The NHS England Proton Service

EU Commission Sub-Group on Proton Therapy

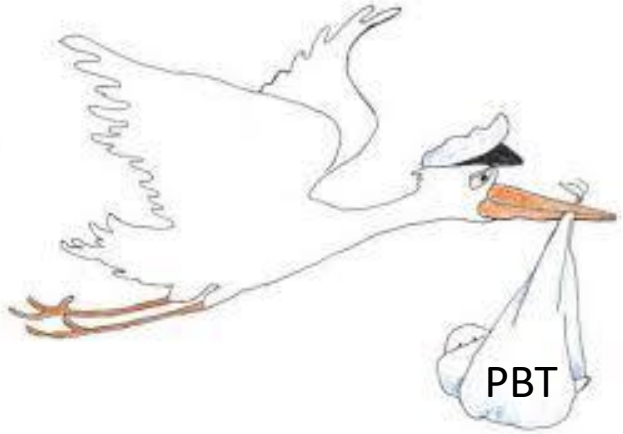
Luxembourg October 2018

NHS England National Clinical Lead PBT

How did we get here?

- 2007 Cancer Reform Strategy
  - Clinical Consensus Document
  - Clinical Policies Developed
  - Recommended Treatment Overseas and Explore Business Case UK based centre(s)

- 2008 Proton Overseas Programme
  - NHS England Highly Specialised Commissioning
  - Scotland NHS National Services



- 2015 FBC - £250M
  - Department of Health
  - Treasury Approved
- State of the Art Equipment & Building
- 1500 Patient Capacity = 1.5% Radical RT

