



National Proton Beam Therapy Service Development Programme

Strategic Outline Case

National PBT Service Development Programme – Strategic Outline Case

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National Proton Beam Therapy Service Development Programme

Strategic Outline Case

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Foreword

On 12 January 2011, we published *Improving Outcomes: A Strategy for Cancer* which sets out how the Coalition Government's reforms of health and care services will drive improvements in cancer outcomes and put patients and the public at the heart of cancer services.

The government recognises that ensuring patients have access to high quality modern radiotherapy techniques such as Proton Beam Therapy (PBT) will support improved outcomes, increase cure rates and improve patient experience by minimising long-term side effects of treatment. The precision of PBT means that it can avoid damaging critical tissues when treating tumours, which is particularly important when they are near the central nervous system.

As PBT services are not available in this country, we have been sending our patients overseas for treatment since 2008. The overseas programme has been enormously successful and will have, by the end of the year, sent over 130 patients, including 100 children, overseas for this treatment.

However, there is a high cost in treating patients overseas, both in treatment costs and in the effects on families, who need to spend up to eight weeks away from their homes. In addition, we are unable to treat all those patients who could benefit from PBT. Capacity in the overseas centres is also limited, so it is important that we find a way to treat these patients here in NHS facilities.

PBT equipment is highly unusual, it has a life span of over 20 years and each machine is uniquely expensive when compared to other equipment. For these reasons, NHS Trusts are unlikely to be able to develop services working alone. It is therefore imperative that we work with potential providers to develop a national, fully integrated PBT service that provides access for patients from all parts of the country.

We have already identified those NHS Trusts that we believe would provide the optimal clinical service and geographical access for patients. We have been working with them to develop a business case for PBT services that examines all of the options for provision of a high quality service for patients and provides value for money for the taxpayer.

This Strategic Outline Case (SOC) represents a small part of our work to-date but it is an important first step in ensuring that patients in this country have access to first class radiotherapy services and that we can contribute to our commitment to deliver outcomes for cancer patients that are comparable with the best in Europe.

Professor Sir Mike Richards CBE
National Cancer Director

1. Executive summary.

- 1.1 Proton Beam Therapy (PBT) is a special form of radiotherapy, using a beam of heavy particles instead of X rays. Proton beams can be very precisely targeted on the tumour and is estimated to reduce the dose to normal tissue by a factor of about two, thereby reducing adverse side effects and giving increased cure rates with higher radiation doses in certain rare cancers. The strongest clinical case for PBT relates to children and young people with brain tumours.

Wider strategy context

- 1.2 The *Improving Outcomes Strategy for Cancer* published January 2011, continued the commitment to consider options for developing PBT services in this country, recognising that access to appropriate treatment, delivered to a high standard, is critical to improving outcomes for cancer patients.

Evidence of benefit

- 1.3 Proton Therapy has not been evaluated by National Institute for Health and Clinical Excellence (NICE); there are very few randomised trials worldwide that include proton therapy. However, there is extensive evidence of the superiority of radiotherapy dose distributions, particularly in paediatric indications, low levels of side effects and good outcomes in small series of patients.
- 1.4 There are 1500 patients in the UK per annum (including approximately 250 paediatric patients) for whom PBT is the treatment of choice with clear evidence of health gain. The cancer indications where the experts' review of evidence identified that patients would benefit from PBT, show benefits in terms of reduced side effects, increased cure rates and reduced morbidity.
- 1.5 Detailed evaluation and modelling of the health gains for the proposed case mix defined for NHS commissioning, suggests that proton therapy is within the NICE Quality Adjusted Life Year (QALY) criteria. The comparative benefits of treating patients using conventional radiotherapy and PBT have been modelled and show that, treating those patients, where there is evidence of benefit, with PBT will generate 48,000 additional QALYs over the lifetime of treated patients. The discounted benefit of PBT over conventional radiotherapy, as measured by the QALY gain, equates to £1bn.

The overseas programme

- 1.6 At the moment, patients with high priority indications are considered by an Expert Panel and treated overseas within the National Specialised Commissioning Team's (NSCT) PBT Overseas Treatment Programme. The NSCT Proton Overseas Programme is unusual, if not unique in the world in using an evidence based and prioritised approach and applying it in a systematic way to a whole population for proton therapy.

Cost Effectiveness

- 1.7 However, capacity in the overseas centres is limited and costs have increased as the international demand increases. It is not always possible to treat patients with complex needs overseas. The increase in potential demand, together with the costs of sending patients abroad now make the case for establishing facilities in this country on the grounds of both quality and cost effectiveness. By 2014 to 2015, the NHS Commissioning Board (NHS CB) will be spending £30m per annum treating up to 400 patients overseas. Our best estimate is that we can treat 1165 patients in England for £37m per annum and with capacity maximised treating patients from the devolved administrations and other countries, the costs of treating English patients could reduce to £30m.
- 1.8 There is therefore a clear need to develop services in this country in order to expand access to all patients for whom this treatment has been identified as the most clinically appropriate. A national service is required with access by clinical teams to facilities across the country.
- 1.9 PBT equipment is highly unusual, it has a life span of over 20 years and each machine is uniquely expensive when compared to other equipment (£60m-£80m for the equipment alone). NHS Trusts are unlikely to be able to develop a national service working alone and will require national leadership. We need to work with the host providers to develop a PBT service managed as part of a national fully integrated network of care that provides access for patients from all parts of the country and to ensure that the impact on existing services is appropriately managed.

Integrated services

- 1.10 There are fewer than 50 PBT centres around the world. Many existing centres are stand-alone treatment delivery facilities and not integrated with other hospital care facilities. This is not the ideal model for the complex case mix of patients proposed for this country.

Number of facilities

- 1.11 Those NHS Trusts that we believe would provide the optimal clinical service and geographical access for patients were identified in 2010. The next step was to assess the number of facilities required to meet the known demand, providing the best use of available resources.
- 1.12 The identified demand is for 1500 patients per annum. Experience from centres around the world is that the maximum capacity for a single centre is 750 patients per annum and this could be lower with a highly complex case mix.
- 1.13 A single centre would not meet the clinical demand and therefore require an ongoing revenue commitment to overseas treatment or re-assessment of the indications list, identifying a new clinical rationale to commission and limit the appropriate numbers for a single centre capacity. A single centre offers limited resilience in the event of breakdown.
- 1.14 Two centres would meet the clinical demand if used at maximum efficiency and provide a degree of resilience in the event of breakdown. There would be some capacity to offer treatment to patients from the devolved administrations and some research capacity.
- 1.15 Three centres would provide the best geographical access, least impact on existing services and allow the likely future expansion of the clinical indications with greater opportunities for research. However, a three-site national service would be more expensive. Greater capital investment would be required with the reduced activity over three sites increasing revenue costs. PBT facilities require the procurement of extremely expensive equipment and while we are constantly reviewing developments of the technology available, there remains a risk that cheaper or smaller technology could become available in the medium term.
- 1.16 For these reasons, with interoperability between two systems, there is scope to deliver a service over two sites in the shorter term, looking to develop a third in the longer term. Demand and capacity on the first two sites can be closely monitored and technological developments kept under review with a business case for a third site developed at the appropriate time.

Conclusion

- 1.17 This strategic outline case therefore concludes that a two-site solution treating 750 patients each per year would meet all of the critical success factors identified. It presents the best and most cost effective solution in the short-term with the option to make a case for a third centre in the medium to long-term as experience with the two sites is reviewed, enabling a third site to make use of any future technological developments.
- 1.18 A National PBT service should be developed on two sites that:
- ensures that all patients, for whom evidence supports proton therapy as the most clinically effective treatment, receive treatment within a clinically appropriate service specification and to nationally agreed standards
 - ensures that services provided enable the continued development of the technologies involved and that workforce and training issues are appropriately addressed
 - delivers improved outcomes by ensuring that patients have access to high quality modern radiotherapy techniques, comparable to those used in other European countries, to improve outcomes and improve patients' experience by minimising any long-term side effects of treatment.

Next steps

- 1.19 We will now develop a co-operation agreement between the two Trusts, The Christie NHS Foundation Trust and University College London Hospitals Partners, the DH and the NHS Commissioning Board Authority. This will set out how these parties will work together to deliver the next phase of the National PBT Service Development Programme and will include a National PBT Service and Investment Framework. The two Trusts will develop individual Outline Business Cases for HMT approval.

2. Strategic Case.

- 2.1 This section provides background information about Proton Beam Therapy (PBT) Treatment and the clinical case for developing a service. It explains the significance of the proposed development of a National PBT service within the context of Government health policies, including the drivers for improvement in the provision of radiotherapy and the associated objectives. It also outlines the overall investment objectives of the PBT programme.

The Treatment

- 2.2 PBT is a special form of radiotherapy, using a beam of heavy particles called protons instead of X rays. Protons are produced by accelerators that can be either cyclotrons or synchrotrons. The advantage of proton beam therapy over radiotherapy given by a linear accelerator is that the proton beam can be very precisely targeted on the tumour. This ensures that nearby normal tissues receive significantly less radiation thereby reducing adverse side effects as well as giving increased cure rates with higher radiation doses in certain rare cancers. PBT is estimated to reduce the dose to normal tissue by a factor of about two. Evidence is growing that PBT can be effective in treating a number of cancers. The strongest clinical case for PBT relates to children and young people with brain tumours
- 2.3 PBT has been mainly used to treat three types of cancer. These are malignant melanomas occurring in the retina at the back of the eye (ocular melanomas) and two very rare cancers: chondrosarcomas and chordomas, affecting the base of the skull and the upper part of the spine respectively. In other countries, many prostate cancer patients have been treated with PBT though the National Radiotherapy Advisory Group considered there is insufficient evidence of benefit for these patients for inclusion on the list of indications considered for treatment overseas.
- 2.4 The only proton facility in the UK is a low energy facility at the Clatterbridge Centre for Oncology, Liverpool; this is suitable for eye tumours only. It treats around 100 patients a year with excellent outcomes and over 90% permanent control (effective local cure and saves enucleating the eye).
- 2.5 There are more than 33 facilities around the world with ten centres in the USA and nine in Europe, a further six are currently in the planning stages and will become operational within the next five years.

There are many facilities in the planning stage but many are not becoming operational – in some cases, drivers are commercial, for example, there are facilities in the USA that treat mainly prostate cancer as patients are prepared to pay for the treatment to avoid side effects of standard treatment. Many are also stand-alone treatment delivery facilities and not integrated with other hospital care facilities. This is not the ideal model for the complex case mix of patients proposed for this country.

- 2.6 PBT is a highly unusual asset: it is both very long-lived and each machine is uniquely expensive when compared to other medical equipment. Investment in PBT facilities is too large and risky for even the largest and best run NHS trust to undertake alone, from £50-80m for the equipment and £40-60m for the building. Historically the private sector would have been used to shoulder part of the financing and risk associated with this type of scheme. It is important that, because of the size, complexity and cost of this new technology, PBT services have a managed introduction in the NHS to ensure that it is available to all patients regardless of where they live and is delivered through a managed network of care.
- 2.7 To match the UK population with the current proposed case mix within safe capacity throughput, minimise reconfiguration of other services and minimise travel and accommodation costs a three site solution would be optimum.

The Clinical Case

- 2.8 The National Radiotherapy Advisory Group (NRAG) considered the case for high-energy proton therapy as part of their report *Radiotherapy: developing a world class service for England* (February 2007) and made recommendations for the establishment of proton therapy facilities in England. The group examined the evidence for PBT in 2006 and identified the clinical diagnoses where PBT is clearly the superior option in terms of clinical outcomes when compared to conventional radiotherapy. The evidence is now even more secure for the use of protons in reducing toxicity and effects from standard radiotherapy. References to the clinical papers providing evidence for PBT for the NRAG report can be found in annex A. This was taken forward by a commitment in the Cancer Reform Strategy (2007) to consider the options for the development of proton therapy services.
- 2.9 A new Advisory Group was established in 2008 to take forward this commitment and that group undertook a further review of evidence to identify the following indications that would benefit from proton beam therapy.

Table 1. Annual caseload for UK population

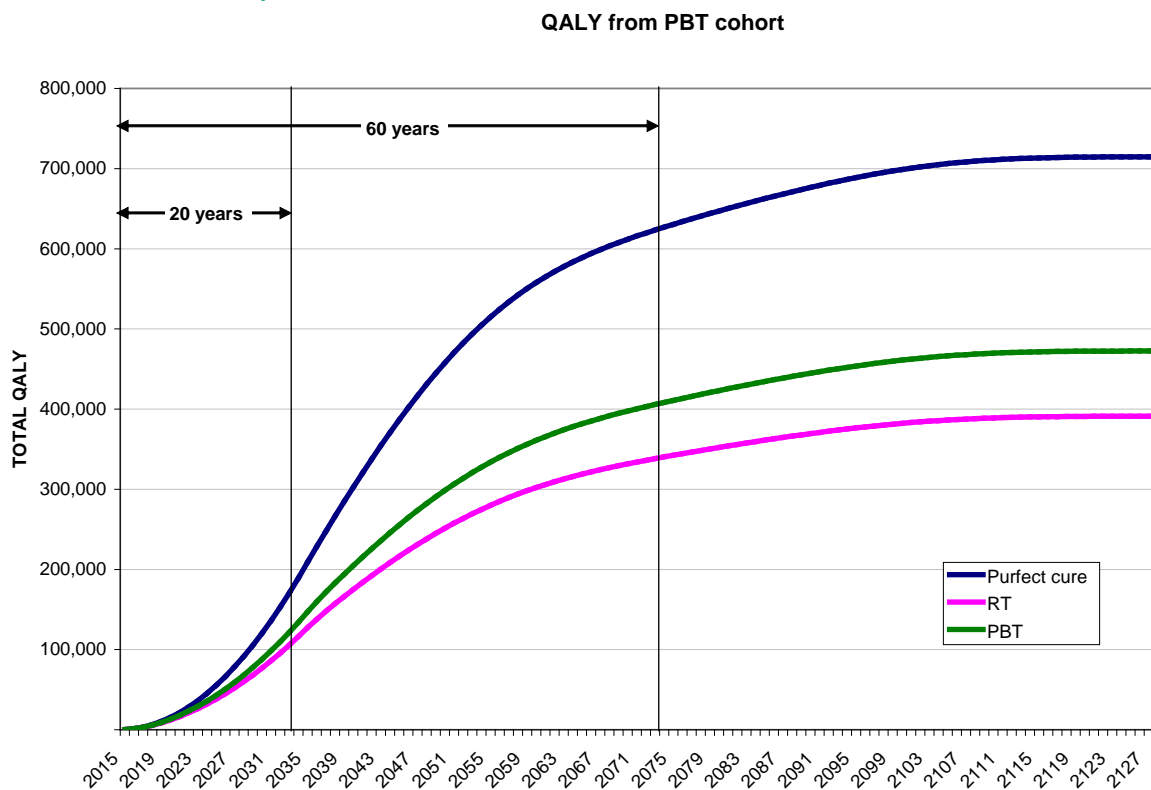
		Note	↓2 ⁰ Ca	↑Cure Rate	↓Morbidity
Paediatric Indications					
Chordoma/Chondrosarcoma		15	1	**	***
Rhabdomyosarcoma	Orbit	5	1	***	*
	Parameningeal & Head & Neck	15	1	***	*
	Pelvis	10	1	***	*
Osteosarcoma		3	1	***	***
Ewings		9	1	***	**
PPNET (Extra-osseous Ewing's)		5	1	***	**
Ependymoma		25	1	**	*
Low Grade Glioma		5	1	**	*
Optic Pathway Glioma		12	1	***	*
Craniphayngioma		15	1	***	*
Medulloblastoma (PNET)		70	1	***	*
Hodgkins		5	1	***	*
Retinoblastoma		5	1	**	*
Meningioma		3	1	***	**
Intracranial Germinoma		10	1	***	*
Nasopharynx (Head & Neck)		15	2	***	**
Difficult Cases (Esthesioneuroblastoma/Neuroblastoma/Liver)		5	3	**	**
Very Young Age (Extra Cases)		20	4	***	***
	Paediatric TOTAL	252		***	**
Adult Indications					
Choroidal melanoma		100	7	*	***
Ocular / Orbital		25	8	*	***
Chordoma	Base of Skull	60	8	*	***
Chondrosarcoma	Base of Skull	30	8	*	***
Para-spinal / Spinal Sarcoma	Including Chordoma	180	8	*	***
Meningioma		100	5	*	*
Acoustic Neuroma		100	5	*	*
Craniospinal NOS (Pineal)		10	8	**	**
Head & Neck & Paranasal Sinuses		300	6	**	***
PNET (medullo/intracranial)		30	5	**	**
Difficult Cases (e.g. young adult, previous radiotherapy treatment, abnormal anatomy)		300	9	**	**
	Adult TOTAL	1235		*	***
	TOTAL	1487			

Notes to table 1 can be found in annex B; the numbers are for the UK and therefore include the devolved administrations (for breakdowns of caseload by country, see paragraph 2.24).

- 2.10 The above table shows the indications where the experts' review of evidence identified that patients would benefit from PBT and indicates the nature of the benefit in terms of reduced side effects, increased cure rates and reduced morbidity.
- 2.11 The National Specialised Commissioning Team (NSCT) Proton Overseas Programme is unusual, if not unique in the world in using an evidence based and prioritised approach and applying it in a systematic way to a whole population for proton therapy. It is becoming clear that because of this, the NHS will soon have the opportunity to report outcomes on series of paediatric cancers that match or exceed any in the world literature. A project has started to evaluate the outcomes from the Overseas Programme. The extension of the diagnostic criteria to include a wider range of highly prioritised cases for treatment in the NHS will ensure the NHS can match the best radiotherapy services in the world.
- 2.12 Proton Therapy has not been evaluated by the National Institute for Health and Clinical Excellence (NICE) and it is unlikely it will do so. There are very few randomised trials that include proton therapy. There is extensive evidence of the superiority of radiotherapy dose distributions, particularly in paediatric indications, low levels of side effects and good outcomes in small series of patients. The rarity of the cancers treated in any one institution or even country, coupled with the scarcity of the resource and the timescales for the expression of late side effects has meant it has not been possible to construct conventional clinical trials and provide the sort of evidence that would lend itself to NICE methodology. However the Department of Health's Clinical Quality and Efficiency Analytical Team have conducted a detailed evaluation and modelling exercise on the health gain for the proposed case mix of patients. This suggests that proton therapy, for the case mix of patients defined for NHS commissioning, comes within the conventional NICE Quality Adjusted Life Year (QALY) criteria.
- 2.13 The comparative benefits of treating patients using conventional radiotherapy and PBT have been assessed by the DH analysts using Monte Carlo simulation modelling. The model is based on treating patients with conditions for which PBT is currently the most clinically effective treatment. In the first year, this is equivalent to the cohort of 1,487 UK patients indicated for PBT. In the model, new treatments are started every year for 20 years.

2.14 The model simulates the course of events for patients from treatment until death (or 100 years of age). QALYs are assigned to each patient, reflecting their quality and quantity of life after receiving conventional radiotherapy and PBT. A higher QALY value indicates higher quality and/or length of life post treatment. Figure 1 below shows the additional QALYs that the cohort of patients would receive with access to PBT rather than conventional radiotherapy.

Figure 1: Results of Monte Carlo simulation modelling comparing the QALY gains of conventional radiotherapy and PBT for patients where PBT is the most clinically effective treatment



The gain from PBT can be measured as the difference between the sum of QALYs obtained under each treatment regime. Based on this approach, enabling highly indicated patients to access PBT will generate 48,000 additional QALYs. Using the DH value of £60,000 per QALY, the discounted benefit of PBT over conventional radiotherapy, as measured by the QALY gain, equates to £1bn.

National Service Context and Objectives

2.15 This section provides an overview of the framework for PBT and for the improvement of radiotherapy services. It addresses broader government health policies and focuses on the key policy objectives.

Government health policies

- 2.16 Commissioning of PBT services from providers in England will support the Government's policies and aims for improving outcomes for cancer patients. Improving Outcomes: A Strategy for Cancer states:

“One example of high quality modern radiotherapy is Proton Beam Therapy (PBT). This is a very precise form of radiotherapy that can be effective in treating a number of cancers and avoiding damage to critical tissues near the tumour. This is particularly important in treating tumours near the central nervous system.

