

E04/S(HSS)/a

**NHS STANDARD CONTRACT  
RETINOBLASTOMA SERVICE (CHILDREN)**

**PARTICULARS, SCHEDULE 2 – THE SERVICES, A – Service Specification**

<b>Service Specification No.</b>	E04/S(HSS)/a
<b>Service</b>	Retinoblastoma service (Children)
<b>Commissioner Lead</b>	
<b>Provider Lead</b>	
<b>Period</b>	12 months
<b>Date of Review</b>	

**1. Population Needs**

**1.1 National/local context and evidence base**

Retinoblastoma is the commonest primary ocular malignancy of childhood, with tumours arising from the developing retina. It typically presents in the first 2-3 years of life, often during infancy. The tumour is confined to the eye in the early stages, and cure rates for intra-ocular retinoblastoma can be as high as 95%. Extra-ocular spread (Figure 1) carries a very poor prognosis, with cure rates below 5-10%. Early diagnosis and prompt treatment is therefore crucial to save life and vision.

Retinoblastoma accounts for up to 1 % of all tumours in infancy. The incidence of sporadic retinoblastoma is 1 in 15,000-20,000 live births, with no gender or racial predilection. There are 40-50 new cases annually in the UK.

50% of cases of retinoblastoma carry the genetic change and could be passed on to the next generation. These cases also carry a lifelong risk of second cancers.

Children with retinoblastoma affecting both eyes often present with poor vision. When only one eye is involved, a white reflex on photographs or squint is the commonest reason for referral. Careful screening of the fellow eye is essential in all such cases through childhood. Advanced cases are rarely seen in the UK. This is more common with unilateral cases.

The relatively small numbers of cases seen even by specialised centres, lack of a satisfactory animal model, and numerous non-comparable staging systems have hindered retinoblastoma research in the past. There is now increasing collaboration between centres nationally and internationally to increase the evidence base for retinoblastoma management.

The structure of the national retinoblastoma service is similar to other large centres in Europe and North America, with multidisciplinary input and treatment modalities of

world class standard. There is good evidence (in the literature) to support the role of such centres of expertise in the management of rare disorders and similar centrally funded services exist for other rare conditions in the UK. The epidemiological data gathered by the two UK centres is analysed at the joint service annual meeting and supports the current service structure.

## **2. Scope**

### **2.1 Aims and objectives of service**

#### **About the condition**

Retinoblastoma is the commonest childhood eye cancer. Early detection and prompt treatment can give cure rates up to 95% for intra-ocular tumours, but extra-ocular disease carries a very high mortality. Treatment requires significant multi-disciplinary input, and lifelong surveillance of mutation carriers is needed due to the risk of second cancers. The last decade has seen tremendous advances in the management of this potentially lethal condition.

#### **What the service aims to achieve and deliver:**

- to offer modern treatment of a rare condition easily accessible by the entire population;
- to concentrate the expertise in two designated centres that are easily accessible from England, Scotland and Wales- this ensures the specialists can build up experience and offer a focused service for a rare condition;
- to share experience between the two centres and work towards similar management protocols;
- to share care with local centres to minimise travel for the families;
- to work closely with vision impairment services, schools and The Childhood Eye Cancer Trust;
- the national artificial eye service which are often involved in the care of these children;
- To ensure continuity of care and adequate transition when the children grow up into young adults and are discharged from the service.

#### **A general overview of the service identifying population served**

The Retinoblastoma service is provided from 2 centres in Birmingham and London that are well positioned geographically and are easily accessible from all over the UK. Both centres have multidisciplinary teams involving oncologists, ophthalmologists, geneticists and nurses, orthoptists, prosthetists and play therapists.

#### **Why the service is needed**

Retinoblastoma is a rare condition with up to 40-50 new cases annually in the UK. A UK ophthalmology consultant would expect to see no more than two new cases in

their career which is not enough to develop or maintain the expertise in dealing with the condition. The treatment is often prolonged and complex, and needs significant multidisciplinary input. Specialised equipment like the retcam, and knowledge of special techniques such as radioactive plaque therapy and intra-arterial chemotherapy are essential for managing this condition to adequate standards. It is therefore essential both from the governance as well as financial viewpoint to concentrate expertise in designated specialised centres with central funding to ensure uniform access to care for patients from all over the country.