- 2018 Christie Hospital Manchester - Opens
- 2020 UCLH London - Opens

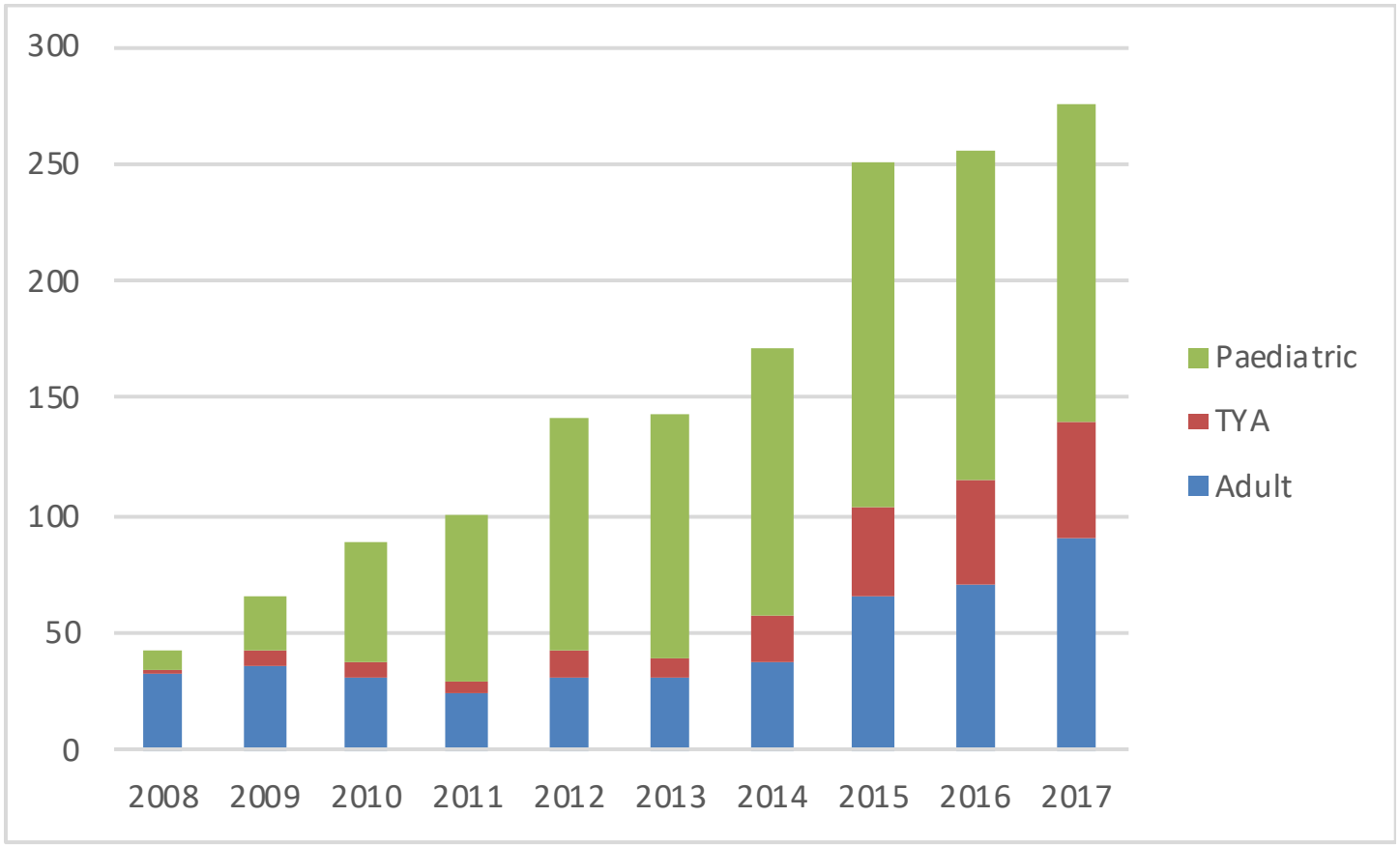
Basic Facts

Overseas Programme

- Total Referred into POP
  - Paediatric 918
  - TYA 215
  - Adult 471
  - Total 1604
- Average Paeds / TYA decision time 4 calendar days for approval
- Approval rates 2015-2018

	Paed	TYA	Adult
Yes	410	142	157
No	30	9	77
% Yes	**92**	**94**	**67**

Referrals into Proton Overseas Programme by Age
2008-2017



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Approvals By Diagnosis - Paeds and TYA

Rhabdomyosarcoma	219
Ependymoma	180
Low Grade Glioma	168
Ewings	160
Craniopharyngioma	121
Chordoma	36
Soft Tissue Sarcoma	29
Chondrosarcoma	20
Nasophargyngeal Carcinoma	12
Salivary Gland	11
Retinoblastoma	9
Osteosarcoma	7
Meningioma	6
Neuroblastoma	6
Non-germinomatous germ cell tumour	6
Pituitary Adenoma	6
Other	20

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Approvals By Diagnosis - Adult

Chordoma	169
Chondrosarcoma	95
Soft Tissue Sarcoma	12
Ewings	9
Adenoid Cystic Carcinoma	4
Nasophargyngeal Carcinoma	3
Adult Other	10

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The Society of Neurological Surgeons

NHS England

bsbs

British Skull Base Society

NHS England Proton Overseas Programme

Chordoma and Chondrosarcoma Pathway - Surgery, High Dose Radiotherapy and Proton Beam Therapy

What does good surgery look like?
Guidelines

- Quality of Resection
- Quality of Imaging
- Pathway Management
- Quality Standards Resection
- Combined Endoscopic / Lateral Cranial Approach
- Cross-refer to high volume expert skull base unit

Referral Process

- Local Cancer Centre MDT
- Local Patient assessment Radiation Oncology

- Refer through NHS Referral Portal
  - Structured data collection
  - Panel and referral function faster
- Imaging through Image Exchange Portal

- NHS England
- NHS Scotland
- NHS N Ireland
- Wales procurement Process

- National Panels
  - Paeds / TYA
  - Skull Base / CNS
  - Sarcoma
  - Head and Neck

- Clinical Policy criteria
- Safety
- Critical Friend ‘MDT’