We are currently exploring options for developing PBT facilities in England to treat up to 1,700 patients per year. However, these facilities will take time to develop. In order to ensure that all high priority patients with a need for PBT get access to this cutting-edge treatment, additional funding will be provided over the next four years to treat patients (predominantly children) abroad. Based on our assessment of clinical need, this will benefit 400 patients per year by 2014 to 2015.”

- 2.17 This policy is in line with the government's emphasis on outcomes, addressing improved survival and improved long term quality of life and based on a range of documents published by the DH including:

- *The National Radiotherapy Advisory Group (NRAG) Report (2007)*
- *The Cancer Reform Strategy 2007 (CRS)*
- *A Framework for the development of PBT services in England (2009)*

- 2.18 The Improving Outcomes Strategy for Cancer continued the commitment to consider options for developing PBT services in this country, recognising that access to appropriate treatment, delivered to a high standard, is critical to improving outcomes for cancer patients. This strategic outline case sets the scene for the future investment programme.

- 2.19 An expert Advisory Group was established to advise the DH on this issue and drafted a *Framework for the development of PBT services in England* (the “Framework”) annex E to advise both the National Specialised Commissioning Team (NSCT) and potential providers of services. The Framework includes a patient pathway and outline specifications for both the technology and infrastructure required to provide a quality service for patients.

- 2.20 In August 2009, the NSCT was asked to move to the next stage in the development of PBT Services in this country by holding a competition to identify a possible provider or providers of proton beam services in England and developing an outline business case. It was made clear at that time that a decision on whether to proceed with the services development would depend on future available funding. It was subsequently agreed that the DH would support the NSCT in developing the business case and the National Cancer Director would undertake the role of Senior Responsible Officer for the Programme. Subsequent changes to potential finance options have led to the need for this to be a DH strategic business case.
- 2.21 Proposals were sought from interested Trusts; a transparent evaluation process was developed in order to identify the sites that demonstrated the clinical and financial capability to deliver these services and provided the optimum geographical locations to ensure equal access to the population of England. The three host Trusts selected are University College London Hospital Partners and the Christie NHS Foundation Trust for a two-site option and University Hospitals Birmingham NHS Foundation Trust for a three site option. The DH has been working with these three Trusts to develop the strategic business case.
- 2.22 In October 2010, the government announced that it would introduce improved treatment, by expanding radiotherapy capacity. It announced the investment of over £50m over the spending review period so that all high priority patients with a need for proton beam therapy would have access to this treatment, benefitting 400 patients per year by the end of the spending review period.

Demand

- 2.23 The PBT Framework includes the clinical indications and associated potential demand figures as set out in Table 1.
- 2.24 The Advisory Group advised that there are 1500 patients (numbers are estimates so rounded up for planning purposes) in the UK per annum (including 250 paediatric patients) for whom PBT is the treatment of choice with clear evidence of health gain and pointed out that this list is conservative. This increase in potential demand, together with the costs of sending patients abroad now make the case for establishing facilities in this country on the grounds of both quality and cost effectiveness.

National PBT Service Development Programme – Strategic Outline Case

	Scotland	Wales	N.Ireland	England	Total UK	5% research	
paediatric	23	13	8	212	252		
Adults	91	57	34	953	1135		
						70	
Total (1)	114	70	42	1165	1387	1457	
Patient numbers to be commissioned by NHS England							1165
Estimated capacity need for purpose of business case (2)							1500

Notes:

The above figures exclude ocular patients which total 100 for the UK. These patients are currently treated at Clatterbridge.

The centres could also potentially treat patients from the Republic of Ireland where there is an estimated need of 108 per annum, with these included there would be a need to build capacity for 1565 patients in total, with 1165 of those being commissioned from the NHS in England.

Above need based on the following population figures:

	Scotland	Wales	N. Ireland	England	Total UK
Population (m)	5.2	3	1.8	51.4	61.4
% population	8	5	3	84	100

- 2.25 The service, once operational from late 2016, (post SOC note: now end 2017) will need to ramp up from year one, a more detailed analysis of potential ramp up will be provided in the Trusts' Outline Business Cases (OBCs).
- 2.26 The indications in the case mix are already conservative and heavily prioritised to those for which there is existing evidence of improved clinical outcomes. Modelled dose distributions show a significantly wider potential with no clinical evidence yet. These indications should be the subject of clinical trials. Without strict prioritisation and trials, there is a risk of pressure for use of PBT capacity way outside that possible for two centres.

What treatment are these patients receiving in the absence of PBT in England?

- 2.27 Clearly, a small proportion of these cases are already having proton treatment abroad within the NSCT Proton Overseas Programme. Within the wider diagnostic criteria proposed for the NHS based service, some patients may currently be receiving conventional radiotherapy but either accepting higher late complication rates or lower doses and so compromised outcomes. In other cases, patients may be having no radiotherapy at all with worse outcomes. For sacral chordomas, highly mutilating surgery may be the only curative alternative to proton beam therapy, all of these alternative treatments are clinically sub-optimal, in some cases severely so and with poor experience for patients.

Meeting the Demand

- 2.28 To meet the demand that the clinical experts have identified, facilities would need to be built in England. A key first step is, therefore, to identify the number of facilities required. Experience from centres around the world is that the maximum capacity for a single centre is 750 patients per annum (dependent on case mix, a highly complex case mix would reduce capacity). Our assessment of the number of centres/ facilities required is therefore as follows:

- A single centre
 - would not meet the clinical demand and would therefore either require an ongoing revenue commitment beyond that currently identified (to continue to supplement the home NHS service with overseas treatment, or, the experts would need to re-assess the indications list and identify a new clinical rationale to commission and limit the appropriate numbers for a single centre capacity
 - would mean that we would prioritise patients in England and require us to deny treatment to patients in the devolved administrations
 - carries the significant risk of lack of resilience and the potential impact on treatment outcomes of interruptions to treatment in the event of machine breakdown.

- **Two centres**
 - would meet the clinical demand if used at maximum efficiency
 - provides a degree of resilience in the event of breakdown
 - provides sufficient capacity to offer treatment to patients from the devolved administrations
 - provides some capacity for research.
- **Three centres**
 - would provide the clinically optimal service
 - provides the best geographical access
 - would have the least impact on existing services
 - provides for the likely future expansion of the clinical indications; and
 - provides greater opportunities for research.

2.29 An alternative approach would be to purchase the service from a private provider. However, the only known private provider with an interest in developing these services does not plan to develop a facility on a hospital site and plans to use a technology which is currently not operational or tested and will not treat the majority of patients on our list of those who could benefit.

2.30 For the above reasons, a National PBT service provided over three sites is clinically the preferred solution. However, it is recognised that, even with the potential to make savings through economies of scale, a three-site national service would be more expensive in terms of the amount of capital required and the impact on revenue costs. However, with total interoperability between two systems, there is scope to deliver a service over two sites in the shorter term, looking to develop a third in the longer term.

Key Policy Objectives

2.31 The high-level objectives for the development of a PBT service in England as set out in the Framework are as follows:

- To ensure that all patients, for whom evidence supports proton therapy as the most clinically effective treatment, receive treatment within a clinically appropriate service specification and to nationally agreed standards.

- To ensure that services provided enable the continued development of the technologies involved and that workforce and training issues are appropriately addressed.
- To deliver improved outcomes by ensuring that patients have access to high quality modern radiotherapy techniques, comparable to those used in other European countries, to improve outcomes and improve patients' experience by minimising any long-term side effects of treatment.

The Current Position

Treatment overseas

- 2.32 The CRS also set out that, while facilities were being established in this country, PBT for a “high priority” list of cancers would be commissioned from overseas centres. The NSCT, established a clinical reference panel, chaired by Dr Adrian Crellin, to advise on individual cases.
- 2.33 It was estimated that about 400 patients in England per annum would have cancers in the “high priority” category. Recognising that not all patients would want to travel overseas and that numbers would take time to build. Some of those patients who could benefit most from PBT are not included in this list because of the complex needs of their care and the unsuitability for travel overseas (e.g. medulloblastoma where the integration with chemotherapy and the timing of radiotherapy are critical, patients with recent cranial surgery or poorer performance status after surgery).
- 2.34 Overall 250 patients have been referred into the programme since its started in 2008 and 160 patients have been referred for proton treatment abroad including nearly 100 paediatric cases. 50 patients travelled overseas for treatment in 2010 to 2011 at a cost of £5m. For 2011 to 2012, in the first seven months, 42 patients from England had begun treatment overseas. The panel is currently carefully managing the programme, recognising that the overseas capacity to treat patients is limited. It was planned that 120 patients would receive treatment overseas in 2011 to 2012 at a cost of £9m; however, the programme is currently estimating 80 patients as USA costs have increased taking the average cost this year to £110,000 per patient (an increase on the planning figure). For these reasons (capacity and cost), the expert reference panel is being deliberately cautious in the cases it sends overseas for treatment.
- 2.35 The following high priority indications are used by the Expert Panel when considering patients referred for PBT. All cases must only be considered for curative indications, have a good life expectation from other conditions and have a good performance status.

Adult

- Base of Skull and Spinal Chordoma
- Base of Skull Chondrosarcoma
- Spinal and Paraspinal Bone and Soft Tissue Sarcomas (Non Ewing's)

Paediatric

- Base of Skull and Spinal Chordoma
- Base of Skull Chondrosarcoma
- Spinal and Paraspinal "adult type" Bone and Soft Tissue Sarcomas
- Rhabdomyosarcoma

Orbit

Parameningeal and Head and Neck

Pelvis

- Ependymoma
- Ewing's Sarcoma
- Retinoblastoma
- Pelvic Sarcoma
- Optic Pathway and other selected Low Grade Glioma
- Craniopharyngioma
- Pineal Parenchymal Tumours (not Pineoblastoma)
- Esthesioneuroblastoma

Cost of treatment overseas

2.36 In October 2010, the government announced additional funding over the next Spending Review period so that all high priority patients have access to this treatment - benefitting 400 patients per year by the end of the spending review period. Estimated spend on overseas PBT treatment by 2014 to 2015 is £30m per annum.

2.37 The NSCT have, to date, commissioned proton beam therapy interventions at sites that have been assessed to ensure clinical and business arrangements are appropriate. Arrangements have been made for a limited number of patients to be treated in Switzerland, France and the USA. Costs for overseas treatment vary greatly, from £42,000 per patient in Switzerland, to over £100,000 at the commercially run centres in the USA. In 2011 to 2012, the average cost is currently nearer £90,000 because of significantly fewer patients being treated in Switzerland and the majority being treated in Florida. Capacity to deliver PBT for non-eye cancers in Europe is still very limited. Difficulties in integrating other treatments and the quality of patient experience have led to France not being used currently. There is a recognised need to increase capacity in Europe and existing services are under increasing pressure to treat their own cases.

The Business Need

Limitations to overseas treatment

2.38 Clinical

- In many cases, it is inappropriate to send patients for overseas treatment because of the complex nature of their cancer treatment, for example, they may require associated surgery, chemotherapy and other supportive treatments. Surgical interventions are undertaken in specialist units in England. For these patients, until facilities are established here, there is a proven clinical advantage to staying in this country for conventional radiotherapy treatment. There are limitations on when a patient may fly after cranial surgery that limit access to treatment abroad.
- The potential for truly collaborative treatments (ie combinations of surgery, chemotherapy and radiotherapy) is severely limited, possibly limiting the effectiveness of treatment. This dislocation in the clinical management of patients within a NHS pathway offers a real risk of the clinical care being compromised.

2.39 Impact on patient experience

- Treatment overseas as a long-term strategy is not ideal. There is significant disruption to family life with an impact on the whole family. Patients treated in the USA will be required to stay for an average six to eight weeks for treatment.
- In some cases, there could be difficulties ensuring full integration of care with the referring Oncology centre and specialists.

- The problem of communication between different countries should also not be underestimated, either due to linguistic or cultural differences. This can potentially also impact on the patient's well-being and the family's experience during treatment. This is one of the reasons that the overseas programme has recently stopped using the facility in France.

2.40 Limited Overseas capacity.

- The ability of the NHS to commission proton therapy as a treatment would remain completely dependent on the capacity business model (and good will) of a number of different continental European and USA proton centres.
- Business plans for many proton/heavy-ion centres currently coming on line in Europe have planned their referral patterns around high throughputs for their own populations. There is a risk that there will not be capacity for patients from the UK and elsewhere to use these facilities.
- At least three of the new, larger particle therapy facilities are designed to offer Proton beam therapy secondary to their design for Carbon Ion Therapy provision. This limits their capacity of offering guaranteed access to Proton Therapy. Two planned heavy ion German centres will now be closed and never treat any patients due to technical failures.
- Many centres in the USA have been developed to deliver different specification and techniques than that required for the NHS complex case-mix. Simple configurations designed to deliver treatment predominantly for prostate cancer for commercial reasons have limited throughput for the UK specification. This limits the ability to guarantee access to the required technology.

2.41 There is also pressure on the current system for determining those patients who should receive proton therapy treatment overseas. The reference panel is currently almost at the maximum number of referrals that it can consider and new arrangements will need to be made to consider the increasing number of referrals as we build to 400 cases per annum. Plans are in place to develop a clinical network that can assist in managing referrals and this will begin to build expertise and lay the foundations for transition to a national service. Having an increasing number of overseas providers is also an issue, managing relationships with multiple providers adds an additional pressure to the programme.

Research

2.42 This country has already contributed much to conventional radiotherapy through innovative research and could contribute significantly to advances in particle therapy. Provision of particle therapy in England would enable clinical and technical radiotherapy research and clinical trials including novel regimes of combined treatments. The overseas programme is already designed to contribute to research and evaluation in delivery, verification and guidance in advanced particle therapy in a way that is already making us world leaders in this area. Opportunities to evaluate treatment provided in this country would allow us to continue to contribute the development of this cutting-edge treatment. There is considerable international level expertise in the UK in advanced particle accelerator development and a lack of matching clinical experience would limit the potential for scientific and commercial developments for the UK.

2.43 Summary of risks of continuing to send patients overseas for treatment:

- risk of cost increases overseas as capacity declines
- treatment not provided for the high priority patients in England because of lack of capacity overseas
- poor quality of overall care package for patients
- unable to meet any further increase in demand
- inability to treat complex cases.

Impact on current services of developing PBT services in England

2.44 In developing PBT services in England there will be an impact both on the current services commissioned overseas and on existing radiotherapy services. It is recognised that the developing service would need to merge as existing referral patterns and pathways of care for the overseas cases and cases receiving alternative treatment will need to change as facilities come on line in England and ramp up their capacity.

2.45 There would also be an impact on paediatric surgery, neurosurgical and spinal surgical services. This impact would need to be managed as part of a wider PBT development programme managed at NHS CB level while the project/programme to build PBT facilities is managed separately but with strong links. This programme will, over the next four to five years, develop a national integrated PBT network and manage the impact on other radiotherapy services. Through the creation of the single integrated clinical network all potential cases for PBT will have common referral process, assessment and

care pathway.

This will ensure common access and treatment protocols and selection of the optimum sub-specialisation of treatment. The creation of the network and establishment of the centres for PBT treatment will define the future integration requirements for the referring Paediatric and Surgical services. The opportunity for synergistic gains in terms of improved survival and qualitative outcomes is very great in these rarer cancers.

Summary of business need

- 2.46 There is therefore a clear need to develop services in this country in order to expand access to all patients for whom this treatment has been identified as the most clinically appropriate. A national service is required with access by clinical teams to facilities across the country. Developing this kind of national service is beyond the ability of a single Trust acting alone and requires national leadership. In developing services in England, there is a need to ensure the impact on existing services is appropriately managed and the new service is managed as part of a national fully integrated network of care.

Investment Objectives

- 2.47 The following investment objectives have been identified from *A Framework for the Development of PBT Services in England 2009* (annex E). The Framework was developed and signed off by the PBT Advisory Group, which included almost all current clinical PBT experts and medical physicists and has been subsequently signed off by the PBT Delivery Board, which includes representatives from Specialised Commissioning, Strategic Health Authority Medical Directors, the Royal College of Radiologists, NSCT and a patient representative.

1 FINANCIAL

To reduce the current costs of treatment per patient and enable more patients to be treated with a minimal increase in the current commissioning budget to treat patients with PBT.

DEMAND

- 2** To provide the capacity to treat 1500 patients in England and eliminate the need to send up to 400 patients overseas from 2017.

ACCESS

- 3** To ensure that all patients, for whom evidence supports proton therapy as the most clinically effective treatment, receive treatment within a clinically appropriate service specification and to nationally agreed standards.

INFRASTRUCTURE

- 4** To ensure that services provided enable the continued development of the technologies involved and that there is a fully trained and skilled workforce to undertake this service in the NHS.

QUALITY

- 5** To deliver improved outcomes by ensuring that patients have access to high quality modern radiotherapy techniques, comparable to those used in other European countries, to improve cure rates and improve patients' experience by minimising any long-term side effects of treatment.

2.48 Equality and other Impact Assessments will be produced as part of Trust Outline Business Cases.

3. The Economic Case.

- 3.1 This section will outline various options for meeting the investment objectives and having regard to the critical success factors, a series of short-listed options for subsequent ratification and detailed evaluation at the Outline Business Case (OBC) stage.

Table 3.1 Critical success factors

No.	Critical success factor
CSF1	A business need for creating Proton Beam Therapy (PBT) capacity in England has been identified.
CSF2	Clinical and therapeutic resource capacity and capability are well integrated and it is a good allocation of resources.
CSF3	There will be an increase in the benefits to cancer patients over the medium and long term, while improving value for money in the short term. All patients will be evaluated within defined treatment protocols and prospective follow up research studies to ensure clinical and economic outcomes are delivered.
CSF4	The institution is capable of developing PBT capacity and being future proofed through the support of clinical and technological research and development.
CSF 5	There is a long term commitment to site, to technology and to supplier.
CSF6	The proposal is affordable.

Long-list options

- 3.2 The range of options to meet the objectives of the programme have been considered within key categories. Each category is discussed in turn below.
- 3.3 The PBT programme’s working assumption, based on the work undertaken to date by the DH analysts, is that creating PBT capacity in England for non-eye patients in England can halve the cost of treatment, compared to the current average price paid overseas.

- 3.4 To put the possible delivery options into context a short explanation of PBT service delivery is required. The best current clinical and technical evidence, from overseas centres, is that the greatest level of throughput for a multi room site is around 750 patients per year. With current technology this is unlikely to increase in the short to medium term and indeed evidence suggests that achieving this throughput is not easy (for optimum efficiency, there should be no more than three chambers).
- 3.5 The basic installation of an accelerator, including the bunker, associated rooms and control equipment, costs around £100m.
- 3.6 There are a number of technological developments that may mean that high-energy protons can be produced at a lower cost and footprint in the future, although not yet proven as feasible, the summary conclusions of a technical review are included at annex C. The Outline Business Case (OBC) will fully consider future technological advances.

Scoping options

Option 1: Do nothing

- 3.7 This option assumes the DH (and, after creation, the NHS Commissioning Board NHS CB)) carries on commissioning treatment abroad for the caseload of currently agreed indications and that there continues to be sufficient overseas capacity at an acceptable price beyond 2015. This is by no means certain.
- 3.8 Capacity in Europe and elsewhere cannot be guaranteed to be available to NHS patients. Holding the line to the current prioritised list is unlikely to be sustainable in that similar arguments apply across a wider range of particularly paediatric cancers. There would be clinical and public pressure to expand the remit for more cases abroad. The adult cases would have to be treated conventionally with surgery alone or conventional radiotherapy with inferior outcomes. There may be pressure for sacral chordomas to be treated with carbon ion therapy in the absence of protons as the catastrophic consequences in terms of quality of life of curative surgery represent the only alternative.

Option 2: Create NHS capacity in England

- 3.9 Creating NHS capacity in England will ensure that PBT treatment is well integrated with other hospital care facilities and treatment is delivered through a managed network of care.
- 3.10 There are currently patients for whom overseas treatment is inappropriate due to the complex nature of their requirements, the availability of PBT in England would enable these patients to access treatment.