Objectives of the service –strategic:

- to make the service accessible to all parts of the UK;
- to concentrate the expertise, and share experience between the two designated centres;
- to provide care closer to home where possible including shared care;
- to adopt a holistic approach working closely with schools and social services, voluntary and patient involvement organisations such as The Childhood Eye Cancer Trust, and other NHS services like the National Artificial Eye service. To contribute actively to the medical literature through audit and research;
- to audit performance against international standards;
- to ensure continued professional development for all team members.

The purposes and goals of the service:

- to offer a comprehensive diagnostic and therapeutic service for the management of retinoblastoma;
- to arrange for long term follow-up of a lifetime disease.

## **2.2 Service description/care pathway**

### **Diagnosis**

The diagnosis of retinoblastoma is essentially clinical, and may be supported by imaging in some cases. Diagnostic biopsy is contra-indicated because of the risk of extra-ocular spread.<sup>14,15</sup> It is important for the child to see an ophthalmologist with experience in retinoblastoma as the diagnosis is not always easy, and often a matter of clinical judgement.

### **Treatment**

Retinoblastoma has evolved from a deadly childhood cancer to a largely curable cancer within the past 40 years. Current treatment strategies aim to salvage the eye and provide the best visual outcome possible. This requires significant multidisciplinary input and should be coordinated by a specialised centre.

The various modalities of treatment are:

- Laser treatment- heat treatment to destroy the tumour;
- Cryotherapy: freezing treatment to destroy the tumour;
- Radiotherapy: external beam of plaque brachytherapy to damage the tumour and control growth;
- Chemotherapy: to shrink the tumours, and is often combined with laser

treatment;

- Enucleation: surgical removal of the eye may be necessary in advanced cases.

#### Newer treatment modalities

The most significant advance in recent years has been the interventional radiological technique of Intra-arterial chemotherapy (IAC). This involves transfemoral artery cannulation to allow delivery of a high dose of the chemotherapeutic agent Melphalan into the ophthalmic artery, avoiding systemic side effects. Although long term experience with this technique is lacking, the initial results are encouraging in selected cases. This is currently being offered to selected cases in the UK as a second line treatment.

#### Research directions

The relatively small numbers of cases seen by each centre, lack of a satisfactory animal model, and numerous non-comparable staging systems have hindered retinoblastoma research in the past. Current research is directed towards:

1. a better understanding of genotype-phenotype relationships in retinoblastoma that will be useful in the multidisciplinary management of this disease;
2. improvements in local drug delivery methods will address the problem of systemic toxicity from existing chemotherapy regimens;
3. minimising the side effects of treatment;
4. developing better animal models;
5. exploring biologic treatment e.g. anti angiogenic agents, growth factors etc.

It is likely future research will be directed towards targeted molecular therapy to individualise treatment and gene therapy to prevent tumour formation.

#### Supportive treatment:

1. prosthesis fitting for enucleated eyes- is an important part of rehabilitation, usually a few weeks after surgery (this service is not funded centrally);
2. psychological support for children and families- to deal with loss of eye, vision and a chronic illness;
3. long term oncological surveillance especially for germ line cases- this is best undertaken by oncologists;
4. Counseling- parents should be counseled soon after diagnosis and the patients when they reach adolescence about the inheritance of retinoblastoma, and risk to siblings and offspring. The risk of secondary malignancies, advice about risk factors like smoking and how to look out for early warning signs should be discussed with adolescent patients and access offered to the Childhood Eye Cancer Trust at the point of diagnosis for information and ongoing support.

