guidance.nice.org.uk/CSGBraincns>

Appendices

Appendix 1: Information Principles for Visually Impaired individuals

Accessing Information in the NHS

- Local Authority (Social Services) Sensory Impairment Teams. Rehab officers provide indoor and outdoor mobility training and training in practical skills i.e. cooking
- Connexions – Career advisory service
- FE colleges / disabled students support services
- Voluntary Sector
- RNIB Group (Includes RNIB and Action for Blind)
- RNIB Helpline 03031239999, helpline@rnib.org.uk
- Your rights (welfare benefits, legal rights and discrimination)
- Regional family support services
- Access technology for computers
- Employment advice (in resource centres and postal delivery service)
- Emotional service
- Talk and support

Leisure

- Vacation scheme (8-17 years)
- Actionaires Clubs (actionforblind.org.uk/children)
- RNIB National Leisure Services (holidays, sport and leisure)
- Library Services (all formats, including Talking Books)
- Soccer sight (audio description at football grounds)
- Audio description: television / theatre / cinema / art galleries
- National Talking Newspapers and Magazine (tel 01435 866102, tnauk.org.uk)
- Action Vision hotels (also them breaks, actionforblindpeople.org.uk/hotels)

Other organisations

Local societies for people for people with sight loss (RNIB Agencies Database <http://info.rnib.org.uk/Agencies/ukagencies.htm>)

Peer Support

- Importance for peer inspiration
- Social networking websites (using access technology)
- Vitalise holidays (group holidays with sighted guides, 0845 330 0149, vitalise.org.uk)
- Traveleyes Holidays (group holidays with sighted guides 0844 8040 221, traveleyes-international.com)
- British Blind Sport for participation and socialising. (britishblindsport.org.uk)
- Social and psychological impact of living with sight loss.

Appendix 2: Endocrinology

Endocrine consequences in rare brain tumours

Endocrine function in patients with rare CNS tumours may be affected either by direct impact of the tumour on the hypothalamic-pituitary axis (HPA) or secondarily as a consequence of treatment with surgery and/or radiotherapy and/or chemotherapy.

Among the treatment options, **surgical interventions** for tumours related to the HPA e.g. (removal and/or decompression of cystic tumours) may cause immediate detrimental effects on the function of the HPA.

Cranial irradiation

Damage to the HPA by **cranial irradiation** is well established (Duffner 1985, Sanaan 1987, Clayton & Shalet 1991, Oberfield 1997). The effects are delayed and may surface many years after therapy. The likelihood of a radiotherapy induced HPA dysfunction critically depends on the total hypothalamic / pituitary irradiation dose and its fractionation. Young children are more sensitive to irradiation than adolescents or adults (Brauner 1986). A threshold dose of > 60 Gy or a fraction dose of > 1.8 Gy to the HPA leads to an 80-100 % chance of pituitary dysfunction (Littley 1989). The various axes differ in sensitivity with posterior pituitary function being very resistant to irradiation (Vladyka et al 2003).

Outcome related to tumour type

There are few data on specific brain tumours and their relation to endocrine dysfunction. The questionnaire based American childhood cancer survivor study (CCSS) provided the most extensive set of data (Gurney 2003). With a mean cranial irradiation dose of 50-55 Gy **medulloblastomas and gliomas** appear to be associated with the highest rate of both hypothyroidism and GH deficiency (GHD), averaging 29% and 39% of patients. For **ependymomas** and **astrocytomas** the rate averaged at 11% and 11.5% for hypothyroidism and 11% and 16.5% for GHD respectively. In all tumours the rate of **osteoporosis** was at 3-5% (Gurney 2003).

Radiation effects on specific endocrine axes

I. GH

The sensitivity of the different endocrine axes towards radiation varies considerably. Growth hormone (GH) secretion is most frequently affected with the lowest irradiation doses followed by gonadotrophins, ACTH and TSH whereas diabetes insipidus is very rarely a problem (Littley, 1989, Clayton & Shalet 1991, Schmiegelow 1999, 2000). GH deficiency, particularly in children, occurs frequently after irradiation doses in excess of 30 Gy. But even with doses as low as 10 Gy a substantial proportion of children have defects in their GH secretion (Costin 1988, Ogilvy-Stuart 1992, Brennan 1998). The interval between irradiation and pituitary dysfunction varies widely and appears to be linked to the dose applied to the hypothalamus.