- 3.11 The provision of NHS PBT services will reduce the costs of treatment. Prices currently paid to overseas providers vary widely, reflecting commercial interests as well as underlying costs, the price for NHS treatment will more closely reflect service costs. Travel and accommodation costs will also be greatly reduced.
- 3.12 The provision of PBT treatment in England will develop relevant clinical expertise, offering the potential for further scientific and commercial developments in the UK. A PBT facility in the UK offers the potential to undertake major research programmes that would be difficult to match in other health care systems in the world. A parallel clinical research funding stream would be required.

Option 3: Stimulate/utilise private sector development

- 3.13 There are no providers of PBT in the UK. Due to the high costs of market entry there is currently limited commercial interest in providing PBT in the UK. Initial feedback implied that private sector involvement would only be achieved by the DH given volume guarantees in the same manner as those given on the early Independent Sector Treatment Centres (ISTCs). Initial feedback on this requirement was that volume guarantees would be unacceptable from a policy perspective.
- 3.14 We are aware of one potential development, this proposes making use of a technical solution that is not yet tested or approved and would not be capable of providing a service for a significant majority of our caseload. The development is not planned for a hospital site and so is unlikely to meet CSF 2, requiring a fully integrated service.
- 3.15 Given the uncertainty as to future private sector capacity, this option is not short-listed as it cannot currently be relied upon to deliver PBT services for NHS patients. As part of Trust OBCs, we will re-assess the market landscape and undertake further discussions with the private sector. If any factors affecting the options have changed, we will re-evaluate the options and the criteria for them to be carried forward to the short-list.

Service solution options

Service solution option 1: Configuration of PBT facilities

- 3.16 There are several configuration options for PBT:
- Each accelerator can service between one and four treatment rooms.
 - Treatment rooms can be fixed or rotating (gantry).
- 3.17 Based on best evidence, PBT sites achieve optimum efficiency when operating with three treatment rooms per accelerator. At this capacity, existing centres achieve maximum throughput of 750 patients per annum.

- 3.18 A room with a gantry typically adds an extra £20m to the capital cost of the facility, but it is clinically more appropriate for the proposed NHS case mix and has greater inbuilt future proofing.
- 3.19 Based on the evidence from existing international PBT facilities, the configuration of PBT centres in England will be based on three treatment rooms with gantries.

Service solution Option 2: Number of PBT facilities

a) Develop three NHS centres

- 3.20 The operational rationale for considering a three-site solution is based on a variety of factors:
- a three-site solution would allow easier access to PBT for the majority of the population
 - providing PBT across multiple site will minimise the impact of the required reconfiguration of feeder services
 - developing three sites minimises the risk that supply will not meet projected demand
 - a small amount of excess capacity will allow the centres to be used for research and training purposes and so is the most future proof in terms of capacity requirements.
- 3.21 There are two options for utilising a three-centre model with capital and clinical arguments for both.
1. Develop three centres each with two operating gantries and subsequent addition of the third gantries:

Each centre would initially utilise two gantries at maximum capacity with the later installation of a third gantry as demand requires. Adding a gantry would require a whole centre shutdown of three months and the transfer of caseload to other centres in the interim.
 2. Develop three centres operating three gantries in a single phase:

This option maximises a flexible run up of demand and avoids complex shut downs whilst new chambers are commissioned as in the two operating gantry model.
- 3.22 A three site solution is the clearly the highest cost option.

b) Develop two NHS centres

- 3.23 Based on best evidence a 2-site solution, each treating 750 patients per year will be at the top end of what has been achieved internationally in terms of throughput and efficiency.
- 3.24 There is little risk of redundant capacity but capacity for research and growth of treatment indications will be potentially limited.
- 3.25 The availability of more than one PBT facility provides for the contingency for breakdown of one site. Due to the complex nature of the technology all international centres have had breakdowns. Many patients with curative radiotherapy will need to have treatment completed within the planned overall time if cure rates are not to be compromised.
- 3.26 A two site solution treating 750 patients each per year would meet all of the Critical success factors.

c) Develop one NHS centre

- 3.27 A one-site solution would provide insufficient capacity to treat all patients for whom PBT has been identified as the most clinically effective treatment. The current treatments could be repatriated and treated in the NHS but there would need to be a dramatic revision to the list of proposed case-mix to reprioritise and reduce treatment indications. The scope for research would be dramatically curtailed.
- 3.28 A waiting list caused by bulges of referral would lead to some cases having ‘advanced conventional radiotherapy’ in order not to delay treatment. The practicality is that the current list of indications would need to be revaluated and prioritised to roll out over a period of time and as the single centre capacity is exceeded referral made abroad again or to the private sector should it be there.
- 3.29 There would be less scope to optimise the patterns of associated specialist services such as surgery and paediatric care, thus potentially reducing the opportunity for maximum clinical gain. This option would also create the most dramatic fragmentation of existing services and referral patterns.
- 3.30 In the event of a breakdown, patients would continue with conventional radiotherapy with an attendant compromise of clinical outcomes.
- 3.31 **This option would not meet CSF 1** but could if supplemented by the continued use of overseas capacity and/or by the stimulation of private sector capacity. Use of overseas capacity to fill demand would not meet the CSF 2 – clinical integration. Use of private sector capacity, were it to be closely integrated, would allow this option to meet all of the Critical Success Factors but would make a significant demand on revenue over that planned for if the additional capacity needs to come from overseas.

Funding options

3.32 The main delivery options as detailed above have additional sub-options that will be considered as part of the OBC development. The high capital cost of building a PBT facility¹ means it would be extremely difficult for a foundation trust, even with large reserves, to fund such a scheme without assistance. There are therefore a variety of funding options that will be assessed.

3.33 The project team has assessed the potential for private finance using the criteria developed by the Confederation of British Industry. Based on these criteria, the project could score quite well, it is an area that is worthy of further investigation as part of the OBC development.

Investment Criteria	High	Medium	Low
1. Output/service-delivery driven	<input type="checkbox"/>		
2. Substantial operating content within the project			<input type="checkbox"/>
3. Significant scope for additional/alternative use of asset			<input type="checkbox"/>
4. Scope for innovation in design		<input type="checkbox"/>	
5. Surplus asset intrinsic to transaction			<input type="checkbox"/>
6. Long term contract available			<input type="checkbox"/>
7. Committed public sector management	<input type="checkbox"/>		
8. Political sensitivities are manageable		<input type="checkbox"/>	
9. Risks primarily commercial in nature		<input type="checkbox"/>	
10. Substantial deal	<input type="checkbox"/>		
11. Complete or stand alone operations to allow maximum synergies			<input type="checkbox"/>

¹ around £150m for each PBT multi-room facility. This is equivalent to around 20 times the cost per treatment room compared to conventional radiotherapy, (but note longer effective working life of proton accelerators)

Private Finance Initiative funding style structure

- 3.34 Using Private Finance Initiative (PFI) funding for large capital schemes has previously been used extensively in the hospital building programme. PFI schemes can deliver better value for money when there is scope to bring innovative solutions and where there is a relatively proven delivery model. For a PBT project, a large percentage of the capital cost is associated with the acquisition of the high-tech PBT equipment, which may limit the private sector interest. Key to the use of an availability style PFI model will be the appetite for technology and potentially demand risk.

Public Private Partnership or Joint Venture

- 3.35 A development of the availability style PFI model may well evolve into a joint venture structure with potentially additional risk than that typically passed under a PFI model early indications show that there is some interest in this type of approach.

Public funding

- 3.36 Following a recent policy steer from Ministers, it is now accepted that, subject to availability and value for money, public funding of an NHS led capacity model would be possible. This is a significant step forward but not without hurdles. The precise form of public funding is yet to be determined and the project may be the first or one of the first to approach public funding this way.

Short-listed options

- 3.37 Based on the above long list options, the table below shows the option specifications that have been carried forward to the short-list:

Table 3.2. Short-listed options

Option	Description	Sub-option
1	Do nothing	
2a	Create NHS capacity in England to treat 1500 patients – three centres	i. Public sector financed ii. Private sector financed (PFI style) iii. Mixture of public and private finance (joint- venture)
2b	Create NHS capacity in England to treat 1500 patients –two centres	i. Public sector financed ii. Private sector financed (PFI style) iii. Mixture of public and private finance (joint- venture)
2c	Create NHS Capacity to treat up to 750 patients – one centre	i. Public sector financed ii. Private sector financed (PFI style) iii. Mixture of public and private finance (joint- venture)

3.38 The costs of all short-listed options are assessed over the same 26-year period. This reflects four years of development and the 22-year operational period of the three site solution which covers the longest time horizon. 26 years reflects the minimum 20-year life span for each asset and the phased implementation of sites.

3.39 Each option is assessed on a baseline of treating 1,165 patients for whom PBT is the most clinically effective treatment (excluding ocular patients). Even without changes to the list of conditions that are strongly indicated for treatment with PBT, demand will increase due to population growth. Population growth of 2% per annum is accounted for.

3.40 Costs are based on treating the “average” patient. Solutions with lower volumes of patients accessing PBT will treat only the highest priority patients with the most severe needs. This more complex case-mix will lead to higher costs per patient. At this stage, we cannot accurately model the costs of treating different types of patients.

Option 1: Do Nothing

3.41 The do nothing option does not meet the CSFs for the project but is retained in the short-list of options to provide a benchmark to assess value for money.

3.42 There is an existing commitment to send up to 400 patients of the highest priority patients abroad for treatment. Under the “do nothing” option it is assumed that this commitment will continue over the full appraisal horizon. The cost of this commitment is

expected to be £90,000 per patient. The total discounted cost of maintaining this commitment over the appraisal period is £619m.

Patients without access to PBT overseas will receive alternative treatments:

In the majority (90%) of cases, these patients will be treated with advanced conventional radiotherapy solutions such as Intensity-Modulated Radiation treatment (IMRT). Treatment doses and clinical outcomes will be inferior.

For two-thirds of the remaining patients, current conventional treatment is with surgery alone but with demonstrated poor outcomes in terms of poor local control and/or quality of life.

For the minority of cases, no alternative to PBT can be offered either due to young age or risk of serious toxicity with conventional radiotherapy.

Maximum, Option 2a: Create NHS capacity in England to treat 1,500 patients – three centres

- 3.43 Developing three PBT facilities will initially create capacity exceeding current demand from NHS patients. The use of spare capacity for research or the treatment of overseas patients will provide income to the programme. There are real opportunities to treat patients from smaller countries in Europe who cannot invest adequate resources eg Republic of Ireland and to undertake major research programmes that would be difficult to match in other health care systems in the world. A parallel clinical research funding stream would be required².

In the period during which all three operational facilities are operational, all strongly indicated patients will have access to PBT, receiving the most clinically effective treatment for their conditions.

Indicative cost estimates are based on three centres with three operational gantries developed in a single phase. The OBC will consider options for the phased implementation of gantries.

Intermediate, Option 2b: Create NHS capacity in England to treat 1,500 patients – two centres

- 3.44 Developing two NHS centres will create capacity exceeding demand from NHS patients in the short term. The use of spare capacity will provide income to the programme.

As population growth increases demand from patients with current indications capacity will be exceeded. Patients without access to PBT will be reliant on advanced conventional radiotherapy and/or surgery.

² Costs and benefits of research are not currently included in modelling.

Minimum, Option 2c: Create NHS capacity in England to treat 750 patients – one centre

- 3.45 One Centre will provide treatment for 750 patients. The high complexity case mix of a limited capacity of a prioritised 750 patients is at the limit of throughput of any centre internationally. Additional demand may be unmet through patients being treated with existing treatment modalities.

In the majority of cases (90%) where patients do not have access to PBT “advanced conventional radiotherapy” solutions such as IMRT will be used. Treatment doses and clinical outcomes will be inferior.

In due course if additional capacity is required, a group of lower dependency and less complicated cases would need to be prioritised to consider for proton treatment abroad or within any private sector capacity. Due to the current lack of private sector capacity, indicative costs are based on overseas treatment for this group of patients.

Summary

- 3.46 The following table summarises the costs of each option.

Costs (£000s)	Do Nothing	2a: NHS capacity, three centres	2b: NHS capacity, two centres	2c: NHS capacity, one centre
Capital & Project costs				
Land		30,000	20,000	10,000
Design & Build		414,000	276,000	138,000
Risk retained		10,500	7,000	3,500
Optimism Bias (25%)		111,000	74,000	37,000
Total		565,500	377,000	188,500
Discounted total		533,369	355,173	177,790
Revenue costs				
Costs	932,970	710,162	494,916	369,531
Income		- 348,225	- 16,751	
Optimism Bias (25%)	204,742	174,000	116,000	68,042
Total	1,137,713	535,937	594,166	437,573
Discounted total	688,393	323,335	366,532	268,526
Total Costs				
Total Costs	1,137,713	1,101,437	971,166	626,073
Discounted Total	688,393	856,703	721,705	446,316

Although clearly the most expensive, the three-site option best meets the critical success factors for the project, delivering capacity to meet demand, providing the best geographical access and having the least impact on existing services.

However, on the basis of affordability issues, a two-site solution can meet demand if used to maximum capacity. Two centres will provide a degree of resilience and provide sufficient capacity to treat patients from the devolved administrations.

4. The Financial Case

- 4.1 Indicative costs only are available for the options described in the Economic Case. These indicative costs come from the market engagement exercise conducted last year. It does not however take into consideration the Public Funding sub-option.

Revenue constraints

- 4.2 The Trusts will be re-imbursed the revenue costs via a national tariff. The service will be commissioned by the NHS Commissioning Board (NHSCB) under its arrangements for specialised commissioning and will therefore be funded out of the NHSCB overall programme budget. Spending on the PBT overseas programme will rise each year over the current spending review period until £30m per annum will be being spent treating 400 patients overseas in 2014 to 2015.
- 4.3 It is assumed that this annual revenue commitment will be available to fund the revenue consequences of options other than the overseas treatment programme. That is if the preferred solution is found to be the development of NHS capacity, it is intended that as the new facilities are commissioned this budget would be diverted to fund the majority of the revenue costs.
- 4.4 The £30m was identified using a cost per case calculated at £75,000. Early work to look at expected costs per case of a facility in England has been undertaken based on a number of scenarios. The cost per case is dependent on two main factors: the source of funds and the total available capacity. A one centre solution does not provide enough capacity for all patients to be treated and there would be additional cost in continuing to treat patients overseas. A two centre and three centre solution enables the full caseload to be treated without requiring the use of overseas facilities.
- 4.5 This has shown that the £30m revenue can support a two centre public financed option. It may also support a three centre option with excess capacity and income used to offset costs. The table below shows our initial estimates of revenue costs and further work will be undertaken to refine this in the Outline Business Case (OBC). A one site solution does not have enough capacity to deliver the expected demand and this option would exceed the current costs of c£30m if c400 patients then required treatment overseas.
- 4.6 The table below compares the revenue costs of each options based on the modelling assumptions set out for each short-listed option in the economic case, along with plans for funding them. The availability of PBT facilities in England will reduce the revenue costs of treating the current list of indications.

Table 1: Estimated Revenue costs

	Options			Notes
	One site	Two sites	Three sites	
Capacity	800	1500	2300	1
Cost per Case (Estimated)	£32k	£32k	£32k	2
Total no of patients requiring treatment	1165	1165	1165	
English Patients that would be treated in UK	800	1165	1165	
Cost pa £m (England) at £17k pp	£26m	£37m	£37m	
No of patients for overseas treatment	365	n/a	n/a	
Overseas costs (at £90k)	£32m	n/a	n/a	
Total costs for 1165 PATIENTS	£58	£37m	£37m	
Current costs (overseas treatment)	£30m	£30m	£30m	
Income from spare capacity (Devolved Administrations only)	n/a	£7m	£7m	3, 4
Costs >£30m FOR 1165 PATIENTS	£28m	(£0m)	(£0m)	

- 1 Three site solutions assumes common number of gantries
Based on preliminary costing work. A one site solution would take more complex cases and therefore have higher unit costs.
The estimated cost per patient includes an appropriate allowance for
- 2 depreciation of assets.
- 3 Assumes Devolved Administrations demand is 226 patients
- 4 Three site solution does not identify further income streams for spare capacity other than Devolved Administrations

The costs are very much outline costs and were developed by University College London Hospital (UCLH), one of the trusts interested in hosting a PBT centre.

Capital Constraints

- 4.7 Under some of the proposed delivery sub-options the DH may be prepared subject to ongoing capital availability and demonstrating value for money to provide public funding for the capital costs involved. At present, the DH finance has confirmed the availability of £150m over this spending review in the profile as shown in Table 2 below. The Secretary of State has confirmed his intention to prioritise sufficient funding to support the development of a two-centre service.
- 4.8 The annual costs for a single PBT unit are, yet, unclear given outline business cases have not been drafted. Best estimate of spend profile is shown below.

Table 2: Estimate of Capital Costs for one, two and three site options

Estimated Capital costs (£m)					
	Year 1	Year 2	Year 3	Year 4	Total
	2012/13	2013/14	2014/15	2015/16	
One Site option		40	69	24	133
Two site option		80	138	48	266
Three site option		120	207	72	399

Notes:

Capital costs exclude:

1. design costs and other revenue costs associated with project delivery
2. Land values, estimated at approx £10m per site.

5. The Commercial Case.

- 5.1 The overall commercial approach will be developed and refined for Trust Outline Business Cases (OBCs). At the same time an evidence based procurement strategy will be developed. The commercial case here focuses on the short listed options and the responses gathered from the market engagement already undertaken.
- 5.2 This commercial case relates to commissioning Proton Beam Therapy (PBT) services for up to 1,500 patients per annum from a variety of possible delivery options. For the sake of clarity, it does not look at the do nothing option of commissioning and sending patients for treatment overseas.
- 5.3 The Department of Health's preferred position is to adopt the position, as a Commissioner, reflected in the NHS Standard Contract and the PBT service be provided under any of the short-listed options by the NHS or by a private sector service provider.
- 5.4 The commercial aspects discussed here relate to both the role of the NHS or private sector as service provider and the role of potential equipment manufacturers/suppliers to the NHS or the private sector.

Market engagement - Assessment of attractiveness to NHS providers

- 5.5 The provision of PBT services within the NHS would be a highly prized facility. The market engagement exercise carried out previously attracted strong interest and the following Foundation Trusts (FTs) and NHS Trusts submitted proposals:

Cambridge University Hospitals NHSFT
Clatterbridge Centre for Oncology NHSFT (joint bid with Alder Hey Hospital NHSFT)
Christie Hospital NHSFT
Imperial College Healthcare NHST (joint bid with Royal Marsden NHSFT)
Leeds Teaching Hospitals NHS Trust
Oxford Radcliffe Hospitals NHS Trust
University of Birmingham Hospitals NHSFT
University College Hospital NHSFT (ULCH Partners)

The evaluation of the proposals concluded that six of the eight proposals were capable of delivering a national PBT service. However, most are not prepared to go ahead without guarantees of activity or a significant capital contribution.

Market engagement - Assessment of attractiveness to private sector providers

- 5.6 The high costs of entry could probably be a significant barrier to entry for potential private sector partners. Having said that, there are credible private sector organisations that are actively following developments of PBT within the UK (see paragraph 3.14)

The extent of private sector interest will be further developed at OBC.

**Market engagement - Assessment of attractiveness to manufacturers/
construction companies**

5.7 There has been no engagement with equipment manufacturers yet. Notwithstanding the equipment procurement may take place by Trusts, a programme wide procurement strategy will be developed at OBC stage.

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*[please note, this information has been redacted for commercial or legal purposes]

5.8 A significant cost within the overall cost of a proton beam centre is the construction cost. This is relatively straightforward but will depend on procurement strategies.

