# Clinical Implementation of PBT through UK Clinical Trials

Lee Harrison-Carey[1],

[1]Radiotherapy Trials Quality Assurance (RTTQA) Group, UCLH

FUNDED BY

NIHR | National Institute for Health and Care Research

The National Radiotherapy Trials Quality Assurance (RTTQA) Group is funded by the NIHR. The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

# Overview

- Role of RTTQA
- Role of RT QA in PBT trials
- Trial QA and Dosimetric Audit
- Current Trials
- Trials in set-up

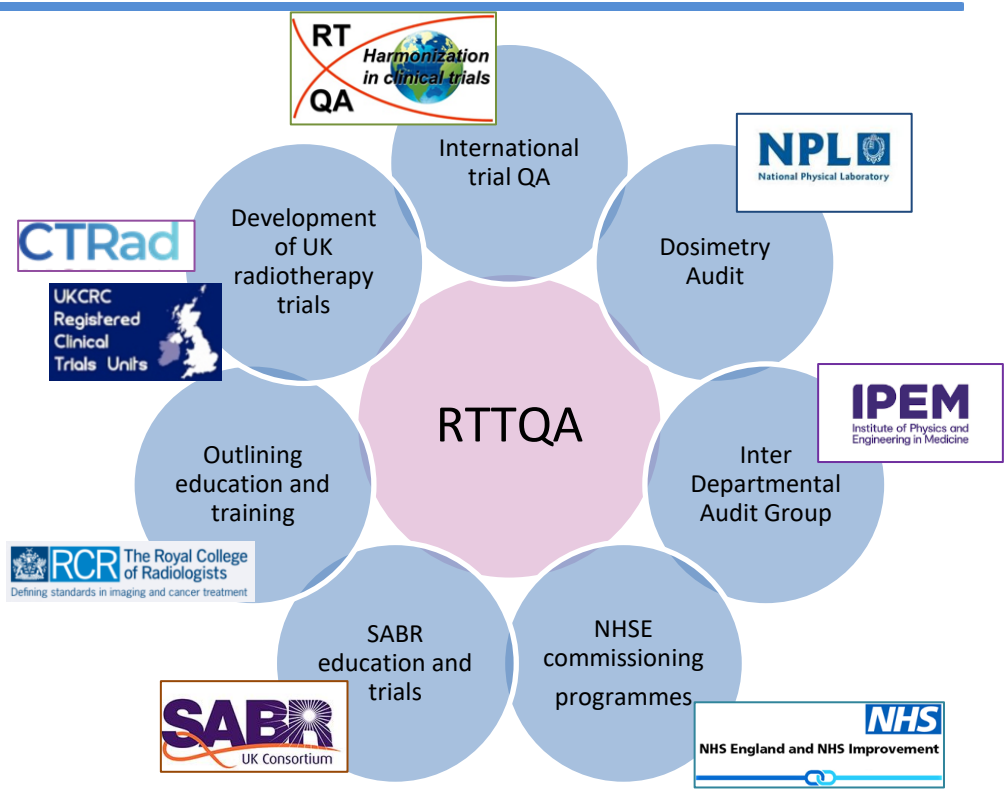
# The Radiotherapy Trials QA (RTTQA) Group

The RTTQA Group is funded by the NIHR

Design and implement QA programmes for NIHR CRN portfolio trials that include radiotherapy

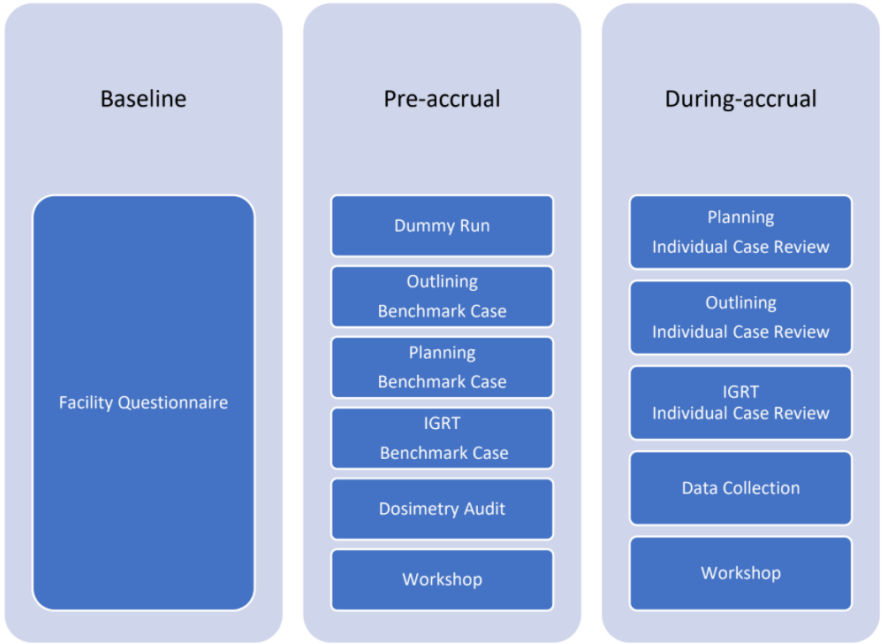
Multi-professional Group across multiple NHS radiotherapy sites:

- Clinician
- Clinical scientist
- Radiographer
- Physicist
- Dosimetrist

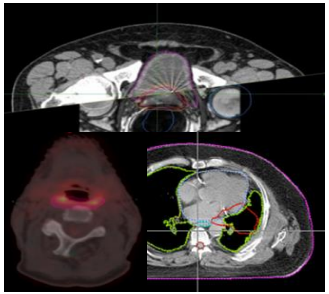


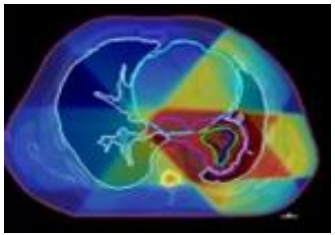
# RTTQA Activity

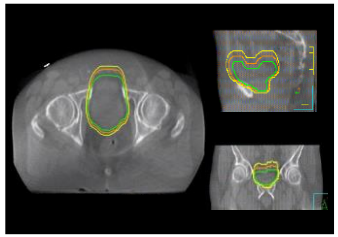
- RT QA is not mandated for RT trials
- Central independent QA is recommended through the RT research community
- CRUK will ask if RT QA has been considered for a trial
- Safety, accuracy, consistency for multi-centre trials across multiple anatomical sites
- Protocol compliance, meaningful endpoints
- Programme of activities

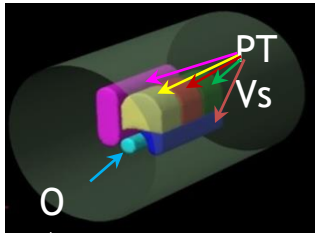


# Key QA Activity Areas








Documentation
FQ
Protocol
RT guidelines

→

Imaging
Target
volume &
OAR Outlining

→

Treatment
planning
and
optimisation

→

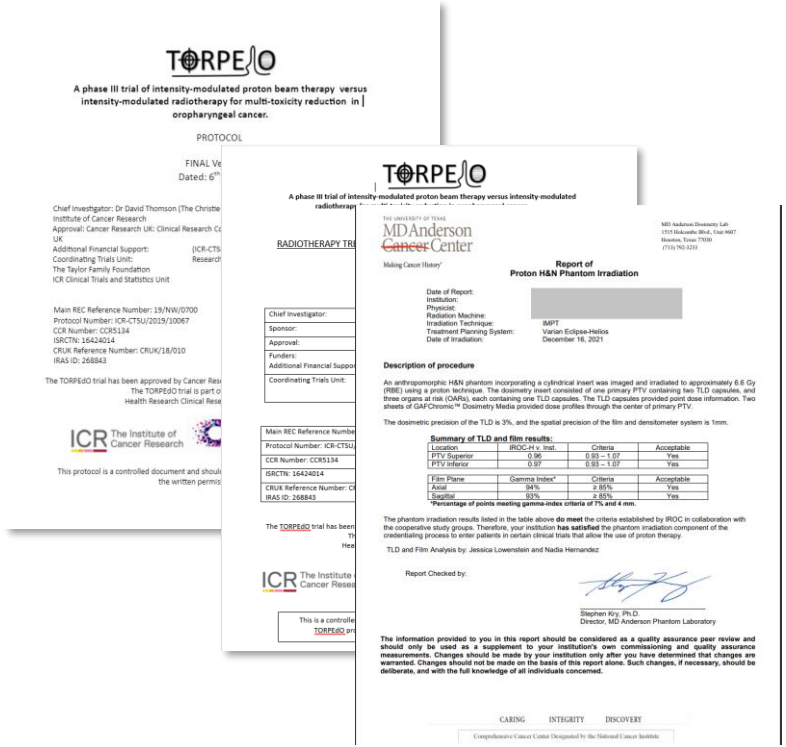
Treatment
delivery
and
verification

→

Dosimetry
audit

# RTTQA Role in PBT Trials

- QA is essential for all RT trials and especially PBT
  - PBT novel in the UK
  - RCT trials help fill knowledge gap
- Ensures compliance with protocol
- Validates trial results
- QA is broken up into pre-trial and on-trial QA
  - Planning and delivery guidance
  - Via RT guidelines document
- How we assess plans
  - Assessment between proton centres or with external assessors
- Dosimetry audit work (e.g. IROC and NPL)


TORPEDO

A phase III trial of intensity-modulated proton beam therapy versus intensity-modulated radiotherapy for multi-toxicity reduction in oropharyngeal cancer.