II. Gonadotrophins

Other hormone axes are less sensitive. The gonadotrophin axis may be transiently or permanently affected and is of particular interest because of its dual response to irradiation. Doses as low as 18 Gy applied to prepubertal children induce premature puberty, predominantly in girls. Higher doses up to 50 Gy may similarly affect both sexes (Leiper 1987, Ogilvy-Stuart 1994, Lannering 1997). A further increase in radiation dose to the HPA results in gonadal failure in children and adults. Thus, dose and timing of irradiation determine effects on puberty (Oberfield 1996). The time interval between radiotherapy and the manifestation of gonadal dysfunction may be many years (Pasqualini 1987, Sanders 1983, Schmiegelow 2001).

III. ACTH and TSH

The frequency of ACTH or TSH deficiencies (21 % and 9 % respectively) is comparable in children and adults (Agha 2005), and is dependent on dose (up to 35 % for ACTH with doses > 50 Gy) and time interval after radiotherapy (Samaan 1982, Lam 1991, Constine 1993). The observation that TSH deficiency is reported with a much lower incidence (Samaan 1982, Chen 1989, Pai 2001) may be explained by the diagnostic approach and highlights the importance of sensitive diagnostic tools to assess pituitary function. It is well known that bioactivity of TSH decreases as a result of hypothalamic-pituitary problems when immunoreactive TSH remains normal or high. This is believed to be based on the glycosylation of the molecule which is controlled by TRH (Beck-Peccoz 1985). For that reason TSH is no longer a sufficiently reliable marker in patients with suspected central hypothyroidism and the diagnosis should rely entirely on free thyroxine.

Metabolic late effects

Hypothalamic damage due to the primary tumour, surgery or irradiation with a dose exceeding 50 Gy is a major risk factor for the development of obesity in CNS tumour survivors. It may be associated with hyperphagia or reduced physical activity (Harz et al 2003). The presence of hormone deficiencies, particularly GH deficiency but also gonadal

and thyroid failure contribute to the changes in body composition (Lustig et al 2003; Ahmet et al 2006). Long-term survivors of childhood brain tumours irradiated with doses of 45 Gy or higher have an increased risk of elevated systolic blood pressure and a less favourable lipid profile (Heikens 2000). The resulting risk of metabolic syndrome is supported in the large CCSS cohort. When comparing patients to their siblings, patients demonstrated an excess increase in BMI of 0.41 kg/m²/yr in females and 0.29 kg/m²/yr in males, giving an average excess weight gain in female patients of more than 6 kg. These effects are seen over a broad range of irradiation doses (Garmey 2008, Shankar 2008).

Table: Risk factors for cancer-related disruption of pubertal timing (Fernandez 2009)

<ul style="list-style-type: none"> - Female sex - Radiation fields involving the hypothalamic region. Doses > 18 Gy can cause early puberty in girls and GHD. Doses > 24 Gy can cause early puberty in boys - Age at radiation exposure < 6 years - Scattered radiation to the thyroid bed (Primary hypothyroidism) can delay puberty - Doses to the gonads > 20 Gy: high risk of primary hypogonadism with pubertal failure. Greater risk in males with prepubertal radiation exposure - Neoplasms in the hypothalamic region: tumour compression, surgical injury and radiation toxicity cause delayed or absent puberty - b-HCG secreting tumours: germ cell tumours secreting b-HCG can induce pubarchia and phallic enlargement in male children, but do not induce early puberty in girls - Chemotherapy regimens with known gonadal toxicity: chlorambucil, melphalan, busulfan, cyclophosphamide, chlorambucil, melphalan and ifosfamide
--

References for Pubertal disorders in Cancer survivors: Nathan & Palmert 2005, Cohen 2005, Gleeson & Shalet 2004