6. The Management Case

- 6.1 This section addresses the achievability of the programme. It will outline the proposed management and governance arrangements to ensure the successful delivery of the identified investment objectives and realisation of the agreed benefits.
- 6.2 The National Specialised Commissioning Team (NSCT) were asked to take forward the process of commissioning a Proton Beam Therapy (PBT) Service in England by 2014 to 2015. The Department of Health agreed to support the NSCT, with specialist procurement, programme and project management expertise and have taken the role as Senior Responsible Officer (SRO) in house to produce a DH business case for the development of a National PBT service.
- 6.3 The proposed management structures and governance framework described in this section reflect the joint responsibilities and accountabilities for Phase I, (Strategic Outline Case SOC)) and Phase II (Outline Business Case (OBC) and Full Business case (FBC)) of the programme.
- 6.4 The organisational structure of both the core DH and NHS is in a period of transition. The proposed management and governance responsibilities for future phases are therefore recommendations based on key assumptions on the future shape of health organisations. The recommendations will need to be reviewed to ensure they are appropriate for each phase of the programme and are likely to require a joint governance structure between the DH and the NHS Commissioning Board (NHS CB), ensuring that any providers or co-funders are represented at the most senior Steering Group/ Delivery Board level.
- 6.5 The programme for the development of PBT Services in England is part of a wider portfolio of programmes to review and improve radiotherapy services and facilities in England, as identified in Improving Outcomes: A Strategy for Cancer in 2011 following on from the Cancer Reform Strategy, 2007. In response to these programme interdependencies, the organisational structures and recommended governance frameworks have been designed to ensure that all key stakeholders in the DH and the future Commissioning organisations are identified and included in the governance arrangements.

Programme Management arrangements for Phase I & II

- 6.6 The proposed organisational structure for the PBT Programme is in line with best programme and project management guidance and has been tailored for the governance requirements of this programme.

- 6.7 Key stakeholders from the NSCT are currently represented on the PBT Delivery Board and the PBT Project Team. The NSCT will continue to maintain strong relationships with key staff within the provider Trusts during the FBC development of Phase I and during Phase II of the programme.

Programme Management arrangements for Phase II & III (delivery).

- 6.8 For the purposes of this Management Case, the assumption has been made that the current Commissioners will become a part of the Specialised Services Portfolio, which will be part of the NHSCB.
- 6.9 The roles of the host programme management organisation implemented for the OBC will need to be replaced for Phase III of the programme, with the Commissioners directing and managing the programme and providing the physical and financial resources for development of the facilities. The DH Cancer Programme Board and Cancer Policy Team (and their successors in NHS CB) will monitor progress as key stakeholders and will lead in managing the impact on existing radiotherapy services and development of the clinical network.

Programme roles, responsibilities and assurances

- 6.10 The existing roles and responsibilities for Phase I of the programme, (SOC) and Phase II (OBC and FBC,) are:

Investment Decision Maker		Secretary of State for Health
Senior Responsible Officer		National Cancer Director
Project Director		
Project Manager		
National Clinical Lead		Consultant Clinical Oncologist
Project Support Office		
Programme Assurance roles		OGC Gateway™ Review Teams National Clinical Advisory Team

PBT Delivery Board

- 6.11 The PBT Delivery Board (now Steering Committee) is the key strategic decision-making forum for the PBT programme. It will retain overall responsibility for delivery of the investment objectives and benefits identified in the Business Case.
- 6.12 The Delivery Board will be chaired by the programme’s SRO and will limit its involvement to providing approval and strategic guidance at key programme milestones. The PBT Delivery Board Terms of Reference are attached at annex D. This Board will need to adapt to reflect the joint governance arrangements between the DH and NHS CB and ensure representation from Trusts and co-funders as the programme progresses.

PBT Project Team

- 6.13 The PBT Project Team will be responsible for planning and delivering the PBT programme and will be chaired by the Project Director. The PBT Project Team will provide leadership and advice and monitor the performance of the Trusts' Project Teams. The PBT Project Team will be responsible for reporting progress, financial forecasts and expenditure and programme delivery data to the PBT Delivery Board.
- 6.14 The memberships for the Delivery Board and Project Team will be reviewed at each stage boundary to ensure the membership is appropriate for the following stage.

Senior Responsible Officer

- 6.15 The SRO is appointed by and accountable to, the Investment Decision Maker, (IDM). The SRO will provide visible commitment and authority to the programme, ensuring appropriate influence and engagement with key stakeholders and a focus on realisation of the benefits identified in the Business Case.
- 6.16 The SRO is responsible for ensuring there are sufficient resources to enable a successful outcome. The role provides the key reporting and decision-making role between the IDM and the PBT Delivery Board. Ultimate decision-making authority sits with the SRO, assisted in an advisory capacity by the Delivery Board.

National Clinical Lead for PBT

- 6.17 The National Clinical Lead (NCL) for PBT role is responsible for defining the clinical work streams and for the coordination of the programme with the other radiotherapy programmes in the portfolio. The NCL is accountable to the SRO for defining the clinical benefits, assessing progress towards realisation and for achieving measured improvements in PBT services in England. The NCL will be responsible for planning and managing the transition of change when the new PBT services become operational.

Outline arrangements for risk management and issues resolution

- 6.18 The Phase One Risk Management Strategy, (RMS), has been developed with reference to the *The Orange Book: the Management of Risk – Principles and Concept*,³ *Management of Risk: Guidance for Practitioners*,⁴ and *Managing risks with delivery partners*⁵. It is consistent with the DH's stewardship risk management framework.
- 6.19 The Delivery Board's risk appetite is described as tolerant of informed risks that have a clear and achievable mitigation plan. For Phase I of the programme, risks are reported and monitored by the Project Manager and the Project Director, who escalates to the Cancer Programme Board and the PBT Delivery Board. During the FBC phase, The

³ HM Treasury (2004)

⁴ Office of Government Commerce (2007)

⁵ HM Treasury and Office of Government Commerce (2005)

NCL and Performance Liaison Manager will also monitor clinical and service delivery risks, in partnership with the provider Trusts and proposed suppliers. The Risk Register will be reviewed monthly as a standard agenda item at the forums identified in the RMS. All risks will be assigned a lead Risk Owner who will be accountable and answerable if the risk materialises.

Transition

- 6.20 It is recognised that the governance arrangements may need to change at FBC and delivery phases as functions and accountabilities change and to reflect financing sources.

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Annex B: Notes to accompany Clinical Indication List

1. The caseload and patient numbers for paediatric cancers suitable for proton treatment are taken from a survey of the Children's Cancer and Leukaemia Group (CCLG) database. It allows an accurate assessment of numbers of cases treated with radiotherapy. It makes assumptions that palliative treatments and specialist regional radiotherapy centres with conventional radiotherapy would still undertake some simple techniques. Proton treatment may allow much younger children to be treated (see note four) Although the paediatric caseload overall (notes one to four) might be viewed as low these cases are necessarily complex, time consuming in terms of both planning and treatment delivery. The proportion of children requiring anaesthesia will be higher than in current practice and is estimated to be 30% (set up and treatment time is longer and with a younger age profile than currently given radiotherapy). This data has been crosschecked with Cancer Registry data although this is relatively crude in terms of such detailed diagnosis information compared with the CCLG data.
2. The addition of this category to the National Radiotherapy Advisory Group (NRAG) lists reflects the changing evidence relating to late second malignancy. There are small numbers of Head and Neck cancer occurring in children, particularly nasopharyngeal cancer. These are treated currently with conventional radiotherapy but it is clear that the site, close to the base of brain and critical dose limiting structures and the risk of second malignancy makes them ideal for treatment with Protons. The numbers are taken from the Yorkshire Cancer Network experience and scaled to the UK population.
3. There are small numbers of extremely rare cancer diagnoses in children that require radiotherapy for curative treatment. It is clear from experience in existing Proton Treatment Centres (PTC) that these special cases are referred where the facility exists. For completeness they therefore need to be included on the diagnostic list although in terms of numbers are insignificant.
4. The majority of the paediatric indications list reflects a shift of caseload currently receiving treatment with conventional radiotherapy. However, the age threshold at which it is felt radiotherapy can be safely given would change significantly if Proton treatment were available in the UK. Whilst the age changes with different diagnoses and situations, there is no doubt from the experience in Europe and the USA that there would be some children given Protons where they currently do not receive radiotherapy as part of their treatment.
5. The numbers for Acoustic Neuroma and Meningioma have been reduced from the original numbers contained within the NRAG report. The use of Gamma Knife will have a role and may take some appropriate cases. However, Gamma Knife has technical limitations in particular the size of a target volume that limits its clinical application. In addition, treatment is delivered in a single fraction and so is highly inappropriate where dose limiting normal tissue structures may be close and where

fractionated radiotherapy is more appropriate. The danger in this assumption is that if Protons were available in the UK it would become the treatment of choice due to its better dose distribution and scattered low dose X-ray, especially in younger patients where the risk of late second malignancy may be of concern. As far as meningioma is concerned, the assumption is that only high-grade tumours will receive radiotherapy. If data emerges from the current European Organisation for Research and Treatment of Cancer (EORTC) trial that higher doses of radiotherapy have higher local control rates then Proton treatment could be the treatment of choice and again these numbers are an underestimate.

6. The addition of selected head and neck cancer and paranasal sinuses cancers is based on good data from case series and better clinical experience from PTCs around the world. The histological types often include a wider variation of subtypes where radiotherapy doses may need to be higher. Many of these cancers have high cure rates and are closely related to the base of skull and other critical dose limiting structures. If available, protons would give a significantly better treatment option and are included in the indications list. Local recurrences of head and neck cancer or second malignancies are not uncommon and may still be curable. Conventional radiotherapy may not be an option but due to its superior dose distribution and dose to surrounding tissues, Proton treatment is an option. Whilst the numbers of paranasal cancers can be accurately estimated (UK numbers 392 on incidence data with assumption of 50% having Proton treatment as opposed to conventional radiotherapy) the numbers of head and neck cancers (100) may be an underestimate when it becomes an accessible option.
7. The numbers of ocular tumours and choroidal melanoma is taken from the current caseload and data from the UK low energy facility at Clatterbridge and is assumed to be stable.
8. The numbers of these standard indications is taken directly from the NRAG report that in turn is based on Cancer Registry data. This makes an assumption that many inoperable sacral chordomas in particular may still receive optimal high dose conventional radiotherapy. New data on particle treatment of these incurable cases does however suggest that higher doses, only deliverable with Protons or carbon ions, may have significantly higher local control rates and survivals and so may be optimally treatment with Protons. Again, whilst the numbers are low it may make this estimate a conservative one.
9. This is the most difficult and variable estimate. There have been several studies looking at how the numbers of rare and common cancers with indications for potentially curative radiotherapy and for whom Proton treatment is a clearly superior option, can be estimated. These cases may be atypical and unusual situations in common cancers where either due to atypical patient anatomy or concurrent conditions or previous radiotherapy treatment, conventional radiotherapy is not an option. Whilst unusual small numbers of common cancers multiply up to be significant. Some of these patients would not wish to travel for Protons and uptake may be lower even if offered so again making estimating numbers more difficult. In other situations there are some tumour types that are difficult to treat and Protons may offer a simpler and much better dose distribution if available and so be the treatment of choice e.g. Thymoma. Some examples are given below.

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- a. Young adults may require radiotherapy for standard radiotherapy indications and although unusual present the same challenges to late side effects from low doses outside the main target volume as in paediatric cancers. The emphasis here is on reducing late second malignancy and fertility.
 - b. Some new cancers may occur close to radiotherapy for a previously treated cancer. Protons may be the only way in which safe radiotherapy may be given so close to previous fields.
 - c. Thymoma radiotherapy indicated for stage II and III post resection. Estimated 80 cases per annum with 40 % invasive so indications for Proton treatment 28 cases.
 - d. Abnormal anatomy - Breast cancer radiotherapy - 'pectus excavatum'. Estimate 25 cases per annum
 - e. Breast cancer radiotherapy on the left side – in those patients estimated to have very high risks due to concurrent cardiac conditions or Herceptin effects or in other atypical situations of previous radiotherapy treatment for other conditions Protons may be a significantly better option than conventional radiotherapy. Even if this amounts to 1% of all radiotherapy treatment for breast cancer the numbers would be 137 cases.
 - f. Basic studies of highly complex cases where conventional radiotherapy has major limitations and so curative treatment compromised currently vary. Estimates vary from 150 per annum in the lowest (three cases per million population) through to 500 per annum. There are studies from Sweden and the UK suggesting that if factors of purely optimum dose distributions are taken into account (with significant impact on significant toxicity, local control rates and second malignancies) then 10%-15% of patients treated with radiotherapy may have an indication for Protons. This is clearly unachievable at present with current costs and technology but is an important indicator for longer term future planning.
10. There is merit on allowing some of these cases early on in the commissioning of a centre in England, as the planning is less complex and would allow a rapid rise in the experience and confidence of new centres. This would enable the more complex cases to be treated with confidence earlier.
11. Highly atypical cases of incurable situations (often limited local recurrence) for younger patients with longer estimates of survival occur and have been prominent in the referrals for referral abroad within the current system. Higher local control rates with significantly lower acute toxicity may make these cases difficult to deny treatment to once Protons are available. These should be restricted to very small numbers.
12. Thus, the figure of 300 included in these figures may be a considerable underestimate. However, the indications in this group would grow with time and clinical evidence and an effective gate-keeping rule needs to be set for referral. The National Commissioning Group (NCG) Proton Clinical Reference Panel have suggested that the criteria for access to Protons in this "Difficult Cases" category is defined tightly. This would be:
- a. normal tissue dose constraints cannot be achieved by optimal conventional radiotherapy techniques with Intensity-modulated radiation therapy (IMRT)

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- b. patients are of good performance status with curable conditions
- c. have a life expectancy from other concurrent conditions of greater than five years.

Conclusion:

- 13. A base figure of 1487 is taken as a minimum to be commissioned for the UK.
- 14. If the Republic Ireland is taken into account as a likely required capacity in the medium term then a base capacity of 1595 is required.
- 15. If a minimum requirement of 5% of capacity is made available for clinical trials then an extra 71 cases and so a required capacity of 1561 cases.
- 16. If both of the factors above are considered a required capacity of 1664 cases is reached.
- 17. Consideration should be given to the need for a back up plans in the event of breakdown and geographical access, especially for the paediatric cases.

Annex C Technology Review – summary conclusions

The Science and Technology Facilities Council (STFC) was commissioned to undertake a short independent review of the existing proposed developments in the technology for Proton Beam Therapy (PBT). The purpose of the review was to assess the available technologies for a clinical service in 2015 to 2016 and what technologies might become available from 2016 to 2026 that might either supersede or prejudice the current investment proposed in PBT within the Strategic Outline Case (SOC). Costs were not included in the review but the main issues were addressed.

The main conclusions are:

[REDACTED]

[REDACTED]

*[please note, this information has been redacted for commercial or legal purposes]

[REDACTED] manufacturers may produce clinical systems within the next five years but their plans for the required scanning beam technology and gantries are uncertain. In many cases, the systems are designed for smaller facilities and a less complex case mix.

There are significant risks associated with the delivery and commissioning of new untested and unlicensed systems in these technologies that could compromise the delivery of a clinical programme.

[REDACTED] compact accelerator technologies such as the [REDACTED] are still too early in their development to assess viability and certainly do not represent a risk of technical redundancy within the medium term.

The physical reduction in gantry size of some new solutions and components should reduce manufacturing cost. The true cost of the systems will only be known following contract negotiation, but may be available within a relevant timescale for 2015 to 2016 commissioning.

The physical size reduction could allow smaller treatment rooms and facilities.

The availability of imaging, treatment planning, robotic positioners and beam switching solutions will need to be addressed for a working clinical solution but were not included in this review and should form part of detailed contract negotiations.

There is not a new technology on the horizon that would make the investment in current technology redundant.

These initial findings and the uncertainty in licensing of the new technology accelerator /delivery systems support the previous view of the Project Team that a service should be developed using the latest generation full gantry systems. This will allow beam delivery for a complex case mix and is the realistic option for ensuring service commencement in 2015 providing a solution that is unlikely to be superseded by new technology in the medium term.

Annex D: Proton Beam Therapy Delivery Board Terms of Reference

National Proton Beam Therapy Service Development Programme Steering Committee Terms of Reference

<p>1. Name Of Group:</p>	<p>National Proton Beam Therapy Service Development Programme Steering Committee.</p>
<p>2. Accountable To:</p>	<p>The Cancer Programme Board to 31 March 2013 and NHS Commissioning Board (NHS CB) subsequently.</p>
<p>3. Aims And Purpose:</p>	<p>To ensure the effective and timely delivery of PBT services in England, managing the impact on other clinical support and radiotherapy services.</p>
<p>4. Objectives And Responsibilities:</p>	<ol style="list-style-type: none"> 1. To develop a PBT service that meets the objectives as stated in the Strategic Outline Case, December 2011. 2. To oversee the facilities projects to ensure that the two sites develop a service that meets Commissioner’s specifications and is delivered to time and budget. 3. To monitor the facilities project financial governance arrangements to ensure that it delivers value for money. 4. To manage the transition from an overseas service to a service in England. 5. To identify and manage the impact of the PBT service on other clinical services. 6. To develop a national clinical network for PBT. 7. To ensure that a research strategy is in place that informs the future development of the service. 8. To manage the impact on workforce across all radiotherapy services. 9. To advise and report to Ministers and NHS CB on progress. <p>In delivering the above the committee will ensure that :</p> <ul style="list-style-type: none"> • there is support from Ministers, NHS CB is obtained at key stages of the programme • there is key stakeholder involvement at all stages of the programme • there are effective stakeholder communications • the programme is properly resourced to achieve its objectives

	<ul style="list-style-type: none"> • the programme is clinically lead with appropriate clinical engagement • risks to the delivery of the programme objectives are identified and effectively managed.
<p>5. PBT Steering Committee Membership:</p>	<p>Co-Chairs</p> <ul style="list-style-type: none"> ▪ National Cancer Director – Mike Richards ▪ DH Director of Clinical Programmes – Gerard Hetherington <p>Department of Health</p> <ul style="list-style-type: none"> ▪ Director of Financial Planning and Allocations – Thomas Nixon ▪ Director Capital Investment Strategy – Ben Masterson ▪ Deputy Director Screening and Specialised Services – Claire Brassington (papers only) ▪ Deputy Director Cancer Programme – Jane Allberry ▪ Project Director Project I – Elizabeth Bisdee ▪ Project Directors Project II and III - tba <p>National Specialised Commissioning Team.</p> <ul style="list-style-type: none"> ▪ Director Specialised Commissioning – Teresa Moss ▪ Finance Director – Jo Sheehan <p>National Specialised Commissioning Group (SCG) Representative</p> <ul style="list-style-type: none"> ▪ An SCG Director – Stephanie Newman <p>NHS Commissioning Board</p> <ul style="list-style-type: none"> ▪ Kathy McLean <p>Clinical Representatives</p> <ul style="list-style-type: none"> ▪ Strategic Health Authority Medical Director –Chris Welsh ▪ National Clinical Lead for PBT – Adrian Crellin ▪ Royal College of Radiologists – Jane Barrett ▪ International and Medical Physics advice – Tony Lomax ▪ National Cancer Research Institute – Neil Burnet <p>Patient Representative nominated by Royal College of Radiologists</p> <ul style="list-style-type: none"> ▪ vacant <p>Additional specialist advice will be obtained as and when required.</p>
<p>6. Decision Making Process:</p>	<p>Decisions will normally be achieved through consensus. Otherwise, a simple majority vote may be taken, in which only full members of the Board may participate.</p>

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<p>7. Quorum:</p>	<p>Formally nominated deputies will be allowed. However, any deputies must be fully briefed and have delegated authority from the organisation that they are representing.</p> <p>The meeting will be deemed quorate when at least four members from the Steering Committee are present.</p>
<p>8. Frequency Of Meetings:</p>	<p>It is envisaged that the group will meet every other month or when key decisions are required.</p>
<p>9. Support:</p>	<p>Secretariat support will be provided by the Cancer Policy Team.</p>
<p>10. Review Date:</p>	<p>The PBT Steering Committee Terms of Reference and Membership will be reviewed by the group at each phase of the programme.</p>
<p>11. Conflict of interest</p>	<ul style="list-style-type: none"> • All members of the Committee and those asked to comment on work produced by the Committee will be asked to declare any conflicts of interest. Any action to be taken on the basis of these declarations will be at the discretion of the Chair. • When key decisions are being made, particularly in relation to the activities outlined in objective three above, appropriate governance arrangements will be put in place.
<p>12. Confidentiality</p>	<ul style="list-style-type: none"> • Records of the Committee meetings and the discussions held, decisions and recommendations made will be kept on file by the Department of Health in line with their normal policies. This information will be available to the public and other interested parties in line with current legislation. • The Committee may from time to time be asked to consider, discuss or review material that, for reasons such as commercial confidentiality, is required to remain confidential. Members will be clearly notified where material is of this nature and will, by virtue of their membership of the Committee and agreement to these Terms of Reference, agree to keep such material confidential.