- Recommend approval or rejection
- Conditions

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Outcomes / Results

- National Dataset Completed
- Vision for Outcomes
- Collections systems
- Funded Analysis
- Sufficient numbers and duration
  - Paediatric overseas - Published
  - Ependymoma – PROS presented
  - Skull Base Chordoma - underway

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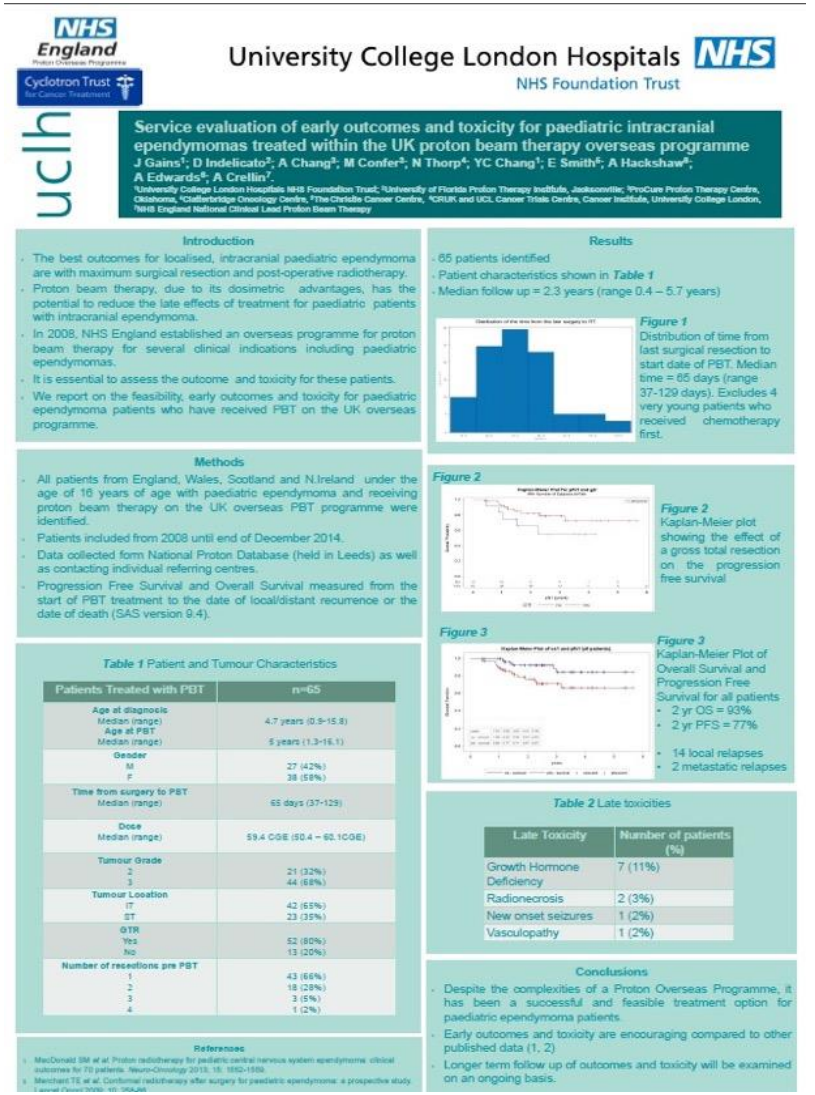
RESEARCH ARTICLE

WILEY Pediatric Blood & Cancer

Clinical outcomes following proton therapy for children with central nervous system tumors referred overseas

Daniel J. Indelicato[1] | Julie A. Bradley[1] | Eric S. Sandler[2] | Philipp R. Aldana[3] | Amy Sapp[1] | Jennifer E. Gains[4] | Adrian Crellin[4] | Ronny L. Rotondo[1]



NHS England Proton Overseas Programme
Cyclotron Trust for Cancer Treatment
uclh
University College London Hospitals NHS Foundation Trust

Service evaluation of early outcomes and toxicity for paediatric intracranial ependymomas treated within the UK proton beam therapy overseas programme