Chemotherapy

The effects of **chemotherapy** are not yet conclusively defined. Large series of childhood cancer survivors suggest an increased frequency of endocrine late effects in patients treated with a combination of radiotherapy and chemotherapy. However, a consistent and independent direct effect of chemotherapy on the hypothalamic-pituitary regulation has not been determined. Only the gonadal axis appears to be sensitive to damage via certain chemotherapeutic agents inducing primary gonadal failure (Schmiegelow 2001, Gurney 2003). The toxicity is dose-dependent and can be induced by alkylating agents (including procarbazine, cisplatin, and vinblastine) or by drugs acting directly on the gonads (including doxorubicin, cyclophosphamide, melphalan, and chlorambucil) (Stava 2007). In addition, the posterior pituitary function may be altered by cancer therapy (Yeung 1998). Cytotoxic treatments with vinca alkaloids, cisplatin, cyclophosphamide, and melphalan may stimulate secretion of antidiuretic hormone (ADH) (Stava 2007).

Clinical assessment and diagnostic tools

The diagnosis of a defect in the HPA may be suggested by the clinical scenario, although symptoms of pituitary insufficiency may be non-specific particularly in adults (e.g. fatigue). Thus assessment based on questionnaires focussing on symptoms such as those used in the CCSS will underestimate the true rate of HPA deficiencies. However in children, growth failure, weight gain or loss, precocious or delayed puberty may provide clinical clues.

1. Symptoms of pituitary dysfunction
 - a. GH deficiency
 - i. In all patients muscle mass and strength may be decreased, visceral fat may be increased, patients are fatigued with a decreased quality of life, impairment of attention and memory. Children have a reduced growth velocity.
 - b. Gonadotrophin deficiency
 - i. Female patients show abnormalities of their cycle with oligo- or amenorrhea, infertility, loss of libido, and dyspareunia.
 - ii. Males lose their libido and show impaired sexual function. There may be mood changes and signs like loss of facial, scrotal, and truncal hair and decreased muscle mass.
 - iii. Children have a delayed or absent puberty.
 - c. ACTH deficiency
 - i. Patients may complain of weakness, nausea, vomiting, anorexia and/or weight loss. There may be circulatory problems such as hypotension, dizziness or collapse.
 - ii. Children may fail to thrive.
 - d. TSH deficiency
 - i. The main symptoms and signs are tiredness, cold intolerance, constipation, hair loss, dry skin, hoarseness and cognitive slowing.
 - ii. A significant sign in children is a reduced growth velocity and weight gain.
2. *Biochemical tests of HPA*
 - a. GH axis
 - i. As measurement of IGF-I alone is not sufficiently sensitive to define the status of the GH axis, dynamic tests are also necessary to delineate GH function. The insulin tolerance test (ITT) is still regarded as the gold standard for the evaluation of the GH axis. In brain tumour patients with epilepsy the ITT may be contraindicated. There are a number of other tests such as the arginine and glucagon stimulation tests that can be used, with the latter also being used (like the ITT) to evaluate the adrenal axis.
 - b. Gonadotrophin secretion

- i. Delayed or absent puberty with prepubertal levels of gonadotrophins and sex steroids indicate gonadal dysfunction
 - ii. Precocious puberty may be a direct consequence of low irradiation doses in prepubertal children.
 - iii. In adults oligomenorrhoea in females with oestradiol levels of <100 pmol/L and inappropriately low LH and FSH levels or lower than expected gonadotrophin levels in postmenopausal females confirm the diagnosis. In men testosterone levels are decreased (<10–12 nmol/L) with inappropriately low LH and FSH levels.
- c. ACTH secretion
 - i. Low morning levels of cortisol (< 100 nmol/l) would suggest the diagnosis.
 - ii. A stimulation test with a low peak cortisol (< 500 nmol/L in the ITT or in a short synacthen test with 250 µg ACTH) confirms the diagnosis.
- d. TSH secretion
 - i. TSH levels cannot reliably be used as a diagnostic marker. A free thyroxine levels < 11 pmol/L on more than one occasion suggests central hypothyroidism.
- e. Prolactin secretion
 - i. An increased prolactin level obtained under stress free conditions suggest hyperprolactinemia.
- f. ADH secretion
 - i. A urine volume of ≥ 40 ml/kg bodyweight per day with a urine osmolality of <300 mOsm/kg water would suggest diabetes insipidus.
 - ii. Water deprivation test until 12 noon following complete fluid restriction after midnight can confirm the diagnosis (urine osmolality <700 mOsm/kg; ratio of urine to plasma osmolality <2)

The demanding nature of these tests warrants referral to an endocrinologist whenever symptoms indicate a potential problem.