Annex E: A Framework for the Development of Proton Beam Therapy in England 2009



A Framework for the Development of Proton Beam Therapy Services in England

Department of Health

27th July 2009

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Executive Summary.

Objectives of the PBT framework

1. This framework for the development of PBT services in England has been developed by the DH following the recommendations made by National Radiotherapy Advisory Group (NRAG) and the commitment in the Cancer Reform Strategy (CRS) to consider options for developing PBT services in this country. It is intended to guide commissioners and potential providers of services by providing advice on the current evidence of benefit from PBT; the current state of the technology; an outline specification of the service likely to be required; workforce and training issues; capital and revenue costs and needs for further research and evaluation.
2. The development of services also addresses the unsustainability of the current process managed by the National Specialised Commissioning Group (NSCG) where an increasing number of patients up to 400 per annum are to be referred overseas for treatment.
3. The objectives of PBT services to be developed are:
 - To ensure that all patients, for whom evidence supports proton therapy as the most clinically effective treatment, receive treatment within a clinically appropriate service specification and to nationally agreed standards.
 - To ensure that services provided enable the continued development of the technologies involved and that workforce and training issues are appropriately addressed.
 - To ensure that services in England match international standards for Radiotherapy, consistent with the CRS Commitment to develop World Class services.

Approach to development of the framework

4. The framework draws heavily on previous detailed work undertaken by expert groups including the Proton Therapy sub-group of the NRAG. A market review was also undertaken by the Centre for Evidence based Purchasing (CEP), the review was carried out using more detailed work undertaken in the USA and approaching the manufacturers re their position in this country.
5. The National Cancer Director convened an advisory group of experts to help develop this framework in September 2008.

6. While the framework addresses revenue costs and sources of funding for these services, it does not make specific recommendations regarding capital solutions for PBT service providers. NHS Trusts will need to consider the relative merits of different public/private sector funding and management approaches in submitting proposals.

Clinical applications and likely demand for PBT

7. The indications where the use of PBT over optimal conventional radiotherapy is the most appropriate treatment have been reviewed and updated. Expert advice indicates that in the immediate future the indications and associated planning numbers support the establishment of facilities in this country so that all appropriate patients can have access to this treatment.
8. Significantly, the revised indications support up to 250 paediatric patients, some of whom, without access to PBT would not access any form of radiotherapy due to their young age and would be likely to experience significantly poorer outcomes. Plans should be made to provide services to treat 1500 adult and paediatric patients in England with, up to an additional 200 from other UK countries and to provide capacity for research trials in the next three to five years or as soon as facilities can be developed. This figure is likely to rise further as the research evidence grows and encompasses more cancer types. The Advisory Group evidence paper also anticipates wider potential for this treatment.
9. The full list of indications is provided at annex A. The review of indications has identified that the current “high priority” or “A” list used to refer patients overseas by the NSCG requires some updates. There is new evidence from existing PBT centres about the prevention of late second malignancy in the treatment of children with conventional radiotherapy. This list has been updated to reflect this and other developments and is attached at annex B. This list should continue to be used until facilities are operational in this country.

Current provision of PBT services in the UK and Overseas

10. The current UK facility at Clatterbridge treats 100–130 patients a year with ocular malignancy in the conserved eye.
11. As a result of the NRAG recommendations, a Proton Therapy Clinical Reference Panel (PTCRP) was established to review clinical cases on behalf of PCTs and recommend/ approve referrals outside the UK while facilities in this country are being established. The panel’s role is to ensure that patients with cancers listed as a high priority have fair and equitable access to overseas treatment by reviewing individual cases and prioritising their need for treatment.

12. The NSCG has commissioned an increasing level of activity from April 2008. The number of cases referred in 2008 to 2009 has exceeded expectations; the planning figure for 2009 to 2010 has, therefore, increased. Due to the complexity of the patient pathway in sending patients abroad, paediatric cases are less represented in terms of numbers.
13. Services are currently commissioned from three overseas centres based in Switzerland, France and the USA. There is limited capacity for treating patients in Europe and the USA, the overseas referral process therefore needs careful management.
14. The NSCG has a remit to refer up to 400 patients overseas for treatment but the process will become increasingly unsustainable as numbers increase:
 - capacity at overseas centres is limited and access is therefore restricted
 - as capacity reduces the costs may increase
 - practicalities of managing complex pathways
 - administrative demands on the clinical reference panel
 - potential further increases in demand particularly in paediatric cases
 - increasing demand for PCTs to fund supporting surgery and chemotherapy of patients referred abroad
 - public demand for appropriate access to PBT being increasingly reflected by media, especially in paediatric caseload.

Current advice on technology

15. Not all manufacturers will want, or be able, to supply PBT equipment in the UK. Because of the indications that the Advisory Group have identified as appropriate for this treatment, a higher specification of equipment is necessary to deliver treatment for these patients. While there are potentially cheaper systems coming on to the market, none are yet clinically available and it is estimated that it could be another 10 to 20 years before these machines are commonplace.
16. The future direction of PBT is likely to extend to heavier particles such as carbon or oxygen ions. Heavy ions have some theoretical benefits over protons. Not all systems currently have heavy ion capability, though most will have that capability in the future. Even more so than proton therapy, there is scope for research into heavy ion therapy and this would help the UK scientific community to be at the forefront of research. However, these systems are likely to be much larger and more expensive than PBT.

Overall requirement for services

17. To treat 1500 patients, services should be co-located with cancer and paediatric services. Transport links should be of the highest quality and accommodation for patients and carers should be available locally. The service must look to the future in terms of enabling further research into use of the technology and development of the science involved to provide value for money, not only for current patients but for services users of the future as the technology develops. There is strong evidence of benefits of integration of new Proton facilities with major conventional radiotherapy services to ensure the most efficient use of staff and other aspects of infrastructure such as planning scans with Computerised Tomography (CT), Magnetic resonance Imaging (MRI) and Positron Emission Tomography (PET) to the highest standards of care. It also facilitates some patients who require both Protons and conventional radiotherapy to have efficient optimal treatment.

Workforce and training

18. There will be a need to begin training staff and ensuring they build experience two years in advance of services becoming operational.

Research and Evaluation

19. Ongoing research and evaluation is needed to maximise the benefits of PBT and to develop the technology. There is a need to establish a baseline for determining future research priorities. Research should be coordinated through the National Cancer Research Institute.

Costs and benefits

20. Revenue costs to treat 1500 patients per annum are estimated at £22.5m. The costs of treating those patients with high-end conventional radiotherapy would be up to £12m, savings made from the avoidance of acute and long-term effects are difficult to quantify. An initial estimate for paediatric patients, even without estimates of increased cure rates and reduced secondary cancers taken into account, is that there is a net benefit of around £40,000 per child for proton therapy if UK facilities were built.

Managing patients while services are being developed

21. The increasing demand for overseas referrals will require careful handling while facilities are being established. Referrals will continue to be made for priority patients but some, for whom the treatment has been identified as appropriate will not have access. For those patients on complex pathways, travel overseas will be inappropriate and for others, improved conventional radiotherapy will be a viable option.

Queries on the Framework

22. Queries about this framework should be sent to Tracy Parker, Cancer Policy Team, Area 402 Wellington House, 133-155 Waterloo Road, London SE1 8UG or to tracy.parker@dh.gsi.gov.uk .

1. Introduction

Objectives

- 1.1 Proton Beam Therapy (PBT) is an advanced form of radiotherapy and its provision is essential in order for world-class radiotherapy services to be offered in this country.
- 1.2 There has been a growing demand for the wider provision of PBT services in England and increasing recognition that the UK is behind the USA and other European countries in relation to the use of this technology. This framework is designed to help National Commissioners to inform decision making regarding the commissioning and provision of PBT services.
- 1.3 The objectives of the PBT services to be developed are:
 - to ensure that all patients, for whom evidence supports proton therapy as the most clinically effective treatment, receive treatment within a clinically appropriate service specification and to nationally agreed standards
 - to ensure that services provided enable the continued development of the technologies involved and that workforce and training issues are appropriately addressed
 - to ensure that services in England match international standards for radiotherapy, consistent with the Cancer Reform Strategy Commitment to develop World Class services.
- 1.4 The aim of the framework is to provide National Specialised Commissioners, Cancer Networks, Primary Care Trusts and NHS Trusts with up to date advice on:
 - the current indications where PBT is appropriate above optimal conventional radiotherapy
 - the process for referring patients overseas
 - the number of patients that are likely to be treated with PBT each year
 - the current state of the technology and the technical specifications required to treat the identified indications
 - infrastructure specifications to provide a quality service to these groups of patients
 - workforce and training issues

- a recommended approach to further evaluation of PBT through high quality research and audit
- indicative revenue costs.

Approach to the development of the Framework

- 1.5 Development of the Framework has drawn heavily from the report of the *National Radiotherapy Advisory Group Proton Beam Therapy sub-group* published in 2007. Work on the clinical indications, the likely demand and technical requirements, has been updated by an Advisory Group established by the National Cancer Director in September 2008.
- 1.6 The Centre for Evidence Based Purchasing has undertaken a Market Review, largely drawing on detailed work undertaken in the USA and applying it to the UK Health service/ market.

Background

Radiotherapy

- 1.7 The Cancer Reform Strategy (2007) mandated a need for major improvements in the capacity of radiotherapy and adoption of new and improved technology for the delivery of radiotherapy in England, to ensure the delivery of World Class radiotherapy. The National Radiotherapy Implementation Group (NRIG) was set up to oversee these improvements.
- 1.8 Radiotherapy is a core modality of both radical (intended for cure) and palliative cancer treatment. Detailed modelling indicates that 52% of cancer patients should receive radiotherapy as part of their treatment. Of those cured of their cancer, radiotherapy contributes to 40% in combination with other treatments such as surgery. A course of radiotherapy may use many small treatments (“fractions”) delivered each day, up to 35 or even more to reach a dose that can cure a tumour but not damage surrounding normal tissues.
- 1.9 The aim of radiotherapy is to deliver a high radiation dose to a tumour in order to deliver potentially curative treatment. Furthermore, great efforts are employed to minimise the radiation dose to healthy tissue to avoid damage and minimise the risk of induction of additional cancers through secondary radiation effects. Linear accelerators (LINAC) are currently the radiotherapy treatment systems of choice. LINACs produce high energy X-rays to deliver the radiation dose to the tumour.
- 1.10 There is a major shortfall of capacity in the UK compared to other western countries. As well as requiring changes in numbers of radiotherapy treatment machines (LINACs), staffing numbers and specialised training, there is a need to

adopt new technologies to ensure best outcomes for patients. The increasing sophistication of computer planning systems and the ability to merge the output of a full range of imaging modalities to identify the exact position of a tumour using Computerised Tomography (CT), Magnetic resonance Imaging (MRI) and Positron Emission Tomography (PET) allows a dramatic improvement in accuracy and improved outcomes. The use of these co-registered images to plan radiotherapy requires rigorous quality assurance and additional clinician and medical physics time in the pre-treatment phase.

The specific technologies are:

- 1 Intensity-modulated radiation therapy (IMRT)
- 2 Image Guided Radiotherapy (IGRT)
- 3 Proton Beam Therapy (PBT)

Intensity-modulated radiation therapy (IMRT)

- 1.11 IMRT is an advanced mode of high-precision radiotherapy. IMRT allows the radiation dose to conform more precisely to the three-dimensional (3-D) shape of the tumour by modulating—or controlling—the intensity of the radiation beam as well as shaping beams precisely to outline only the target area. Treatment is carefully planned by taking 3-D data from CT images of the patient to determine the exact location of the tumour and important normal tissue structures near to the tumour, or potentially within the path of the treatment beams. Typically, combinations of several intensity-modulated fields coming from different beam directions allow radiotherapy dose to be deposited on a pixel-by-pixel distribution within the target area of the body and allow less normal tissues to be affected and so reduce side effects. It can also allow higher doses to be delivered safely to some tumours so improving local cure rates.
- 1.12 IMRT is not suitable or necessary for all radiotherapy treatments but has significant advantages for better outcomes for patients particularly in cancers of the prostate, head and neck and central nervous system.

Image Guided Radiotherapy (IGRT)

- 1.13 Image guided radiotherapy takes many of the principles of IMRT and adds the ability to track tumours that are within tissues that may be in slightly different positions on a day-to-day basis or are within tissue that moves naturally with functions such as breathing. New imaging technology added to linear accelerators (such as cone beam CT) can see the position of the tumour and allow the treatment beams to be targeted and moved to the tumour in real time such as during respiration, or each day to confirm the accuracy of each daily treatment. This ensures that the tumour is not missed; improving cure rates and allowing smaller target areas to be treated as a new degree of certainty is introduced into the

process. In some cases, this can even mean that “stereotactic” treatments can be delivered using fewer high doses of radiation. It is self-evident that treating the tumour more reliably will improve outcomes and reduce the side effects of treatment.

- 1.14 IMRT and IGRT are important components of new and advanced radiotherapy treatment that will lead to improved outcomes for many patients. However, they are not appropriate for all circumstances. IMRT can lead to larger areas of very low dose X-Rays deposited outside the tumour area (integral dose). In most circumstances that may have little or no harmful clinical effect but in children and younger adults it is known that this can lead to a higher rate of second “radiation induced second malignancy”. For this reason in the majority of indications for radiotherapy in such patients, the most modern technologies of proton treatment can deliver the accuracy of dose within the tumour area but with a low integral dose and so have a major clinical advantage. In other situations, in adults, even better accuracy of dose distribution can be achieved with protons as compared to IMRT that allows higher doses to the tumour where it is situated immediately adjacent to dose limiting normal tissue structures.

Proton Beam Therapy

- 1.15 PBT is an advanced form of radiotherapy and was introduced over 20 years ago. Not only can protons deliver the radiation dose to the tumour, they have significant advantages in reducing the radiation dose to healthy tissue and improved clinical effectiveness.
- 1.16 Although PBT has clear advantages for selected cases compared with a standard LINAC, the capital costs and resources required are extremely high compared with a LINAC which limits its more widespread use:
- a large PBT facility requires about 25 times more space than that for a LINAC
 - the purchase and installation of a large PBT facility requires significant capital investment compared with a LINAC (including building costs) of £2 to £4 million
 - the running costs and resources required may be higher for PBT, though there are publications which conclude that the running costs are not much more than for a conventional centre
 - there is a delay of between three and five years between deciding to buy a system and the first treatment
 - higher staffing levels are required to operate the system and to plan the treatments, though staffing levels are comparable to modern delivery techniques such as IMRT and IGRT.

National PBT Service Development Programme – Strategic Outline Case – Annex E

It is worth noting that the expected life of a cyclotron/ synchrotron is 20-30 years compared to 10 for a LINAC.

2. Clinical Applications and Likely Demand for Proton Beam Therapy.

Potential utility of Proton Beam Therapy for cancer

- 2.1 Proton Beam Therapy (PBT) is a rapidly evolving technology. Evidence is accumulating in existing centres in the USA that spot scanning technology most effectively reduces integral dose (and therefore probably late malignancy) although this aspect of the technology is still not commonly available in the USA.
- 2.2 The proportion of radiotherapy patients for whom PBT is essential is very small (1-2%). The figures given in annex A reflect the overall numbers of specific cancers for whom the clinical case is overwhelming. Whilst there may be advantages and reduced treatment morbidity in wider clinical scenarios, further justification is necessary from clinical trials designed to look at cost effectiveness. Radiotherapy in children requires general anaesthesia in 30% of cases. Preparation or play-therapy time is also required. All of these requirements dictate the need for a higher specification for the technology used in order to maintain a quality service and appropriate throughput and is reflected in the service requirements set out in section three.
- 2.3 There are certain widely accepted indications for proton therapy; where proximity to critical dose limiting normal tissues and/or in children growth, vision, hearing and mental retardation effects, or risks of second malignancy are paramount. For skull base chordoma and chondrosarcoma or paraspinal tumours there is very little acceptable alternative treatment.
- 2.4 The high priority list developed in the National Radiotherapy Advisory Group (NRAG) report that has been used to refer patients overseas requires revision in the light of developments since the report was published and a revised list is included at annex B.
- 2.5 In paediatric cancer patients, increasing knowledge of the risk of inducing late second malignancy and the detrimental effects on growth and endocrine function with existing radiotherapy makes PBT the clinical solution of choice.
- 2.6 It is worth noting that the establishment of services in England, with the recommended paediatric service adjacencies is likely to impact on existing paediatric services. It is recommended that work is undertaken to revise the current assumptions and pathways for paediatric cancer patients so that, where surgery and chemotherapy are also required, the most appropriate care can continue to be delivered locally wherever possible. A multi-professional working group is being set up by the National Radiotherapy Implementation Group and National Cancer Action Team to address this issue.

Estimated demand for PT services

- 2.7 An Advisory Group was established by the National Cancer Director in September 2008 to update the report originally commissioned by NRAG and to provide professional and technical advice on the development of the framework. This Group included experts from the Royal College of Radiologists, the British Nuclear Medicine Society and the Institute of Physics and Engineering in Medicine, Oncology and Paediatric specialists. The Group has identified the need to commission services for 1500 cancer patients in England and recommend that services should be developed to support an additional 200 patients from other UK countries and patients being treated as part of research trials.
- 2.8 It should be noted that there is also a potential public demand for proton therapy, particularly in the treatment of prostate cancer, though there is no evidence to support the NHS commissioning for prostate cancer patients outside of clinical trials.

3 Current provision of Proton Beam Therapy services in the UK and Overseas

PBT services in the UK

- 3.1 The UK currently has one Proton Beam Therapy (PBT) system at Clatterbridge Hospital, Wirral; it is 25 years old and does not have the energy capability of a modern system. The centre at Clatterbridge treats 100-130 patients a year with ocular malignancy in the conserved eye. Other selected patients are being sent to abroad for treatment.
- 3.2 Scotland and Wales currently make use of the National Referral Process operated by the National Specialised Commissioning Group (NSCG) and it is anticipated that they would make use of any facilities developed in England. It is also likely, that for reasons of cost and limited capacity overseas already stated, that Northern Ireland would also refer patients to England.

PBT services in Europe and the USA

- 3.3 A list of current facilities operating in Europe is attached at annex C. Capacity at these facilities is limited. There is some capacity at centres in the USA, however, costs are commercially based and are much higher than those in the European centres. Patients on complex pathways are also difficult to manage in the USA with supporting treatments provided by different centres not collocated with the Proton

Beam facilities. There are likely to be more than 20 facilities in the USA in ten years from now.

The NSCG Process for overseas referral

- 3.4 National Commissioning of PBT has applied since 2008-2009. A clinical reference panel was established in April 2008 to review clinical cases on behalf of PCTs and recommend/approve referrals outside the UK while facilities in this country are established. The panel's role is to ensure that patients have fair and equitable access to overseas treatment by reviewing individual cases and prioritising their need for treatment. A patient pathway for referral to the European Union is included at annex D.
- 3.5 The National Specialised Commissioning Group (NSCG) planned to commission an increasing level of activity in each year from 2008 to 2009 onwards with funding requirements increasing accordingly. The number of cases referred in 2008 to 2009 exceeded expectations; the planning figure for 2009 to 2010 has been increased and numbers are expected to increase in each year of the programme.
- 3.6 Services are currently being commissioned from two overseas centres based in Switzerland and France and it is expected that patients will be treated in the USA in 2009 to 2010. A new centre is due to begin operating in Essen in Germany in late 2009. However, there is limited capacity for treating patients in Europe and the priority for new centres will be treating patients in their own country. Facilities in the USA have commercially based costs unlike those in Europe and the limited capacity there is comparatively expensive. The overseas referral process therefore needs careful management and is unsustainable in the longer term.
- 3.7 The NSCG has a remit to refer up to 400 patients overseas for treatment but the process is becoming increasingly unsustainable:
- capacity at overseas centres is limited and access is therefore restricted
 - as capacity reduces the costs increase
 - practicalities of managing complex pathways
 - administrative burden on panel members
 - Potential further increases in demand
 - increasing demand for Primary Care Trusts (PCTs) to fund supporting surgery and chemotherapy of patients referred abroad
 - public demand for appropriate access to PBT being increasingly reflected by media, especially in paediatric caseload.