J Gains[1]; D Indelicato[2]; A Chang[3]; M Confer[3]; N Thorp[4]; YC Chang[1]; E Smith[5]; A Hackshaw[6]; A Edwards[6]; A Crellin[7].
[1]University College London Hospitals NHS Foundation Trust; [2]University of Florida Proton Therapy Institute, Jacksonville; [3]ProCure Proton Therapy Centre, Oklahoma, [4]Clatterbridge Oncology Centre, [5]The Christie Cancer Centre, [6]CRUK and UCL Cancer Trials Centre, Cancer Institute, University College London, [7]NHS England National Clinical Lead Proton Beam Therapy

Introduction

- The best outcomes for localised, intracranial paediatric ependymoma are with maximum surgical resection and post-operative radiotherapy.
- Proton beam therapy, due to its dosimetric advantages, has the potential to reduce the late effects of treatment for paediatric patients with intracranial ependymoma.
- In 2008, NHS England established an overseas programme for proton beam therapy for several clinical indications including paediatric ependymomas.
- It is essential to assess the outcome and toxicity for these patients.
- We report on the feasibility, early outcomes and toxicity for paediatric ependymoma patients who have received PBT on the UK overseas programme.

Methods

- All patients from England, Wales, Scotland and N.Ireland under the age of 16 years of age with paediatric ependymoma and receiving proton beam therapy on the UK overseas PBT programme were identified.
- Patients included from 2008 until end of December 2014.
- Data collected form National Proton Database (held in Leeds) as well as contacting individual referring centres.
- Progression Free Survival and Overall Survival measured from the start of PBT treatment to the date of local/distant recurrence or the date of death (SAS version 9.4).

Table 1 Patient and Tumour Characteristics

Patients Treated with PBT	n=65
Age at diagnosis Median (range) Age at PBT Median (range)	4.7 years (0.9-15.8) 5 years (1.3-16.1)
Gender M F	27 (42%) 38 (58%)
Time from surgery to PBT Median (range)	65 days (37-129)
Dose Median (range)	59.4 CGE (50.4 – 60.1CGE)
Tumour Grade 2 3	21 (32%) 44 (68%)
Tumour Location IT ST	42 (65%) 23 (35%)
GTR Yes No	52 (80%) 13 (20%)
Number of resections pre PBT 1 2 3 4	43 (66%) 18 (28%) 3 (5%) 1 (2%)

References

1. MacDonald SM et al. Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients. Neuro-Oncology 2013; 15: 1552-1559.
2. Merchant TE et al. Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study. Lancet Oncol 2009; 10: 258-66.

Results

- 65 patients identified
- Patient characteristics shown in *Table 1*
- Median follow up = 2.3 years (range 0.4 – 5.7 years)

Figure 1 Distribution of time from last surgical resection to start date of PBT. Median time = 65 days (range 37-129 days). Excludes 4 very young patients who received chemotherapy first.

Figure 2

Figure 2 Kaplan-Meier plot showing the effect of a gross total resection on the progression free survival

Figure 3

Figure 3 Kaplan-Meier Plot of Overall Survival and Progression Free Survival for all patients

- 2 yr OS = 93%
- 2 yr PFS = 77%
- 14 local relapses
- 2 metastatic relapses

Table 2 Late toxicities

Late Toxicity	Number of patients (%)
Growth Hormone Deficiency	7 (11%)
Radionecrosis	2 (3%)
New onset seizures	1 (2%)
Vasculopathy	1 (2%)

Conclusions

- Despite the complexities of a Proton Overseas Programme, it has been a successful and feasible treatment option for paediatric ependymoma patients.
- Early outcomes and toxicity are encouraging compared to other published data (1, 2)
- Longer term follow up of outcomes and toxicity will be examined on an ongoing basis.