Diagnosis of Hypopituitarism (Fernandez 2009)

Pituitary function	Tests	Diagnostic value	Comments
Growth Hormone Deficiency (Billir <i>et al</i> 2002, Hartman <i>et al</i> 2002, Ghigo <i>et al</i> 2007)*	IGF-I (Hartman <i>et al</i> 2002)	41-69% Sensitivity, 95% Specificity	A normal result does not exclude GHD, but a low value in patients with multiple pituitary deficiencies makes a stimulation test unnecessary
	Insulin Tolerance Test (ITT) (Billir <i>et al</i> 2002, Clayton <i>et al</i> 2005, Maghnie <i>et al</i> 2005a)	-Sensitivity 89%, Specificity 95% for a cut-off of 9 mU/l (Billir <i>et al</i> 2002) in adult patients - In the transition period, cutoffs of 15 mU/l (Clayton <i>et al</i> 2005) and 18 mU/l (Maghnie <i>et al</i> 2005) have been advocated	- Gold standard for the diagnosis of GHD - Evaluates cortisol and growth hormone reserve - Only valid if nadir glucose value <2.2 mmol/l, close supervision required (Greenwood <i>et al</i> 1966) - Contraindicated in patients with stroke, epilepsy, coronary heart disease or heart failure - Lack of body mass index-adjusted reference values - Repeated hypoglycaemias can offset the stimulatory input of ITT in non growth hormone deficient subjects (Davis <i>et al</i> 2000, Davis & Tate 2001)
	Glucagon Test (Leong <i>et al</i> 2001, Gomez <i>et al</i> 2002, Conceicao <i>et al</i> 2003)	Sensitivity 97-100%, Specificity 88-100% for a cut-off of 9 mU/l	- Safe and accurate alternative to ITT - Evaluates cortisol and growth hormone reserve - Contraindicated if fasting >48 hours or clinical suspicion of pheochromocytoma or insulinoma - Lack of normative data for the transition period and obese patients
	GHRH + Arginine (Aimaretti <i>et al</i> 1998, Darzy <i>et al</i> 2003, Ghigo <i>et al</i> 2007)	- 95% Sensitivity and 85% Specificity for a cut-off of 13.8 mU/l (Billir <i>et al</i> 2002) - 100% Sensitivity and Specificity for a cut-off of 27 mU/l (Aimaretti <i>et al</i> 1998)	- Safe and accurate - Body mass index-related normative data are available - Less sensitive than ITT in initial phases of radiation-induced GHD (Darzy <i>et al</i> 2003) - Optimal performance requires specific cut-offs (Aimaretti <i>et al</i> 1998, Ghigo <i>et al</i> 2007)
Gonadotroph deficiency (Verga 2002, Bhasin <i>et al</i> 2006, Kazi <i>et al</i> 2007)	-Men: 9 am Total Testosterone, FSH, LH - Clinical assessment of symptoms of androgen deficiency	Low testosterone values in at least 2 consecutive measurements are required for diagnosis	- Prior to biochemical measurements, intercurrent illnesses need to be excluded - Drugs and conditions affecting sex-hormone-binding globulin values can interfere with total testosterone levels. Estimated free testosterone index is recommended in those instances - Age-related total testosterone reference ranges currently lacking
	-Premenopausal women: FSH, LH, Oestradiol + Menstrual History (Verga 2002)	- Low oestradiol levels + low/normal FSH and LH levels in the follicular phase of the menstrual cycle - Oligoamenorrhoea	Clinically and/or biochemically oriented exclusion of other causes of menstrual disorders is required: functional hypothalamic hypogonadism, hyperprolactinaemia, primary ovarian failure (premature, menopausal), hyperandrogenism and drug interference