#### Prenatal diagnosis- the role of imaging and tissue sampling

If there is a family history of retinoblastoma and the mutation in the affected parent is known, there are several options to prevent retinoblastoma or enable early detection

- i. Pre-implantation genetic diagnosis (PIGD) involves screening embryos  
.Unaffected embryos are selectively implanted ensuring the foetus is born free

of the retinoblastoma mutation and does not require screening. Additionally, there is no risk of second cancers, and no risk to future generations. The obvious disadvantage of this technique is the need for in-vitro fertilization (IVF) to produce and then select embryos.<sup>31</sup>

- ii. Chorion villous sampling (CVS) or amniocentesis
- iii. Prenatal ultrasound- In cases with a family history, and particularly if the child is shown to carry the mutation on CVS or amniocentesis, B scan ultrasonography may be advisable in the later stages of pregnancy to look for development of tumours. Although the sensitivity of this technique is quite low, in experienced hands, it may be possible to detect large tumours developing in the last few weeks of pregnancy.
- iv. Cord blood testing. The obstetric team can collect cord blood and send it to a reference laboratory to test for the retinoblastoma (Rb) mutation.

### **Screening for retinoblastoma**

As 50% of retinoblastoma cases are genetic and heritable, screening close relatives who are at risk of the disease is invaluable in early detection and treatment, saving eyes and lives. If the mutation for the index case is known, testing can be offered to relatives to determine if they are at risk of suffering/passing on the disease.

Screening is offered if:

- mutation positive or
- if the mutation is not known for the index case and risk cannot be excluded.
- both centres have protocols for screening. Screening is not needed if the relative does not carry the mutation. This approach helps avoid unnecessary screening, and focuses resources. Ideally the first screening exam for neonates with a close family history of retinoblastoma is performed in the obstetric unit before discharge, and subsequent examinations can be arranged with ophthalmic units familiar with retinoblastoma management.

### **Prognosis**

#### **Prognosis for life**

Most untreated tumours proceed to local invasion and metastasis to cause death within 2 years. Most small/medium tumours can be successfully treated while preserving useful vision. Overall there is a 95% survival rate (in the developed world). Poor prognostic factors include: size of tumour, optic nerve involvement, extraocular spread and older age at presentation.

#### **Prognosis for vision**

The prognosis for vision in retinoblastoma survivors is good, with better than 6/12 vision in the better seeing/remaining eye in over 80% of cases (Birmingham Children's Hospital audit data).

#### **Recurrence**

Recurrence can develop within the eye in previously treated tumours, and regular follow-up examinations are essential.

### **Risk of second cancers and the role of long term surveillance**

Patients with germ-line mutations are at increased risk of developing secondary malignancies such as pinealblastoma (trilateral retinoblastoma) ectopic intracranial retinoblastoma, and osteogenic or soft tissue sarcomas, melanoma and bladder cancer. The cumulative risk of second cancers has been reported as being between 20% to 48% over 50 years in various studies. This risk is increased with radiation exposure. The role of long term screening of retinoblastoma survivors is not clearly defined in the literature. Patient education and health awareness play a key role in minimising delay in diagnosis and treatment of second malignancies in these patients.

### **Days/Hours of operation**

#### **Birmingham**

The Birmingham service accepts patients through the week, with

- operating lists on Monday and Friday am
- retinoblastoma clinic on Wednesday pm
- intra-arterial chemotherapy on Tuesday
- weekly multidisciplinary team meeting is on Friday afternoon
- artificial eye service clinic on one Wednesday a month.
- in addition to the above, ad hoc additional lists are arranged on some Friday afternoons to meet additional demands on the service when needed.
- all enucleations and radioactive plaque treatment are undertaken on the planned emergency list.
- all socket repairs and allied oculoplastic procedures are undertaken on the routine operating lists on Tuesday am
- systemic chemotherapy is typically given on Friday for West Midlands patients, and remotely located patients usually receive chemotherapy from their local paediatric oncology service with close liaison with BCH oncologists.
- the Childhood Eye Cancer Trust Support Worker is available on the wards on Monday and Friday mornings, the out patients clinic on Wednesday afternoon

#### **London**

The London service is organised with

- operating lists all day Wednesday.
- all enucleations and plaques taking place during Wednesday between 8:30 and 6pm.
- National Artificial Eye Service joins theatre once a month.
- an ad hoc overflow operating list to be developed on a Monday morning.
- Intra Arterial Melphalan organised weekly.
- systemic chemotherapy organised for London based patients at GOSH.
- mini-multi-disciplinary teams involving both ophthalmologists and sometimes oncologist during the Examination Under Anaesthetic (EUA) of each patient.
- full MDT including pathologist once a month Monday pm to discuss enucleations etc.
- the team is regularly audited, including communication.