Protons - Low Energy

- Eyes – Choroidal Melanoma
- Clatterbridge 1989
- First hospital based cyclotron in world
  - 2830 + Patients

- Excellent Results
  - 95% local control
  - 90% preservation of eye
  - 80% preservation sight

- Complex service
- Durability of expensive equipment

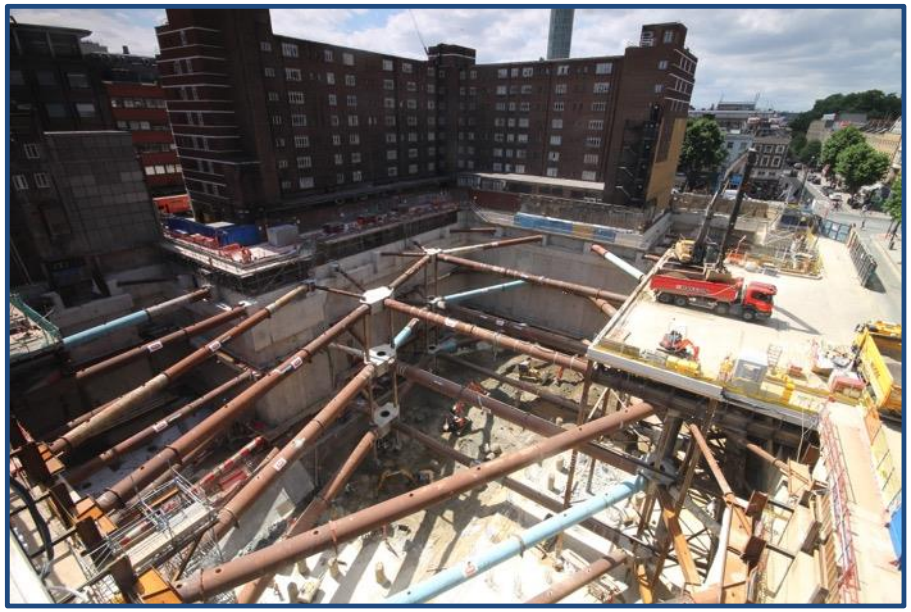
Expansion of PBT in UK

- NHS
- Clatterbridge
  - Low Energy - Eyes
- Christie 2018
- UCLH 2020

- Commercial
- Rutherford Centres
  - Newport
  - Northumberland
  - Reading
  - Liverpool
  - London
- AVO
  - London
- Proton Therapy UK - Prague
- Munich