Minimal requirements for endocrine follow-up

- It is desirable that pituitary hormones are measured before the initial tumour therapy in all cases where the tumour affects hypothalamic or pituitary structures and may thus have induced pituitary dysfunction.
- Patients, who received chemotherapy only, should be scrutinized for
 - Disorders of the gonadal axis such as delay in menarche, pubertal development, oligo-, amenorrhea, infertility or loss of libido.
 - Uncharacteristic symptoms like fatigue indicative of other pituitary dysfunction such as central hypothyroidism or GH deficiency
- In patients treated with brain irradiation
 - Weight, blood pressure, serum glucose and lipid levels should be monitored regularly.
 - Basal pituitary function should be checked at 2-yearly intervals even in the absence of any symptoms during the first 10 years following radiotherapy. Minimal evaluation in adults should include morning cortisol, TSH, fT4, and IGF-I. Females should be screened for changes in regular menstrual cycles. In males morning testosterone levels needs to be assessed.
 - As early HPA dysfunction may be difficult to diagnose further dynamic testing of the pituitary axis may be warranted in all subjects with any of the non-specific clinical symptoms or signs of an endocrine disorder. Referral to a specialist in endocrinology should be mandatory.
 - In children, evaluation of growth velocity and pubertal development should be undertaken at least 6 monthly with pituitary function testing if there is any concern. It is important to recognise that early puberty may lead to a relatively normal growth rate in the presence of GH deficiency.
 - 10 years after radiotherapy, treatment should be stratified according to symptoms indicative of pituitary dysfunction.

Appendix 3: Additional support for brain tumour patients and carers

Additionally, patients and carers may substantially benefit from early contact (as soon after diagnosis as possible) with dedicated brain tumour-specific charities and not-for-profit organisations which offer face-to-face, telephone and online support opportunities as well as a wide range of comprehensive, practical information regarding brain tumours. Talking through the challenges of brain tumours with other patients and carers who are on the same journey can provide a unique level of emotional support and hope. Appropriate local spiritual support and bereavement care services support should be accessed (NICE 2004, NICE 2006).

Brain tumour charities and not-for-profit organisations:

Astro Fund (information and support for low grade glioma patients and carers)	http://www.astrofund.org.uk/	01485 57 27 67
Brain Tumour Research (an umbrella group of UK brain tumour charities, many of which provide information and support)	http://www.braintumourresearch.org/	01296 733011
Brain Tumour UK (provides information and support)	http://www.braintumouruk.org.uk/	0845 4500 386
International Brain Tumour Alliance (IBTA) (maintains links on its website to numerous brain tumour support groups)	http://www.theibta.org	01737 813872
PLGA Foundation (Pediatric Low Grade Astrocytoma Foundation, USA. Aimed at younger pediatric patients but covers low grade glioma patients up to the age of 19)	http://www.fightplga.org/	contact@fightplga.org
Samantha Dickson Brain Tumour Trust (provides information and support)	http://braintumourtrust.co.uk/	0845 130 9733
Virtualtrials.com (an international website providing information and online support/discussion groups)	http://www.virtualtrials.com	

Additionally, the **Teenage Cancer Trust**, a UK charity devoted to improving the lives of teenagers and young adults with cancer, offers opportunities (including a family support

network) to young people up to 24 years old. See <http://www.teenagecancertrust.org> or telephone 020 7612 0370.

Appendix 4

Symptom related referral pathway to supportive care services for patients with Optic Glioma tumours

Referral to appropriate supportive care services at any stage of the patient pathway dependent on symptoms/function:

Stage of pathway (NICE 2004)	Optic Glioma Tumour	
	Symptom	Support services
Pre-diagnosis	↓ vision affecting function	OT/ SS Sensory teams
Diagnosis	↓ vision affecting function psychosocial issues	OT/ SS Sensory teams
Initial/during treatment	↓ vision affecting function psychosocial issues emotional /mobility/pain issues	OT/ SS Sensory teams SS /PC PS/ CT/C/PC
Post treatment	↓ vision affecting function emotional /mobility/pain issues ↓ cognition psychosocial issues	OT/ SS Sensory teams PS/ CT/C/PC OT/PS SS/PC
Disease progression	↓ cognition psychosocial issues emotional /mobility/pain issues	OT/PS SS/PC PS/ CT/C/PC
End of life care	↓ function/nutrition emotional /mobility/pain issues psychosocial issues	PT/OT/SLT/D/PC PS/ CT/C/PC SS/PC