4 Current advice on technology and Design.

High Level Technical Specification

- 4.1 The technology related to Proton Beam Therapy (PBT) is advancing rapidly. Up to date advice was therefore sought from experts during the development of this framework.
- 4.2 The case mix recommended by the Advisory Group concentrates on the most complex clinical indications. The technical solution to provide a quality service for these groups of patients therefore requires gantries and the infrastructure required to cope with the needs for anaesthetics requires the highest specification. Although large numbers of patients have been treated with PBT, uncertainties remain, especially in proton range and dose in patients. Careful treatment planning is required to mitigate against these uncertainties. The flexibility of beam directions offered by gantries is an important factor.
- 4.3 It is recommended that the specification for a PBT service includes the following technical requirements, more detail can be found in annex E:
- well defined spectrum of protons with minimal contamination from other radiations
 - minimum 230MeV, higher if possible
 - passive scattering and spot scanning
 - gantry (s)
 - efficient
 - integrated with conventional radiotherapy
 - dedicated planning resources CT/MRI/PET
 - staffing
 - photon mix
 - image guided – in-room 3d/4d imaging
 - respiratory gating
 - dose archiving and retrieval

4.4 The following are also recommended:

- any centre operating from one treatment room should have a plan for extending the number of treatment rooms without cessation of therapy. This would require the investment in a switching magnet for the primary beam and adequate space for expansion with reasonable radioprotection. Switching times should be well under a minute (10 to 20 seconds optimally)
- all centres should plan for an extended working day and have a first class arrangement for technical repairs/service/maintenance
- it is self-evident that back up linear accelerators should be available for prolonged unintended treatment interruptions due to synchrotron or cyclotron failure. Local linear accelerator capacity should be sufficient to ensure minimum further treatment delays.

Technology and Design

Technology

- 4.5 The main particle accelerators used to generate the proton beam are the cyclotron and synchrotron. These are large complicated pieces of equipment; they can be greater than seven metres in diameter. It may be possible to bury the cyclotron or synchrotron underground to reduce the footprint of the department.
- 4.6 Cyclotrons and synchrotrons accelerate particles using different methods; each has their advantages and disadvantages. Cyclotrons accelerate particle to a fixed maximum energy, subsequently, the proton beam energy can be reduced to the required energy using degraders. However, radioactivity can build up in the degrader. A synchrotron produces particle at a range of energies that can then be used directly. While both synchrotrons and cyclotrons can produce heavier charged particles, it is more straightforward for a suitably designed synchrotron. Cyclotrons do however tend to be have lower maintenance requirements and hence lower running costs. Some new technologies are being developed which are much smaller than these systems. However, cyclotrons are generally advantageous for scanning due to the fact that they operate in continuous wave mode.
- 4.7 It is advised that reliability of the system and guaranteed system up-time should be determined before purchase. Radiotherapy is delivered to the patient over a number of fractions. Ideally, the fractionation regimen should not be interrupted; otherwise, the treatment may not be as effective.

Pencil beam – spot scanning

- 4.8 Pencil beam scanning (PBS) or spot/ raster scanning uses a beam smaller than the tumour size. The proton beam is then scanned over the tumour. PBS allows more accurate treatment of the tumour. In 2008, at the time of the innovations report [1] only the Hitachi PBS was in routine clinical use. Other systems have been approved by the Food and Drug Administration (FDA), while others are beginning to be used clinically. Evidence from Villigen and the use of Intensity Modulated Proton Treatment (IMPT) would suggest that there are significant advantages in optimising dose distributions. There is also evidence that scattered neutron production is less, so allowing even lower potential risks of second malignancy induction.

Image guidance

- 4.9 Image Guided Proton Therapy (IGPT) is considered important. The tumour volume is highly targeted and any change in size or position of the tumour could mean that healthy tissue is being irradiated instead of the tumour. Imaging of the tumour prior to treatment can ensure that the patient is positioned correctly and that the tumour is still in the beam.

Respiration gating

- 4.10 Tumours in or near the lungs will move as the patient breathes. Therefore, a fixed proton beam will irradiate the tumour and healthy tissue depending on the point in the breathing cycle. Respiration gating will monitor the breathing cycle and switch off the beam when the tumour is not expected to be in the proton beam, thereby sparing healthy tissue.

Installation

- 4.11 The installation and building work for a large project such as PBT presents many challenges and is costly. The planning for such a large site must not only include the treatment facilities but also all the other facilities such as treatment planning, imaging and waiting areas. As with all radiotherapy systems, there needs to be sufficient shielding to reduce the radiation levels outside of the treatment rooms and particle (proton) accelerator. The timescale for building the facilities, installing the equipment and commissioning the equipment is very long. Specialised planners of PBT facilities may be required.
- 4.12 A large cyclotron or synchrotron can supply proton beams to many rooms, therefore one room can be built with the particle accelerator; further rooms can be added to expand the treatment capability over a scheduled period of years. Similarly, single room systems can be installed over a period of time. This installation programme can allow the time to develop experience and build up the associated expertise and resources required.

Treatment rooms

- 4.13 A single cyclotron or synchrotron can be connected to several treatment rooms. The protons can be piped to the treatment rooms. Large cyclotrons and synchrotrons are very expensive and therefore several treatment rooms need to be connected to justify the cost. Normally the proton accelerator can have up to four or five rooms attached. In addition, there can be the possibility of connecting to a research room.
- 4.14 There are two manufacturers offering systems that are considerably smaller than a standard cyclotron or synchrotron. Both these systems will fit into a space similar to that of a standard LINAC room. This offers the opportunity for having smaller centres with one or two rooms, but could allow multiple centres to be developed. The concern for these novel systems is that neither system has been installed for clinical use anywhere in the world to date so neither independent confirmation of manufacturer performance, nor reliability data in clinical use is available.

Treatment room design

- 4.15 There are three main options for rooms:

Gantry system: the beam can be rotated to any angle around a centre point. However, the gantries used are very expensive and very heavy.

Fixed beam: the beam enters the room in one direction only, at installation the direction is chosen – horizontal, vertical or an oblique angle. This is cheaper than a gantry system but is less comfortable for the patient and the outcomes are poorer.

Fixed beam combined with robotic couch: instead of moving the beam the patient is moved into position, this makes the system easier to operate with fixed beam.

- 4.16 The caseload that is proposed for the UK has a very high proportion of the most demanding and complicated planning solutions to optimise treatment. This makes a gantry-based solution necessary for most of the capacity. It ensures maximum flexibility for the introduction of multiple angled beams and minimum patient movement, essential to maximise the gain for Protons. It is likely to be more future proof in a very rapidly moving field. There is evidence that some indications for Proton treatment can be adequately treated by other less expensive solutions without compromise of quality and it is likely that this could be an area of research for the UK to explore in parallel with a secure core service.

Treatment planning system (TPS)

- 4.17 All radiotherapy treatments are planned individually. If changes are required during a treatment, then it will need to be re-planned. PBT is more complex than the currently used photon therapy. In addition, photon therapy planning systems have improved over many iterations of the software. Proton treatment planning systems

are still in development and are not as user friendly. There are four manufacturers who can supply TPS.

Facility upgrades

- 4.18 Technology will advance and demand increase over the life of the facility and it will be essential that it is upgradeable. It would need to have the potential for new beam-lines and rooms to be added and acceleration upgraded to allow for the acceleration of heavier particles with minimum disruption to services. Providers should be able to demonstrate a clear technological development roadmap, or at least be willing and open to new developments for the next 10 to 15 years.

Future developments

Heavy ions

- 4.19 The future direction of PBT is likely to extend to heavier particles such as carbon or oxygen ions. Heavy ions have some theoretical benefits over protons. Not all systems currently have heavy ion capability, though most will have that capability in the future. Even more so than proton therapy, there is scope for research into heavy ion therapy and this would help the UK scientific community to be at the forefront of research. However, these systems are likely to be much larger and more expensive than PBT.

Multi-leaf collimator

- 4.20 Each treatment is tailored to the patient. The proton beam needs to be shaped to match the area to be irradiated. Currently, for passively scattered PBT, collimators are made for each patient to shape the beam and attached to the exit port for the protons. A multi-leaf collimator is integrated into the system and can be programmed to create a collimator for each patient in situ. Such a capability would be useful for both passive and scanning delivery.

Accumulated Delivered Dose Archiving & Retrieval (ADDAR)

- 4.21 The system should have a mechanism for accumulating the daily delivered doses, along with the daily positional/guidance images (and recorded daily residual set-up inaccuracies) into a final "delivered treatment plan" showing delivered dose, the accumulated delivered dose (ADD). In addition to showing the actual delivered dose, it will be necessary for this information to be archived, along with all the relevant imaging and be retrievable within a matter of a few minutes. The retrieval of archived data is essential in order to provide the opportunity to compare the location of recurrences and of normal tissue damage in relation to the dose actually delivered to the relevant structures. This system of accumulated delivered dose archiving and retrieval might be known as ADDAR. By meeting this requirement

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particle therapy centres will be placing themselves at the forefront of the International requirements on record keeping and analysis of radiotherapy dose delivery

5 Overall requirements for services

Patient Pathways

- 5.1 Services should be commissioned to treat 1500 patients from England with additional capacity for 200 patients from the rest of the UK and for clinical trials, against an agreed pathway. The current pathway for overseas referral is set out in annex D together with a referral pathway for a UK service.
- 5.2 This includes capacity of 5% for research into new applications of the treatment. It is also anticipated that high quality prospective studies will also be undertaken on the impact on clinical management of all patients undergoing Proton Beam Therapy (PBT) treatment. Facilities established should provide a base for training and education as well as clinical research and technical development.
- 5.3 The planning of new facilities will need to take account of the case mix recommended by the Advisory Group which concentrates on the most complex clinical indications. The technical solution to provide a quality service for these groups of patients therefore requires gantries and the infrastructure required to cope with the needs for anaesthetics requires the highest specification.
- 5.4 It is recommended that the specification for a PBT service include the following technical requirements (see paragraph 4.3):
 - well defined spectrum of protons with minimal contamination from other radiations
 - minimum 230MeV, higher if possible
 - passive scattering and spot scanning
 - gantry(s)
 - efficient
 - integrated with conventional radiotherapy
 - dedicated planning resources CT/MRI/PET
 - staffing
 - photon mix
 - image guided – in-room 3d/4d imaging

- respiratory gating
- dose archiving and retrieval.

Infrastructure requirements

- 5.5 New treatment facilities should be developed on the site of an Integrated Cancer Centre with access to full Multidisciplinary Cancer Care, including paediatric oncology and “host” academic radiotherapy and medical physics departments. Partnerships with academic physics and engineering disciplines would be advantageous.
- 5.6 The link to a major radiotherapy centre will avoid duplication of Computerised Tomography (CT) simulation, Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) fusion for treatment planning, with additional advantages in terms of training, experience, research, rotation and cross cover with the host centre. Some dedicated staff will be required.
- 5.7 The impact on current patterns of service provision needs to be recognised in paediatric oncology and radiotherapy. A greater degree of centralisation to a limited number of national or regional centres seems inevitable. In other areas, there will be a need for strong links to local Multidisciplinary Team (MDT) support and initial diagnostic and staging work to ensure patients can access the national referral centre within clinically acceptable timescales. A wider network of clinical and medical physics expertise across the country would facilitate this. Close follow up, essential for this group of patients could then be devolved locally to minimise travel and inconvenience to patients. Accelerated pathway and collaborative management will be required to deal with referrals.
- 5.8 The relative complexity of paediatric cancer care where surgery, chemotherapy and radiotherapy (including paediatric anaesthesia) are required in close sequence, with all the requirements of supportive care, makes referral abroad for larger numbers of children unsustainable. Hence, any UK centre would need to address the complexities of multimodality treatment and interconnections with local paediatric cancer services as well as the practicalities of good administration and communication. Hotel accommodation and specialist supporting services for paediatric oncology and neurosurgery will be essential for a Proton Treatment Centre (PTC).
- 5.9 It is recommended that the specification for PBT services includes the following requirements for siting/co-location and adjacencies.
- participation in clinical trials
 - radiotherapy support services on site
 - paediatric Oncology – integrated physical care and supervision

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- neurosurgery – if not on site, with links to a major unit/ centre
- paediatric Anaesthesia – and physical infrastructure of playrooms, recovery areas
- paediatric experience
- hostel Accommodation – for patients and carers for stays of up to seven weeks
- NHS clinical service
- properly constituted MDTs for all site specialisation and integrated modalities
- innovative approaches to communication strategies between MDTs and for both aftercare and follow up
- patients treated within defined protocols and prospective data collection.

6. Workforce and Training

- 6.1 It will be necessary to ensure that appropriately trained staff are available to deliver the service. Staff will need to be trained and provided with experience at overseas centres. Potential providers will be invited to make proposals for staff training.
- 6.2 Staff groups identified in the National Radiotherapy Advisory Group (NRAG) report included:
Physics, engineering and workshop staff
Dosimetrists
Immobilisation technicians
Therapy radiographers
Nurses
Doctors, including Proton Beam Therapy (PBT) specialists, paediatric oncologists, anaesthetists.
- 6.3 There will be a need for a structured system for increasing the knowledge and experience of the above staff groups which can be rolled out prior to facilities becoming operational in this country to ensure that they are up and running at full capacity as quickly as possible because of the unsustainability of the overseas referral process.
- 6.4 In the shorter term, more training is required for a wider group of clinicians to support the current overseas referral process and provide the after care for patients on return to the UK.
- 6.5 There are few staff that are trained in PBT. Hiring previously trained staff in PBT may be difficult, especially due to the future international increase in PBT centres who will also be seeking experienced staff. Suitable staff may need to be sent to other existing centres to gain experience. Once a system is running it can take several years to produce standard clinical protocols and to streamline the operating procedures in the department.

7. Research and Evaluation

- 7.1 The overriding priority for developing facilities in this country is that they will provide an NHS clinical service. However, the provision of proton radiotherapy facilities in the UK will have the added value of providing opportunities for contributing to the international knowledge on the use of this treatment modality and improving outcomes for patients in the UK. Research undertaken should not only focus on improving outcomes for new groups of patients with the existing technology but also on understanding the technologies better with a view to improving patient outcomes. In addition, there should be commitment to technological research for maximising treatment quality over the lifetime of the facility (20 years) in order to stay competitive with other developments in Radiotherapy (RT) technology in the same timeframe.
- 7.2 This added value is welcomed and appropriate links should be made with basic applied and clinical research proposals
- 7.3 It is recommended that future research into Proton Beam Therapy (PBT) treatment should be coordinated through the National Cancer Research Institute (NCRI). It is strongly recommended that prospective audit of the impact of proton therapy on clinical management becomes a requirement and that research groups start to identify priorities for future research so there is no delay before studies begin once services are operational. The NCRI Radiotherapy and Radiobiology research initiative has included consideration of PBT protocols within the New Technologies work-stream of the Clinical and Translational Radiotherapy Research Working Group.

8. Costs v benefits

Costs

- 8.1 The costs of sending patients abroad vary considerably from £20,000 in Switzerland to an expected £60,000 in Paris and over £100,000 in the USA. These variable costs reflect the origins of some existing centres within nationally funded physics research settings (no residual capital cost element) and the individual nature of treatment requirements (planning and daily general anaesthetic etc). Providing current providers do not change their prices, it is estimated that the gross costs of sending 400 patients abroad would be between £16m - £36m per year without travel and subsistence costs. The net cost would be £1.7m less, the saving of not giving photon therapy in England.
- 8.2 It is difficult to estimate the cost for a UK centre given that the market is untested, some national centres overseas are subsidised from physics budgets and healthcare prices in the USA are usually higher than NHS costs.
- 8.3 The offsetting cost-benefit arises from avoidance of the health care costs of damage to non-target organs and from second cancers. Both are well-recognised effects of radiation therapy.
- 8.4 To gain the necessary medical, physics and technical expertise required to run an effective proton therapy service, key appointments would need to be made and significant revenue made available up to two years ahead of any clinical service to allow training and commissioning.
- 8.5 Costs will be significantly affected by centre design, construction and configuration, length of working day and fractionation. Estimates internationally seem remarkably consistent.

Cost Effectiveness

- 8.6 In addition to the high capital investment required to build a proton unit there are also higher running costs compared to a conventional radiotherapy treatment unit. The unit cost per patient can be reduced by running an extended hours system and by using multiple chambers and preparation facilities to allow efficient use of a single proton beam line for a number of patients.
- 8.7 Proton Beam Therapy (PBT) in the USA is covered by Medicare. The cost per treatment paid by Medicare fell in 2007 from \$33,482 (£22,000) to \$24,054 (£16,000) per patient. The French government are currently paying €40,635 (£35,000) per typical proton patient. Children frequently need anaesthesia during radiotherapy, which can raise the cost per treatment by up to 30%.
- 8.8 The DH analysts have estimated that a proton facility built in the UK could deliver treatment for 400 patients per year at around £21,000 per patient; giving a total annual revenue cost of £8.5m per year gross. Larger facilities with extra treatment

rooms and running for extended hours would have the capacity to treat 1500 patients per year at £15,000 each, giving a total cost of £22.5m per year.

- 8.9 An option to have two smaller centres in the UK would be more expensive than a single large facility, but would give greater resilience to breakdown and would be much more convenient for patients, particularly for paediatric cases who may have to travel to the unit daily for eight weeks. This option may have a 25% premium to the costs. (ie 1500 patients at £27m per year).
- 8.10 Conventional complex radiotherapy typically costs £5,000 per patient without anaesthesia and £8,000 with anaesthesia. However, it might not be possible to release all the cash quickly from switching from radiotherapy to proton therapy given that much of the expense is associated with the capital costs of linear accelerators. Service alignment with the current 20 paediatric radiotherapy centres and any new proton facility would be needed to maximise the benefit of the scheme.
- 8.11 Monetising the benefits that the extra cost of PBT has over conventional radiotherapy is difficult because conducting clinical trials on rare and complex tumours is not always possible or takes many years to complete. PBT is being used for more common conditions in the USA, particularly prostate cancer. There is little evidence yet to suggest that it provides more than nominal medical benefit to the patient. However, there has been a large demand from patients in the USA who are willing to pay for PBT because of its perceived Rolls-Royce status.
- 8.12 The benefit case for PBT is strongest for a range of complex childhood cancers. The side effects of conventional radiotherapy include hypothyroidism, hearing loss and growth defects. The Department of Health analysis gives a lifetime weighted average cost saving of £13,919 per child of providing healthcare for the side effects from PBT compared to conventional radiotherapy. In addition to the direct cost saving of reducing side effects a monetary value of the Quality Adjusted Life Year (QALY) can be estimated for the health impact PBT gives compared to radiotherapy. In this case, the lifetime weighted average health 'loss' is £42,554 less for PBT. In addition to these benefits, there are claims that patients receiving PBT have increased cure rates and a reduced chance of developing induced secondary cancers. We are unable to estimate the cost of these benefits without further information.
- 8.13 Even without the estimates of increased cure rates and reduced secondary cancers taken into account, this initial estimate suggests a net benefit of around £40,000 per child for PBT if a UK facility was built.
- 8.14 In the absence of published benefits for adults, the monetised benefits could be estimated using a combination of clinical assumptions and modelling techniques. This will require further analysis.
- 8.15 Currently we are paying for around 40 patients a year to receive PBT abroad. Costs of sending patients abroad have been up to £60,000 per patient (including travel and accommodation) but this could rise to over £100,000 per patient as capacity in Europe becomes scarce. There are currently 20 radiotherapy centres providing services to paediatric patients but the development of PBT facilities is likely to reduce the need for these services with potential savings.