PROTOCOL

TORPEDO

A phase III trial of intensity-modulated proton beam therapy versus intensity-modulated

RADIOTHERAPY TR

MD Anderson Cancer Center

Making Cancer History®

Report of
Proton H&N Phantom Irradiation

Date of Report:
Institution:
Physicist:
Radiation Machine:
Irradiation Technique: IMPT
Treatment Planning System: Varian Eclipse-Helios
Date of Irradiation: December 16, 2021

Description of procedure

An anthropomorphic H&N phantom incorporating a cylindrical insert was imaged and irradiated to approximately 6.6 Gy (RBE) using a proton technique. The dosimetry insert consisted of one primary PTV containing two TLD capsules, and three organs at risk (OARs), each containing one TLD capsules. The TLD capsules provided point dose information. Two sheets of GAFChromic™ Dosimetry Media provided dose profiles through the center of primary PTV.

The dosimetric precision of the TLD is 3%, and the spatial precision of the film and densitometer system is 1mm.

Summary of TLD and film results:

| Location | IROC-H v. Inst. | Criteria | Acceptable |
|---|---|---|---|
| PTV Superior | 0.96 | 0.93 – 1.07 | Yes |
| PTV Inferior | 0.97 | 0.93 – 1.07 | Yes |

| Film Plane | Gamma Index* | Criteria | Acceptable |
|---|---|---|---|
| Axial | 94% | ≥ 85% | Yes |
| Sagittal | 93% | ≥ 85% | Yes |

*Percentage of points meeting gamma-index criteria of 7% and 4 mm.

The phantom irradiation results listed in the table above **do meet** the criteria established by IROC in collaboration with the cooperative study groups. Therefore, your institution **has satisfied** the phantom irradiation component of the credentialing process to enter patients in certain clinical trials that allow the use of proton therapy.

TLD and Film Analysis by: Jessica Lowenstein and Nadia Hernandez

Report Checked by:

Stephen Kry, Ph.D.
Director, MD Anderson Phantom Laboratory

**The information provided to you in this report should be considered as a quality assurance peer review and should only be used as a supplement to your institution's own commissioning and quality assurance measurements. Changes should be made by your institution only after you have determined that changes are warranted. Changes should not be made on the basis of this report alone. Such changes, if necessary, should be deliberate, and with the full knowledge of all individuals concerned.**

CARING INTEGRITY DISCOVERY

# Current Trials

***Completed Recruitment:***

- TORPEdO: Toxicity Reduction using Proton bEam therapy for Oropharyngeal cancer
  - 19 sites opened
  - 204 patients recruited, 135 PBT, 69 IMRT
  - Imaging and biology sub-studies recruiting
  - Comprehensive RT QA programme

***Open Trials:***

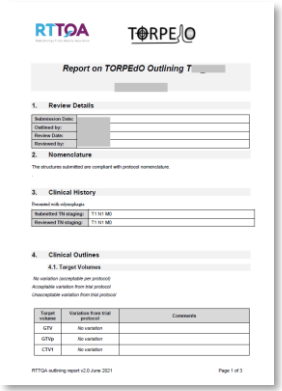
- Parable: Proton beam therapy in patients with breast cancer: evaluating early and late effects
  - 10 sites opened
  - 31 patients recruited, 15 PBT, 16 IMRT

# TORPEDO

- Assess whether IMPT compared with IMRT reduces treatment-related toxicities in patients with locally advanced oropharyngeal squamous cell carcinoma
- First UK PBT trial - defined methodology and process for future UK trials
- Pre-trial QA
  - Contouring Benchmark (vs gold standard)
    - Unless streamlined by previous H&N trial QA
  - Planning benchmark case
    - Pre-contoured with target and OAR volumes
  - Dosimetry Audit
- On-trial QA
  - Prospective Contouring review
  - Prospective plan review for first IMRT and IMPT at each centre with external review
  - Timely retrospective plan review (ideally before mandated week 3 rescan)

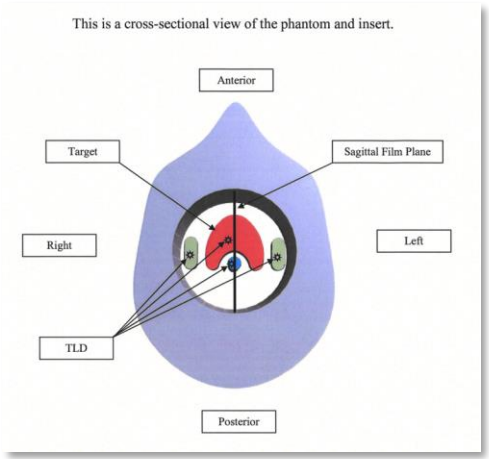
- Needed to be sure we had optimal VMAT plans vs PBT or you haven't shown a real benefit