Key:

- | | |
|----------------------------|--|
| A = Appliances | - requiring appliances – prosthetics/wigs |
| C = Chaplaincy | - spiritual/emotional issues |
| CT = Complementary Therapy | - emotional/mobility/pain issues |
| D = Dietitian | - ↓ appetite/weight changes |
| OT = Occupational Therapy | - ↓ ADL/ cognitive deficits/ anxiety issues |
| PC = Palliative Care | - Symptom Control, Advance Care Planning, end of life care |

PT = Physiotherapy	- weakness and/ or sensory deficits/↓ balance/ ↓ exercise tolerance/ fatigue affecting functional mobility & arm function
PS = Psychological Support Services	- psychological issues/anxiety/ depression
SS = Social Services	- psychosocial issues & welfare benefits
SLT = Speech & Language Therapy	- ↓ speech/language/swallow function

Appendix 5: Imaging guidelines

Optic pathway imaging guidelines

All new presentations of patients with optic pathway tumours must be imaged using a consistent and comprehensive protocol. This is to ensure that optimal diagnostic information can be obtained, consistency is maintained allowing for direct comparability between studies, and that all cases can be recruited into nationally driven studies. It is equally important that follow up imaging is undertaken in a consistent and timely manner. Lack of a consistent protocol has led to difficulties in analysing the imaging of patients enrolled into tumour studies from different UK and international centres.

Lack of adherence to the national CCLG imaging protocol will jeopardize recruitment of new cases into research studies. The protocol given below is adapted from the imaging protocol published in 2001¹ but reflects recent advances in imaging techniques (DTI, perfusion MRI, MRS). Not all centres can or will wish to use the newer techniques, and therefore these are given as optional sequences. Many centres will have their own preferred imaging sequences; this protocol is not intended to be prescriptive or to exclude other sequences and techniques, however it is essential that a standard basic set of sequences is used nationally.

Newly diagnosed patients:

Brain

Axial T1, T2

Coronal or sagittal FLAIR

DWI and/or DTI (with ADC maps)

Orbits (for tumours mainly confined to the orbits)

Cor T1, STIR/T2 FS

Post Gadolinium (Gd) coronal T1 FS

Post Gd brain axial, sagittal T1 (1.5T)

Post Gd brain axial T1, axial 3D T1 volume (3T)

Optional sequences (according to local capacity/availability or CCLG trial involvement)

Coronal/sagittal T2 brain, Ax STIR/T2 FS orbits

Perfusion MRI (requires placement of blue or pink cannula)

MRS (Magnetic Resonance Spectroscopy)

Spine (for NF1+ve cases and/or when intracranial leptomeningeal disease is identified)

Post Gd sagittal T1, T2

Coronal T1 FS

Immediate post-op (within 48 hours)

Brain

Axial T1, T2

Coronal or sagittal FLAIR

DWI (with ADC maps)

Post Gd axial, sagittal T1 (1.5T)

Post Gd axial T1, axial T1 volume (3T)

Follow-up examinations (dependent upon treatment protocols/clinical progress)

Brain

Axial T1, T2

Coronal FLAIR

DWI and/or DTI (with ADC maps)

Orbits (for tumours mainly confined to the orbits)

Coronal T1, STIR/T2 FS

Post Gd orbits coronal T1 FS

Post Gd brain axial, coronal, sagittal T1 (1.5T)

Post Gd brain axial T1, 3D T1 volume (3T)

Optional (according to local site preference or enrolment into trial)

Coronal/sagittal T2

Perfusion MRI (requires placement of blue or pink cannula)

MRS if tumour size $\geq 1.0\text{cm}$ (and dependent on tumour type/protocol)

Spine (dependent on presence of spinal disease identified at presentation and/or leptomeningeal disease)

Post Gd sagittal T1, T2

Coronal T1 FS

REFERENCE

Thiesse P, Jaspan T, Couanet D, Bracard S, Neuenschwander S, Griffiths PD. Un protocole d'imagerie des tumeurs cerebrales de l'enfant (A protocol for imaging pediatric brain tumors). J Radiol 2001;82:11-16.