NHS England


FIRE EX
NHS




KING LIFTING
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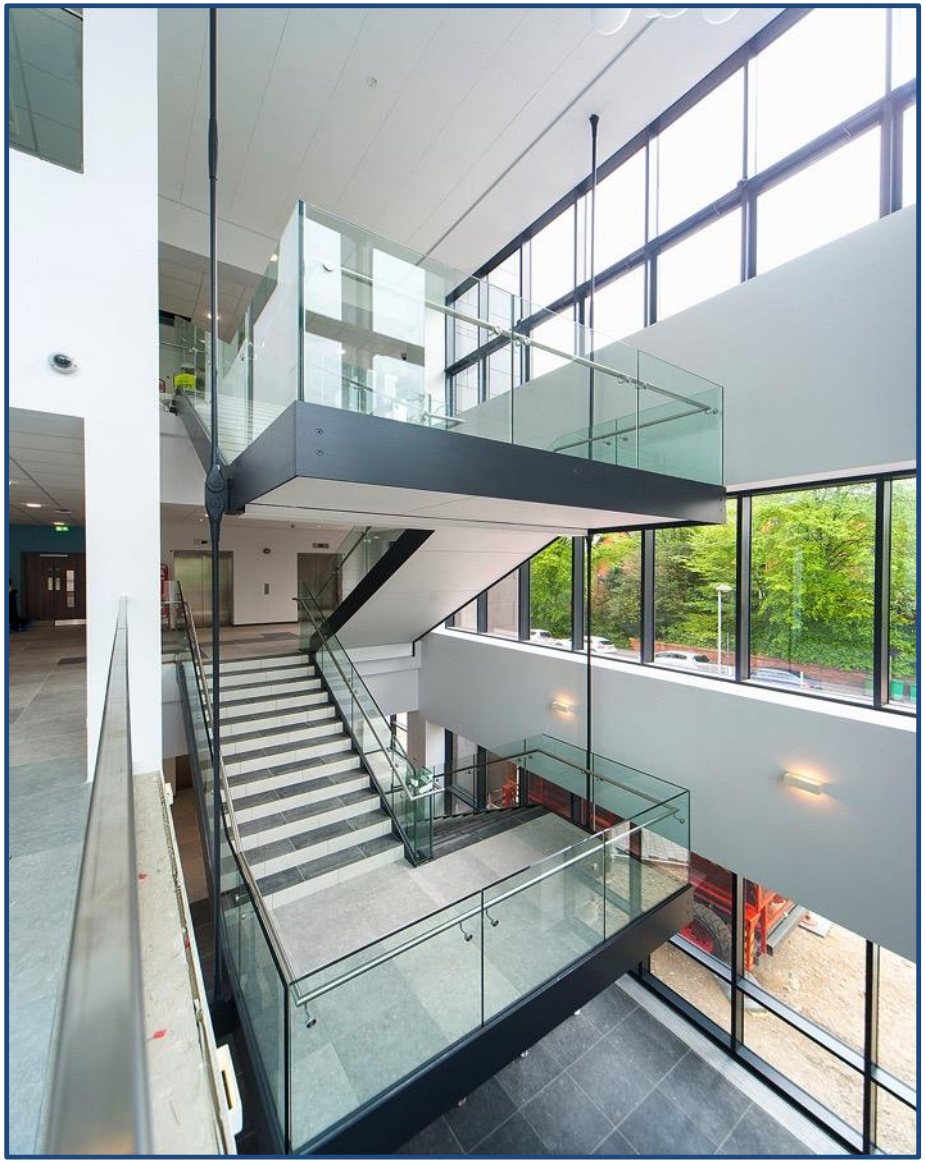
NHS


PROTON BEAM
THERAPY CENTRE


proBEAM



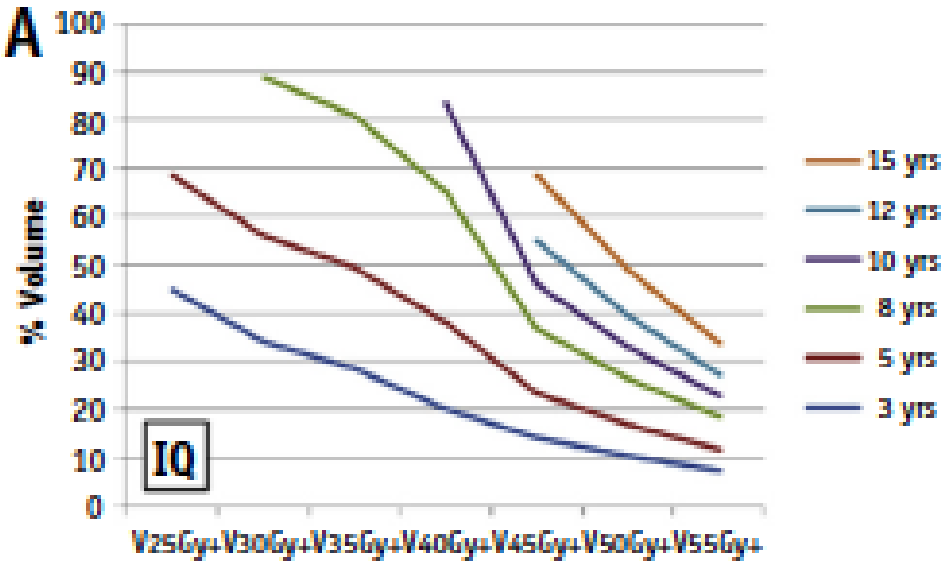
What is missing?