9. Managing Patients while services are developed.

- 9.1 The revised list of indications, the limited capacity for referral of patients overseas for Proton Beam Therapy (PBT) treatment and the long lead-time in establishing facilities will require careful handling. There is potential for many patients being denied access to treatment that has been identified as the most appropriate for their cancer. Handling will be particularly difficult for paediatric patients where PBT would improve outcomes of treatment or potentially prevent acute and late effects such as deafness and impaired IQ.
- 9.2 For some patients on the revised list, referral overseas is not suitable due to complex pathways requiring packages of treatment including chemotherapy and surgery; for others, more advanced conventional radiotherapy may be a viable alternative.
- 9.3 The following issues are relevant.
- We now have the evidence justifying the benefits of investing such a significant amount of funding in UK facilities, especially given the current economic circumstances and it has been a complex process to establish this case.
 - The evidence around proton therapy treatment is now established and we have improved our understanding of the most effective ways of using protons to treat selected group of patients with cancer.
 - The National Specialised Commissioning Group (NSCG) has already established a proton therapy clinical reference panel to advise on suitable cancer cases to be referred overseas for treatment from April 2008.
 - Funding has been made available to the NSCG to support increasing numbers of patients being treated abroad. Twenty-two patients were referred by the panel for overseas treatment in 2008/09. Provision has been made for more patients to be referred in 2009 to 2010 though there is potential for a significant increase in demand. The NSCG has a remit to refer up to 400 patients per annum.
 - There is limited overseas capacity to send patients for PBT and although it is expensive, until facilities can be built in the UK, we will continue to follow very specialised clinical criteria to determine those patients who should be sent overseas for proton beam therapy.
 - In many cases, it is inappropriate to send patients for overseas treatment because of the complex nature of their cancer treatment, for example, they may require associated surgery, chemotherapy and other supportive treatments. For those patients, until facilities are established here, there is a proven clinical advantage to staying in the UK for conventional radiotherapy treatment.

Clinical indications in oncology for proton therapy

Indications and Caseload for Proton Treatment for the UK

The National Radiotherapy Advisory Group (NRAG) working group report on Proton treatment was included in the final NRAG report of Feb 2007 and incorporated in to the Cancer Reform Strategy (CRS) of Dec 2007. This included estimates of clinical diagnoses and patents for which Proton treatment was seen as a clearly superior option in terms of clinical outcomes when compared to conventional radiotherapy.

The National Commissioning Group (NCG) has taken forward the first CRS recommendation, endorsed by Ministers to send a highly selected sub-group of patients with specific diagnosis and indications for treatment abroad prior to a Proton Treatment Centre (PTC) being available in the UK. This paper updates and enlarges on the list of diagnoses and clinical situations where Proton treatment should be available and would be commissioned by the NCG with NHS funding in the first Proton facilities in the UK.

The field of proton radiotherapy is fast moving in terms of technology, new treatment centres and clinical experience. The range of experience and treatment capacity worldwide has meant that there is a need for some minor adjustments to the list contained within the 2007 reports. In some cases, there are other emerging technologies such as Stereotactic Radio Surgery (single fractions – Gamma Knife) that might be alternatives for selected diagnoses (acoustic neuroma and meningioma) and Stereotactic Radiotherapy (multiple fractions – Linear Accelerator or Cyber Knife). However for the majority of clinical diagnoses and situations within the list below, the quite specific characteristics of Protons to allow high doses of fractionated radiotherapy to tumours and tumour bearing tissue, close to critical dose limiting normal tissues makes it unchallenged and would be the standard list of accepted diagnoses for all major PTCs in the world. The world experience with Protons is now over 45,000 patients treated over the last 30 years. Much of this experience is with a particular range of diagnoses which forms the highest priority for provision within the UK, many of whom would already have approval for treatment abroad. In other cases, the evidence is now more secure that protons provide a better alternative to conventional radiotherapy. Para-nasal sinus tumours and other selected Head & Neck cancer has been added to the NRAG list on this basis.

The attached list includes those indications currently treated at the low energy Proton facility at the Clatterbridge Hospital in Liverpool.

In paediatric cancer there is already data that now makes Protons the treatment of choice where radiotherapy is required for curative treatment, with reduced late side effects such as growth deformity, endocrine dysfunction and neuropsychological effects and loss of intellectual function. Emerging data has demonstrated that the late effects of low doses of X Rays in the induction of late second malignancies is important with a the higher rate than was previously recognised, particularly in children and young adults with more susceptible tissues and greater life expectancy post treatment. This makes Proton treatment a particular priority where the magnitude and extent of dose outside the target volume can be markedly less than conventional radiotherapy. The table includes a 'star' rating (one to three) of the clinical areas (reduced second malignancy, increased cure rates and reduced late side effects) where health gain may be delivered when compared to best conventional radiotherapy. The secondary issue of reduced acute side effects has not been qualified but is important for wide field paediatric radiotherapy and can reduce costs significantly.

International opinion generally bases planning for treatment capacity for PTCs on similar diagnostic categories. The list here is based on diagnoses where there is felt to be clear evidence of health

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gain and is possibly at the most conservative end of the spectrum. Whilst it may be possible to demonstrate dose distributions that are clearly better than even the best conventional radiotherapy with IMRT for a much wider list of diagnoses and treatment sites, the high relative cost of Protons and the lack of evidence of a major improvement in outcome means that these indications should be seen as scope for clinical trials and a lower priority for the UK at this stage.

The most rapidly expanding indication, particularly in the USA is for prostate cancer for which there is relatively little evidence, with market forces driving the model rather than one of clinical need. It would not therefore be viewed as a priority for the UK, outside clinical trials. It might however be a driver for the private/independent sector to provide treatment capacity greater than that funded by the NHS commissioning process.

Published estimates of required Proton capacity for the population in Sweden have much higher numbers and indeed there are similar publications for the UK. Italy has an initial assessment of numbers similar to the UK conclusion.

Whilst there is much interest in other charged particles such as Carbon Ions, there is less clinical experience, the indications less secure and such treatments are more a focus of ongoing research.

Whilst the DH and the NCG can only commission for the population of England, there is every indication through the NCG and through the existing agreement to use the NCG Clinical Reference Panel for making decisions about patients selected for treatment abroad, that Scotland, Wales and Northern Ireland would commission for PTC capacity based in England for the foreseeable future. These estimates are based on the whole population of the UK of 60M rather than the 80% of the population in England. In reaching conclusions about the capacity required in the UK it should be noted that there is the possibility that the Republic of Ireland (population 4.4M) may consider commissioning Proton treatment in England with all the advantages of language and cost. This would require an additional 7.3% capacity from that listed below.

It seems difficult to imagine that clinical trials and research would not be funded for indications outside those listed below. This might be in the form of prospective case series or randomised clinical trials. The National Cancer Research Institute (NCRI) initiative on Radiotherapy and Radiobiology Research was launched in 2009 and some work stream on Particle treatment would seem unlikely in the future. Thus, some capacity for clinical trials should be assumed over and above that listed below with funding streams yet to be determined.

Table 1. Annual caseload for UK population

Paediatric Indications		Note	↓2 ⁰ Ca	↑ Cure Rate	↓ Morbidity
Chordoma/Chondrosarcoma		15	1	**	***
Rhabdomyosarcoma	Orbit	5	1	***	*
	Parameningeal & Head & Neck	15	1	***	*
	Pelvis	10	1	***	*
Osteosarcoma		3	1	***	***
Ewings		9	1	***	**
PPNET (Extra-osseous Ewing's)		5	1	***	**
Ependymoma		25	1	**	*
Low Grade Glioma		5	1	**	*
Optic Pathway Glioma		12	1	***	*
Craniphayngioma		15	1	***	*
Medulloblastoma (PNET)		70	1	***	*
Hodgkins		5	1	***	*
Retinoblastoma		5	1	**	*
Meningioma		3	1	***	**
Intracranial Germinoma		10	1	***	*
Nasopharynx (Head & Neck)		15	2	***	**
Difficult Cases (Esthesioneuroblastoma/Neuroblastoma/Liver)		5	3	**	**
Very Young Age (Extra Cases)		20	4	***	***
	Paediatric TOTAL	252		***	**
Adult Indications					
Choroidal melanoma		100	7	*	***
Ocular / Orbital		25	8	*	***
Chordoma	Base of Skull	60	8	*	***
Chondrosarcoma	Base of Skull	30	8	*	***
Para-spinal / Spinal Sarcoma	Including Chordoma	180	8	*	***
Meningioma		100	5	*	*
Acoustic Neuroma		100	5	*	*
Craniospinal NOS (Pineal)		10	8	**	**
Head & Neck & Paranasal Sinuses		300	6	**	***
PNET (medullo/intracranial)		30	5	**	**
Difficult Cases		300	9	**	**
	Adult TOTAL	1235		*	***
	TOTAL	1487			

Notes to table 1

- The caseload and patient numbers for paediatric cancers suitable for proton treatment are taken from a survey of the Children's Cancer and Leukaemia Group (CCLG) database. It allows an accurate assessment of numbers of cases treated with radiotherapy. It makes assumptions that palliative treatments and specialist regional radiotherapy centres with conventional radiotherapy would still undertake some simple techniques. Proton treatment may allow much younger children to be treated (see note four) Although the paediatric

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caseload overall (notes one to four) might be viewed as low these cases are necessarily complex, time consuming in terms of both planning and treatment delivery. The proportion of children requiring anaesthesia will be higher than in current practice and is estimated to be 30% (set up and treatment time is longer and with a younger age profile than currently given radiotherapy). This data has been crosschecked with cancer Registry data although this is relatively crude in terms of such detailed diagnosis information compared with the CCLG data.

2. The addition of this category to the NRAG lists reflects the changing evidence relating to late second malignancy. There are small numbers of head and neck cancer occurring in children, particularly nasopharyngeal cancer. These are treated currently with conventional radiotherapy but it is clear that the site, close to the base of brain and critical dose limiting structures and the risk of second malignancy makes them ideal for treatment with Protons. The numbers are taken from the Yorkshire Cancer Network experience and scaled to the UK population.
3. There are small numbers of extremely rare cancer diagnoses in children that require radiotherapy for curative treatment. It is clear from experience in existing Proton Treatment Centres (PTC) that these special cases are referred where the facility exists. For completeness they therefore need to be included on the diagnostic list although in terms of numbers are insignificant.
4. The majority of the paediatric indications list reflects a shift of caseload currently receiving treatment with conventional radiotherapy. However, the age threshold at which it is felt radiotherapy can be safely given would change significantly if Proton treatment were available in the UK. Whilst the age changes with different diagnoses and situations, there is no doubt from the experience in Europe and the USA that there would be some children given Protons where they currently do not receive radiotherapy as part of their treatment.
5. The numbers for Acoustic Neuroma and Meningioma have been reduced from the original numbers contained within the NRAG report. The use of Gamma Knife will have a role and may take some appropriate cases. However, Gamma Knife has technical limitations in particular the size of a target volume that limits its clinical application. In addition, treatment is delivered in a single fraction and so is highly inappropriate where dose limiting normal tissue structures may be close and where fractionated radiotherapy is more appropriate. The danger in this assumption is that if Protons were available in the UK it would become the treatment of choice due to its better dose distribution and scattered low dose X-ray, especially in younger patients where the risk of late second malignancy may be of concern. As far as meningioma is concerned, the assumption is that only high-grade tumours will receive radiotherapy. If data emerges from the current EORTC trial that higher doses of radiotherapy have higher local control rates then Proton treatment could be the treatment of choice and again these numbers an underestimate.
6. The addition of selected head and neck cancer and paranasal sinuses cancers is based on good data from case series and better clinical experience from PTC around the world. The histological types often include a wider variation of subtypes where radiotherapy doses may need to be higher. Many of these cancers have high cure rates and are closely related to the base of skull and other critical dose limiting structures. If available protons would give a significantly better treatment option and so are included in the indications list. Local recurrences of head and neck cancer or second malignancies are not uncommon and may still be curable. Conventional radiotherapy may not be an option but due to its superior dose distribution and dose to surrounding tissues, Proton treatment is an option. Whilst the numbers of paranasal cancers can be accurately estimated (UK numbers 392 on incidence data with assumption of 50% having Proton treatment as opposed to conventional radiotherapy) the numbers of head and neck cancers (100) may be an underestimate when it becomes an accessible option.
7. The numbers of ocular tumours and choroidal melanoma is taken from the current caseload and data from the UK low energy facility at Clatterbridge and is assumed to be stable.
8. The numbers of these standard indications is taken directly from the NRAG report that in turn is based on cancer registry data. This makes an assumption that many inoperable sacral chordomas in particular may still receive optimal high dose conventional radiotherapy. New data on particle treatment of these incurable cases does however suggest that higher dose, only deliverable with Protons or carbon ions may have significantly higher local control rates and survivals and so may be optimally treatment with Protons. Again, whilst the numbers are low it may make this estimate a conservative one.
9. This is the most difficult and variable estimate. There have been several studies looking at how the numbers of rare and common cancers with indications for potentially curative radiotherapy and for whom Proton treatment is a clearly superior option, can be estimated. These cases may be atypical and unusual situations

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in common cancers where either due to atypical patient anatomy or concurrent conditions or previous radiotherapy treatment, conventional radiotherapy is not an option. Whilst unusual small numbers of common cancers multiply up to be significant. Some of these patients would not wish to travel for Protons and uptake may be lower even if offered so again estimating numbers more difficult. In other situations there are some tumour types that are difficult to treat and Protons may offer a simpler and much better dose distribution if available and so be the treatment of choice e.g. Thymoma. Some examples are given below.

- a. Thymoma radiotherapy indicated for stage II and III post resection. Estimated 80 cases per annum with 40 % invasive so indications for Proton treatment 28 cases.
- b. Breast cancer radiotherapy - 'pectus excavatum'. Estimate 25 cases per annum.
- c. Breast cancer radiotherapy on the left side – in those patients estimated to have very high risks due to concurrent cardiac conditions or herceptin effects or in other atypical situations of previous radiotherapy treatment for other conditions Protons may be a significantly better option than conventional radiotherapy. Even if this amounts to 1% of all radiotherapy treatment for breast cancer the numbers would be 137 cases.
- d. Basic studies of highly complex cases where conventional radiotherapy has major limitations and so curative treatment compromised currently vary. Estimates vary from 150 per annum in the lowest (three cases per million population) through to 500 per annum. There are studies from Sweden and the UK suggesting that if factors of purely optimum dose distributions are taken into account (with significant impact on significant toxicity, local control rates and second malignancies) then 10%-15% of patients treated with radiotherapy may have an indication for Protons. This is clearly unachievable at present with current costs and technology but is an important indicator for longer term future planning.

There is merit on allowing some of these cases early on in the commissioning of a UK centre, as the planning is less complex and would allow a rapid rise in the experience and confidence of new centres. This would enable the more complex cases to be treated with confidence earlier.

Highly atypical cases of incurable situations (often limited local recurrence) for younger patients with longer estimates of survival occur and have been prominent in the referrals for referral abroad within the current system. Higher local control rates with significantly lower acute toxicity may make these cases difficult to deny treatment to once Protons are available. These should be restricted to very small numbers.

Thus, the figure of 300 included in these figures may be a considerable underestimate. However, the indications in this group would grow with time and clinical evidence and an effective gate-keeping rule needs to be set for referral. The NCG Proton Clinical Reference Panel have suggested that the criteria for access to Protons in this "Difficult Cases" category is defined tightly. This would be:

1. Normal tissue dose constraints cannot be achieved by optimal conventional radiotherapy techniques with IMRT.
2. Patients are of good performance status with curable conditions.
3. Have a life expectancy from other concurrent conditions of greater than five years

Conclusion:

1. A base figure of 1487 is taken as a minimum to be commissioned for the UK.
2. If the Republic Ireland is taken into account as a likely required capacity in the medium term then a base capacity of 1595 is required.
3. If a minimum requirement of 5% of capacity is made available for clinical trials then an extra 71 cases and so a required capacity of 1561 cases.
4. If both of the factors above are considered a required capacity of 1664 cases is reached.
5. Consideration should be given to the need for a back up plans in the event of breakdown and geographical access, especially for the paediatric cases.

Revised list of indications for NCG referral overseas

Adult

- base of Skull & Spinal Chordoma
- base of Skull Chondrosarcoma
- spinal & Paraspinal Bone and Soft Tissue Sarcomas.

Paediatric

- base of Skull & Spinal Chordoma
- base of Skull Chondrosarcoma
- base of Skull, Spinal & Paraspinal Bone and Soft Tissue Sarcomas
- orbital Rhabdomyosarcoma
- parameningeal Rhabdomyosarcoma
- retinoblastoma
- pineal
- sarcomas arising from the Pelvis (pelvic Ewings)
- central Optic Path and selected low grade Glioma.

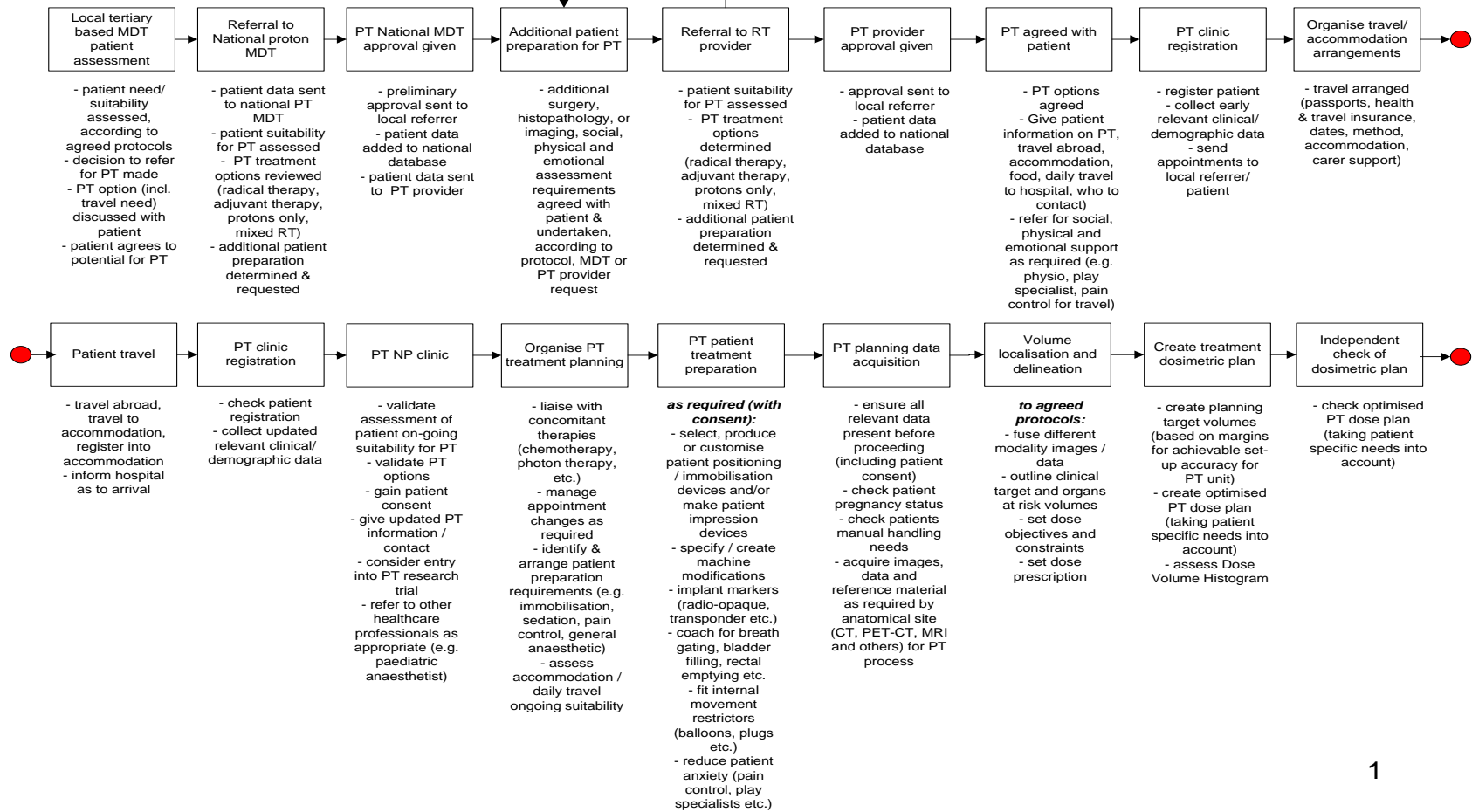
Particle Therapy - Centres in Other Countries

Country	Working Centres (+ number)	Planning	Approved and being built/commissioned	Proton and/or Carbon	
				Protons	Carbons
France	2	1	1	2	2
Switzerland	1	1		1	
Germany	1		5	3	3
Italy	1	1	1	1	1
Japan	4		6	7	3
Sweden	1	1		1	
Slovakia		1	1	1	
USA	5	13	4	22	
Russia	1	1	?	1	
Austria			1	1	1
South Africa	1			1	
Spain		1		1	
China + Hong Kong	2		2	4	

Belgium and the Netherlands are less advanced than the above in terms of planning and are at about the same stage as the UK.