## **Risk Management**

There are clinical and non-clinical risks that need to be managed within the service. Clinical risks include shared care, transition of care into local units and long term follow-up of young adults.

*Non clinical risks include personnel issues as there are very few professionals familiar with retinoblastoma management and long term absence of key members can place considerable pressure on the service. Limited access to artificial eye services in certain parts of the country can affect the quality of care.*

## **2.3 Population covered**

The service covers the entire UK population including Northern Ireland. For logistic reasons, Northern Irish patients, although entitled to treatment in both the national centres, are often treated in the Irish Republic (Dublin). Although both the centres are located in England, there is easy access for Welsh, Irish and Scottish patients to both services. Residents of the European Union are eligible for treatment in the NHS under reciprocal arrangements. All other international patients are treated as private patients, and charged by the individual services.

## **2.4 Any acceptance and exclusion criteria**

Assessments as a requirement of race, gender, sexual orientation, religion and disability equality legislation.

The provider has a duty to co-operate with the commissioner in undertaking Equality Impact Assessments as a requirement of race, gender, sexual orientation, religion and disability equality legislation. Universal accessibility and equitable provision of service regardless of age, culture and gender are carefully monitored.

Providers require staff to attend mandatory training on equality and diversity and the facilities provided offer appropriate disabled access for patients, family and carers. When required the providers will use translators and printed information is available in multiple languages.

## **Referral criteria, sources and routes**

The service will accept referral from any healthcare professional including GPs and optometrists who might suspect the diagnosis. It is not possible for every case of white reflex to be seen in the service, as there is a high proportion of false positives from non- ophthalmologists. Such cases are typically seen in a general clinic and care transferred into the service if retinoblastoma is diagnosed,

The commonest route of referral is from a consultant ophthalmologist, either in a district general hospital or the larger regional centres (teaching hospitals). The child has often been seen by the GP, health visitor or optometrist or in the eye casualty

prior to seeing the ophthalmologist. For all referrals from ophthalmologists, the child will either have been seen in clinic awake, or had an examination under anaesthesia (EUA).

### **Investigations**

Most children will have undergone ultrasound B scan imaging, and some children might have undergone **computed tomography** (CT) or magnetic resonance imaging (MRI) scans although this is not necessary prior to making the referral. No blood tests are needed prior to making the referral. Some cases will have undergone retinal photography at the referring unit. Referrals are typically phoned or faxed through from the referrer, and all referrals are triaged by the consultant ophthalmologist, with a view to seeing the child within 1 week, typically sooner on the next available operating list. If retinoblastoma is considered unlikely, the child might be seen in clinic prior to arranging an EUA if needed.

A detailed eye examination under general anaesthesia (EUA) is mandatory to make the diagnosis and plan management. An examination with the child awake can be incomplete in young children. It also affords the opportunity to document findings with retinal photography, perform ultrasound examination and collect blood for testing.

### **Exclusion criteria**

There is no age exclusion criterion for the service as adult retinoblastoma is extremely rare. For adults who have been treated for retinoblastoma in the past, and have new or ongoing problems, they may be seen by the Retinoblastoma specialists but out with the RB service, either within the adult ocular oncology services in London, or seen by the Retinoblastoma surgeons in Birmingham at the Birmingham and Midland Eye Centre. This is to ensure that professionals familiar with retinoblastoma management provide care for such rare and complex cases in adult centres.

Adults with retinoblastoma related problems such as socket disorders and radiation related conditions are however excluded from the service.

### **Criteria for discharge**

One year event free follow up for unilateral cases and two year event free follow up for bilateral cases before discharge back to the local paediatric ophthalmologist. Suggested follow up till the age of 16 yrs for all affected cases. Screening for unaffected relatives or mutation carriers till the age of seven years.