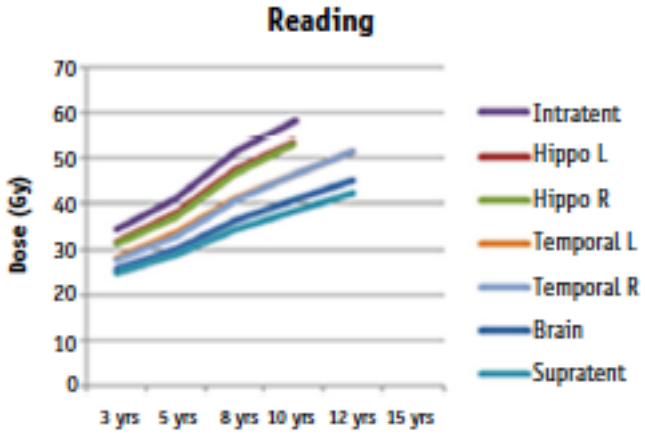
- Conventional Evidence Base
  - Direct Clinical Comparison
  - Randomised Controlled Trials
- Incremental gain adult most common cancers difficult
- Very High cost

Cost per case	£40,000
Excess Annual Cost 10% All RT	£540M

- Size of facilities – even one room
- Incomplete Technical Evolution

Evidence Base - Is this proof?





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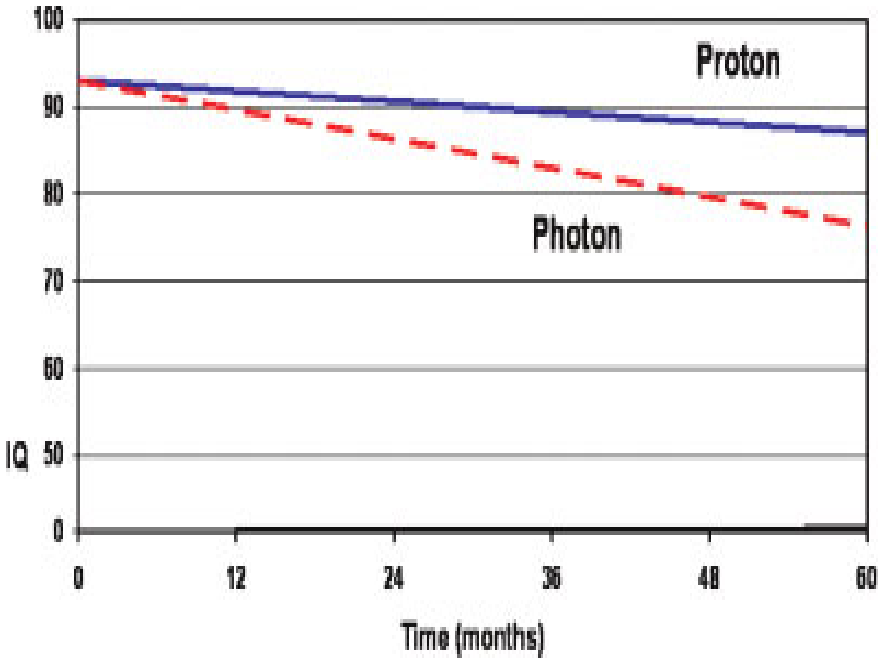
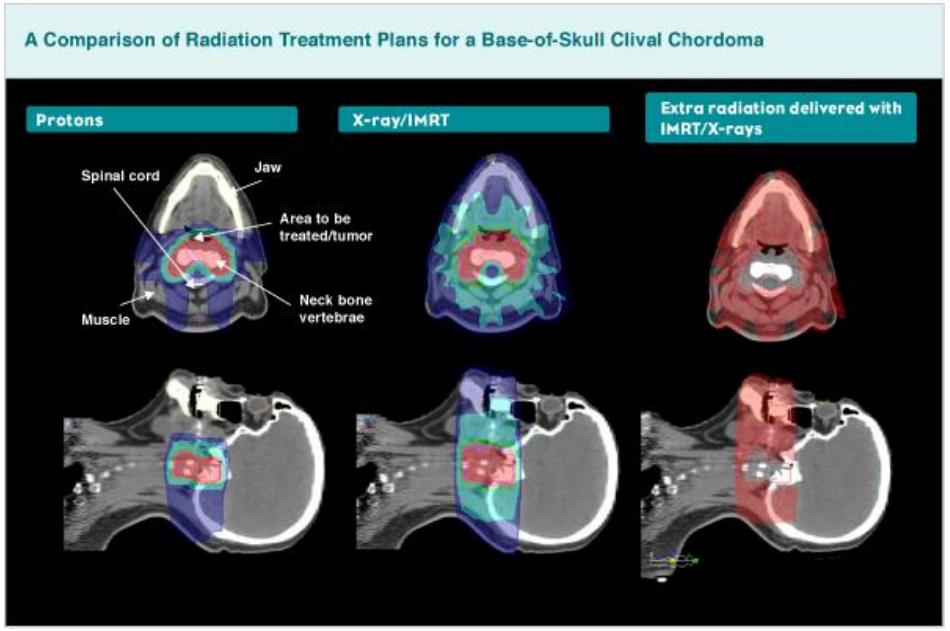