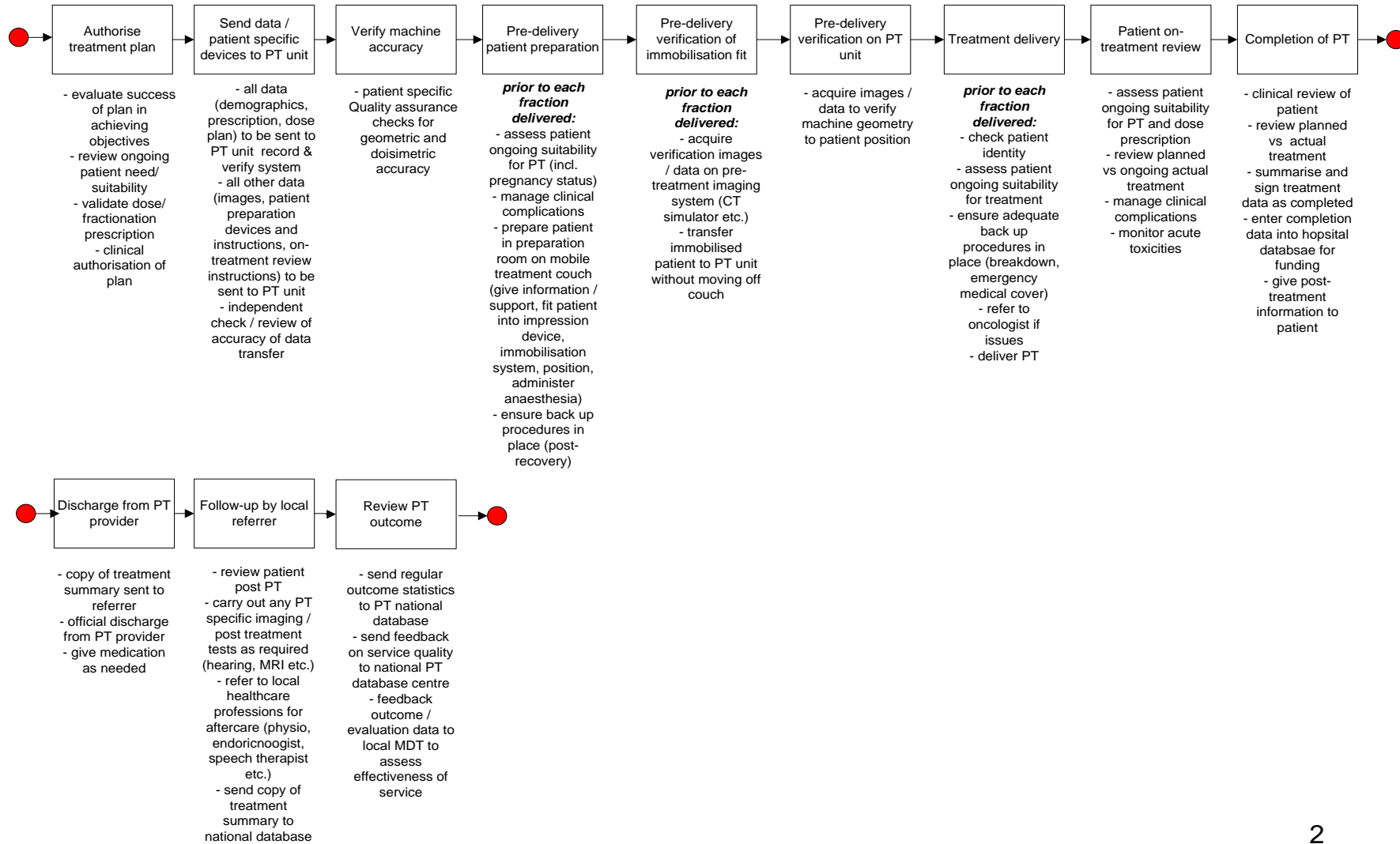
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Proton therapy (PT) pathway - EU (with process details)



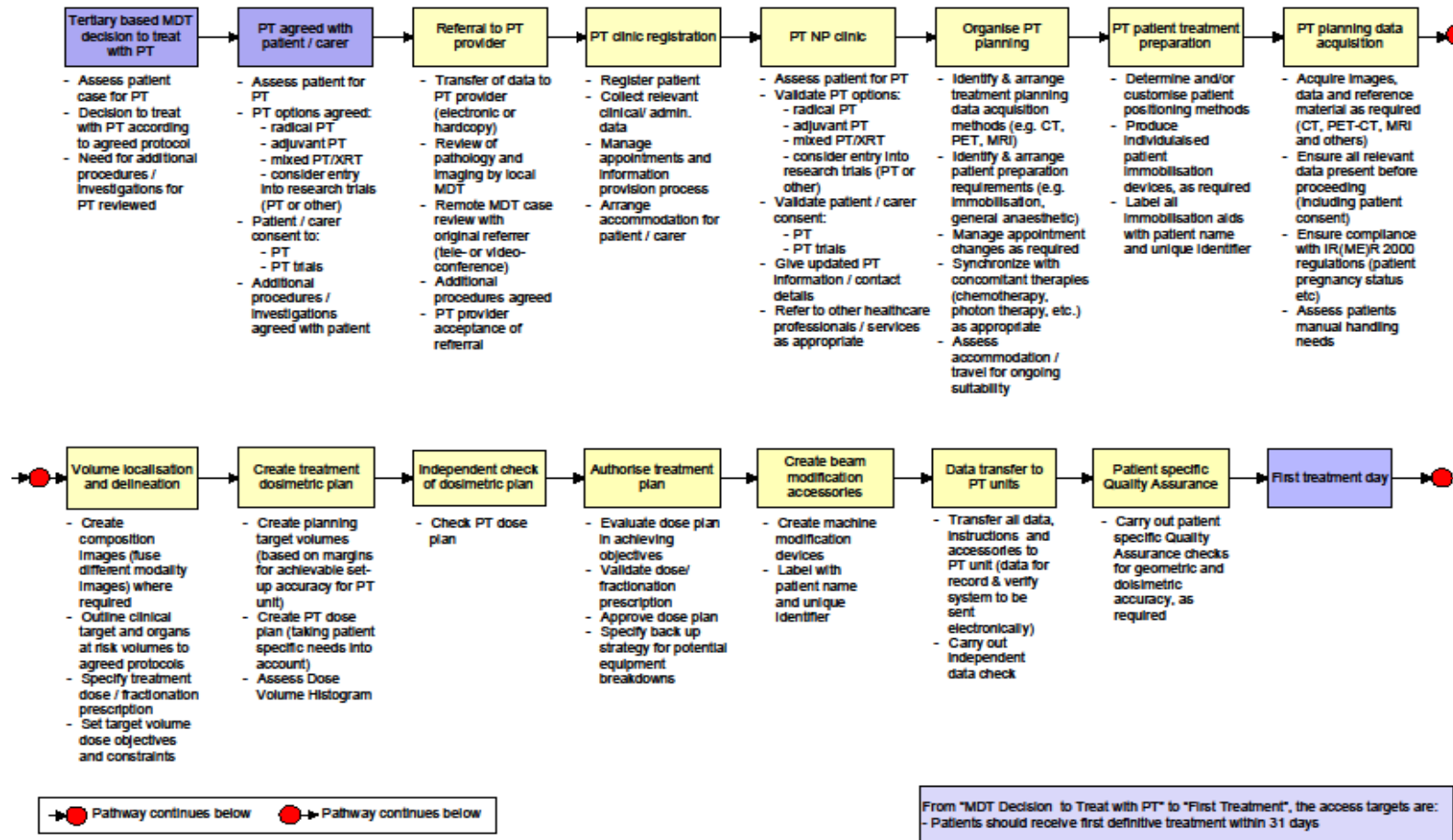
National PBT Service Development Programme – Strategic Outline Case – Annex E

Proton therapy (PT) pathway - EU (with process details)



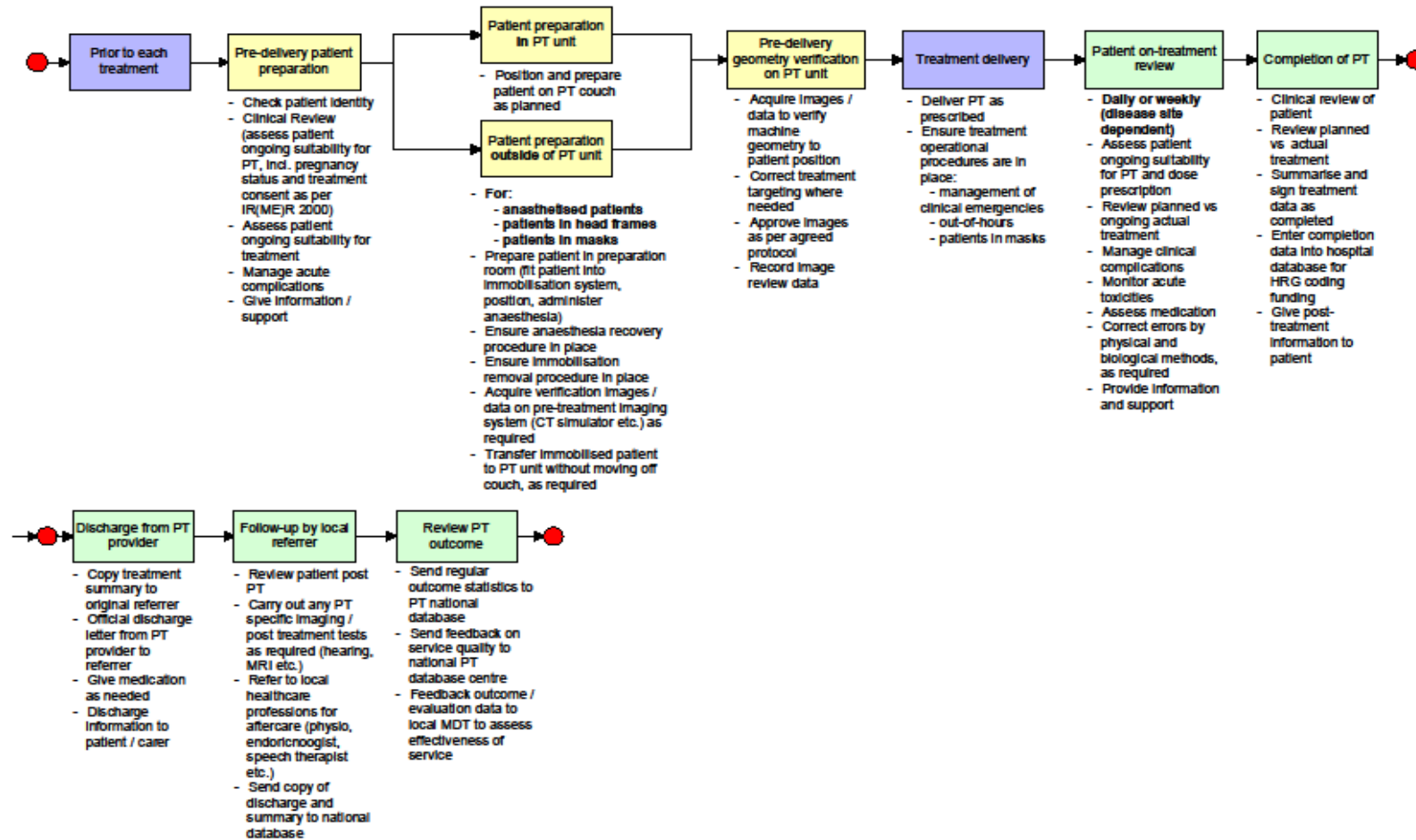
National PBT Service Development Programme – Strategic Outline Case – Annex E

Proton Therapy (PT) UK pathway - Planning



National PBT Service Development Programme – Strategic Outline Case – Annex E

Proton Therapy (PT) UK pathway - Treatment



Suggested Guideline Specifications for UK Proton Therapy.

The accelerator system should use proven technology, which has been used successfully in a hospital/clinical setting with peer reviewed publications of the physical characteristics and patient treatment outcomes. For the other features, such as nozzles, the most up-to-date equipment should be included, with passive and active scanning capabilities.

Where possible the facility/facilities should meet or exceed the following:-

1. Beam energy: maximum proton energy should be at least 230 MeV, with minimum energy of 40-70 MeV following any beam modification devices in the nozzle. Energy steps of 1 MeV are desirable. Energy changes should be as fast as possible, but no slower than 1 MeV/second.
2. A desirable feature might be the availability of higher energy particle source (300-350MeV) for radiography/range probes.
3. All gantries at one facility would be expected to be identical for maximum operational flexibility.
4. Passive scattering and spot/raster scanning capabilities must be available in all treatment rooms.
5. Where possible, the use of collimators and compensators should also be available in scanning mode.
6. For spot/raster scanning, the use of a preabsorber and/or ripple filter to aid the delivery of low energy pencil beams should be provided. This should have the ability of being driven in or out of the beam fully automatically without staff having to enter the treatment room or interrupt treatment.
7. Average Dose Rate for passive scattering: minimum of around one Gy per minute uniformly to a 5cm thick target, the centre of which is at a depth of 10cm when treated with a 10 cm×10cm field. Maximum dose rate of around 6 Gy per minute to same target.
8. For scanning, delivery should be as fast as possible, but no slower than one Gy/Litre/Minute.
9. A desirable feature for spot/raster scanning would be the capability for high-speed 2D scanning including fast energy variation (~100ms/5mm water equivalent step).
10. A desirable feature would be a high intensity source ($\gg 1\mu\text{A}$) with continuous beam or high frequency pulse rate (kHz).
11. Field dimensions: for passive scattering a minimum field size of 4 cm diameter with an upper limit of 35 cm or more. For spot/raster scanning the spot size should be of the order of 5mm FWHM in air at isocentre.

12. For both passive scattering and spot/raster scanning, the option of Multi-Leaf Collimation should be available.
13. Beam monitoring should include beam position to 0.5 mm and dose to a level of 0.1 cGy.
14. All appropriate standard specifications from the IEC for radiotherapy equipment will apply. Examples include:
 - (a) two independent dosimetry systems capable of beam termination should be incorporated as a minimum requirement.
 - (b) dose rate at one metre from the field centre should be less than 0.1% of the primary beam, including appropriate ICRP recommended weighting factors for biological effects.
15. Beam uniformity should be within a 2% tolerance across the field for passively scattered beam or equivalent with spot/raster scanning.
16. A minimum of one gantry per centre is required, with an average national provision of 75-80% of rooms with full rotating gantries. For operational efficiency, the patient and staff must be able to mount the treatment couch from within the gantry ring (so a false floor will be required).
17. Beam switching between rooms should be as fast as possible but no slower than 25 seconds.
18. Reliability should be guaranteed at above 95% and is anticipated to be 98% in most working months. Note that reliability should be defined in terms of clinical availability within the prescribed hours of operation (eg 8am to 8pm).
19. Servicing and technical alterations should be performed with no interference of treatment delivery during normal working hours.
20. Quality assurance tests and patient-specific monitor unit calibration measurements need to be included as part of the treatment process but with minimum disruption.
21. Treatment planning should include passive and spot/raster scanning algorithms based on established physics models, together with the capability for planning Intensity Modulated Proton Therapy treatments. These should accurately reproduce real measured beam data across the full energy range and include advanced computations using Monte Carlo techniques when available.
22. The treatment planning system should match the functionality and operability of a state-of-the-art system for conventional x-ray therapy. It should allow adaptive planning methods, 4D planning, robust planning and provide high quality QA tools etc.
23. There must be excellent on-site access to advanced MRI, PET and CT imaging facilities for target volume definition and post-treatment proton-range confirmation imaging.
24. Image guidance systems should be state of the art and available for daily position verification for all patients. These may vary in implementation but have capabilities for

respiratory gating / motion tracking. For operational efficiency and improved patient experience, the x-ray imaging control area should be within the main gantry room (although control should also be possible from outside the room for imaging to track respiratory motion etc). 3D/4D imaging should be possible on a daily basis, either in the treatment room or in treatment position outside of the treatment room.

25. On-line imaging for organ tracking should where possible make maximum use of technologies which deliver minimum or zero radiation dose, while providing clinically effective functionality.
26. Treatment planning and patient information systems must integrate with NHS IT strategy with connection to local PACS system etc.
27. Building construction must be of sufficient quality to ensure stability and accuracy of all components over the estimated working life of the facility (minimum of 30 years).
28. Local Electricity infrastructure must be capable of supporting the initial facility and any proposed expansion. If this is not so, it should be included in the business case.
29. Independent verification of all treatment related parameters must be demonstrated and compared with the manufacturer specifications and peer-reviewed.
30. Maintenance and servicing contracts should include on site engineers, with flexibility for increasing local involvement with time.
31. Overall responsibility for accuracy of dosimetry and treatment planning should be provided by a medical physics expert under the terms of UK regulations, ie IR(ME)R 2000.
32. Building construction must meet radiation safety limits required by IRR99 and respect local environment.

ANNEX F

Key References

Information in this Framework has been drawn from the following publications and reports on PT:

Department of Health: *Radiotherapy: developing a world class service for England*, February 2007

Department of Health: *Proton Treatment for cancer: a report for the national radiotherapy advisory group*, April 2006

For other references, please see individual papers.

Glossary of Terms used in the Framework

Proton	A proton is a heavy charged particle which has a different depth dose to the photons used in conventional radiotherapy. They have a steeper dose fall off rate with greater sparing of dose to healthy tissue surrounding the tumour target.
Photon	Photons are the x-rays used in modern cancer radiotherapy treatment.
Neutron	Neutrons are produced as a by-product of proton beam therapy accelerators, a neutron dose to a patient is undesirable.
Cyclotron	A cyclotron is a particle accelerator. It is a large and complicated piece of equipment and can be greater than seven metres in diameter. Cyclotrons accelerate particle to a fixed maximum energy, subsequently, the proton beam energy can be reduced to the required energy using degraders. However, the use of degraders will not give a mono-energetic beam and radioactivity can build up in the degrader
Synchrotron	A synchrotron is also used to accelerate particles. It produces particle at a range of energies that can then be used directly. While both synchrotrons and cyclotrons can produce charged particles, it is more straightforward for synchrotrons. Cyclotrons do however tend to be have lower maintenance requirements and hence lower running costs.
NCG	The National Commissioning Group, has representation from the professional bodies and provides clinical advise to the NSCG.
NSCG	The NSCG was established in April 2007, following the recommendations of an independent review chaired by Sir David Carter. The Carter Review recommended that the national commissioning function transfer from the DH to the NHS to strengthen its links with NHS commissioning and to provide for improved coherence between the different levels of commissioning from local, through regional and supra-regional, up to national and to bring about greater accountability and transparency.
NSCT	The National Specialised Commissioning Team is hosted by NHS London. It leads the national commissioning function on behalf of all ten SHAs and undertakes the national commissioning and contracting for highly specialised healthcare services. It also provides the secretariat for the National Commission Group (NCG), which advises Ministers on additions or changes to the portfolio of nationally commissioned services
NCRI	National Cancer Research Institute. Partnership of the major cancer funding bodies. Takes a strategic oversight of cancer research in the UK, identifying gaps and opportunities in current research and facilitating collaboration between funding bodies.

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