## **2.5 Interdependencies with other services**

Although the service is based out of Birmingham and London, there is a wider network of health professionals across the country that is key to its success. This includes GPs, health visitors, optometrists who might help make the referral, paediatric ophthalmologists who make the diagnosis and refer to the two centres,



The interdependencies for the service should be described, for example with general

practice, hospital services, Clinical Commissioning Group (CCG) commissioned services and/or wider inter agency services such as wheelchairs, equipment, interpreter services etc...

- GP
- Community Paediatricians
- Paediatric oncologists
- Paediatric Ophthalmologists
- Artificial Eye Service
- Oculoplastic Surgeons
- Vision Impairment Services
- Childhood Eye Cancer Trust

#### **Relevant networks and screening programmes**

- Cancer Networks
- **Cancer and Leukaemia Group (CCLG)**
- Childhood Eye Cancer Trust (CHECT) - patient involvement
- Joint annual meeting of both services
- Screening programmes- genetic surveillance and links with maternity units for cord blood testing
- Antenatal testing
- Lifelong surveillance- role of the transition clinic

### **3. Applicable Service Standards**

#### **3.1 Applicable national standards e.g. NICE, Royal College**

Response times will be in line with national policy on cancer waits.

The service aims to provide prompt access to care without any waiting time. New referrals are received by phone, email or fax; The team aims to respond within 24 hours, making contact with the family to arrange transport and accommodation. All new cases will be seen within one week on the next operating list or rarely in clinic prior to performing an EUA.

Treatment is instituted promptly, with enucleations up to one week after the decision is made, brachytherapy within two weeks (to allow dose calculation), and chemotherapy within 1-2 weeks. All cases with aggressive disease and where extra-ocular extension is suspected are prioritised.

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#### 4. Key Service Outcomes

Intra-ocular Retinoblastoma has a very high cure rate to the order of 95-98% in specialised centres. The service aims to maintain and improve on this already high level outcome, with constant effort to save eyes (reduce enucleation rate) and vision.

Recent advances have focused on reducing morbidity with the use of local therapy such as brachytherapy and intra-arterial chemotherapy. The wider aim is to improve awareness, and enable timely diagnosis and prompt referral, optimum management, and seamless delivery of care shared between the specialist and local centres to minimise disruption to the families.

The service will be compliant with national cancer standards.

The service will be compliant with national key performance indicators (KPIs).

##### **Outcome data**

The Retinoblastoma service will report on:

##### Deaths

- Metastatic disease
- Number of bilateral Rb patients with bilateral enucleation
- Primary enucleation (removal of the eye as first-line treatment)
- Secondary enucleation (removal of the eye after other treatment has been unsuccessful)
- Eyes preserved
- External beam radiotherapy

*Notes: 1) Reporting will be done separately for unilateral and bilateral retinoblastoma; 2) According to disease classification*

Patient level reports will be submitted for patients undergoing Intra-Arterial Chemotherapy (IAC) treatment, detailing:

- secondary enucleation of the treated eye
- secondary systemic chemotherapy
- external beam radiotherapy treatment
- plaque treatment (brachytherapy)

##### **Governance**

The nationally designated Retinoblastoma providers must be fully integrated into their trust's corporate and clinical governance arrangements.

NHS England and the provider will conduct a formal Joint Service Review at each centre at least annually and would expect to meet with the national clinical teams along with CHECT annually.

See also NHS England Service Standards for Retinoblastoma.

The nationally designated providers of the Retinoblastoma service are required to demonstrate continual improvement in patient care and service delivery. This process will be informed by clinical and service audit, patient and public engagement and awareness of national and international clinical and policy developments that could inform service development. Where appropriate the two nationally designated providers will work together to develop shared protocols and guidelines.

The services will agree service development improvement plans with the NHS England and demonstrate progress at Joint Service Review meetings.

## 5. Location of Provider Premises

Birmingham Children's Hospital NHS Foundation Trust  
Barts Health NHS Trust

### Sub-contractors

National Genetic Reference Laboratory- Manchester  
National Artificial Eye Service

Who delivers the service:

- ophthalmologists
- oncologists
- geneticists
- anaesthetists
- psychologists
- specialist orthoptists
- specialist nurses
- play therapists
- prosthetists