Conflict in Assessing Evidence for PBT

Randomised Controlled Trials?

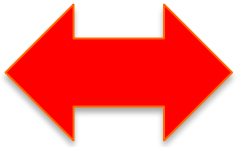
Direct Clinical Comparison?

Rapid Evidence Reviews

Not Systematic Reviews

Insufficient

NHS Clinical Policies



Radiotherapy is a Deterministic Based Science?

Modelling = Treatment Planning
Dose
NTCP - Late effects
Dose Response Curves
Radiation Exposure – Integral Dose

Clinical Consensus

But Uncertainties – Greater and Lesser

- Fractionation ?
- Addition of systemic agents ?

- Spot Scanning
- Evidence is with passive scattering

- Range Uncertainty – where does it stop?
- Imaging
- Movement
- Target Volumes different
- Metal work

- Model based approach?

- Re-imaging and Re-planning

- **RBE**

- Assumption Protons are better – commercial centres, media and marketing – 'No side Effects'

- ***'Dose planning studies without robust evaluation and optimisation are little more than a beauty pageant'***

- CTRad PBT Trials Strategy Group
  - David Sebag-Montefiore

- Myth Busting
- Patient Groups and Equipoise
- **Photon RT Improving**

CTRad
Clinical and Translational Radiotherapy
Research Working Group

- Strict Higher Priority = where dose distribution suggests could address problem or limitation in conventional RT?
- Accept Consensus and Higher principles 'Physics' where overwhelming
- Resist Commercial Model ahead of evidence base
- Create evidence base for future
- Open to collaboration - International Studies
- Cost-Effectiveness assessment AFTER studies assessing clinical gain

Pragmatic Solution

- ‘Routine Commissioning’
- Overwhelming Opinion of benefit and dose distribution
  - Paediatric and TYA
  - Adult Skull Base
  - Adult Spinal Sarcoma
  - Adult Craniospinal

- Trials
  - TORPEDO (oropharynx)
  - L Breast – IMC
  - Mediastinal Lymphoma
  - ABC07 IHCC
  - Anal Cancer
  - Lung – NSCLC
  - Oesophagus
- Evaluative Commissioning
  - Liver - HCC
  - Advanced Nasopharynx
  - Re-Irradiation
  - Common Cancers - TYA

Frontiers in Oncology 2017

The NHS model for Protons

- Academic High Quality Framework
- Integrated Major Cancer Centre Hospital Environment
- All patients in Prospective Studies / Trials
- Routine Formal Evaluation of Outcomes and Late Effects Treatment
- Technical developments and underpinning translational research
- This strategy can allow the future role of protons to be developed in the UK, based on sound clinical evidence, in a safe, sustainable and affordable way.

NHS England 70 YEARS OF THE NHS 1948 - 2018