- Detailed planning guidance issued in the form of RT guidelines (for both PBT and VMAT)
- Outlining was prospectively reviewed for all cases (72 hour turnaround)
- At least the first IMRT and IMPT plans reviewed prospectively by international partner
- As this was a new site external retrospective review was done for all plans
- Dosimetry audit from IROC and MedAustron to validate site as these were the available audits at the start of the trial
- Subsequent NPL reference and H&N audit



# TORPEDO - Audit

- IROC Proton Head and Neck Phantom was used as part of the credentialling process for clinical trials
- Purpose of the phantom treatment experiment is confirm the dose distribution planned by an institution can be delivered correctly




MD Anderson Cancer Center
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**Report of**
**Proton H&N Phantom Irradiation**

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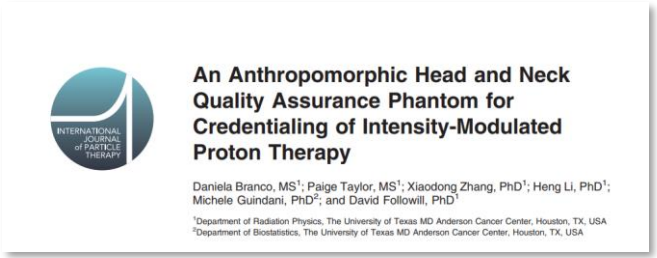
CARING INTEGRITY DISCOVERY

Comprehensive Cancer Center Designated by the National Cancer Institute



INTERNATIONAL JOURNAL of PARTICLE THERAPY

**An Anthropomorphic Head and Neck Quality Assurance Phantom for Credentialing of Intensity-Modulated Proton Therapy**

Daniela Branco, MS[1]; Paige Taylor, MS[1]; Xiaodong Zhang, PhD[1]; Heng Li, PhD[1]; Michele Guindani, PhD[2]; and David Followill, PhD[1]

[1]Department of Radiation Physics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA
[2]Department of Biostatistics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

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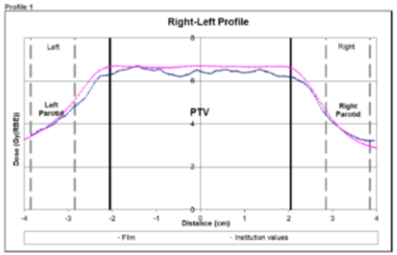
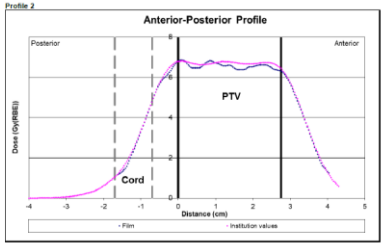
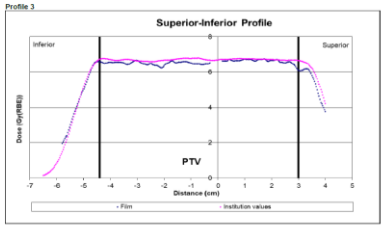
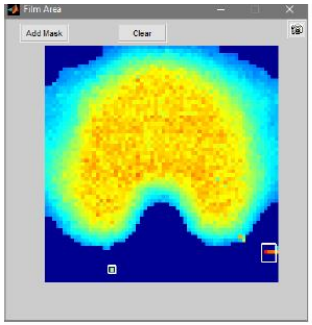
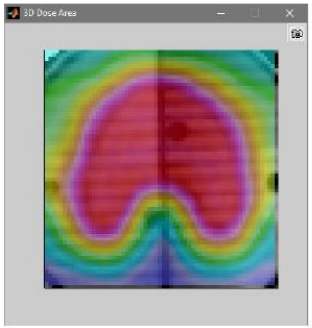
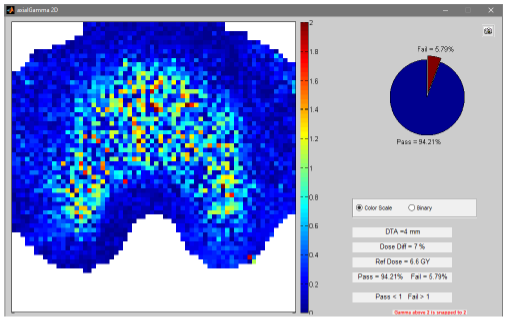


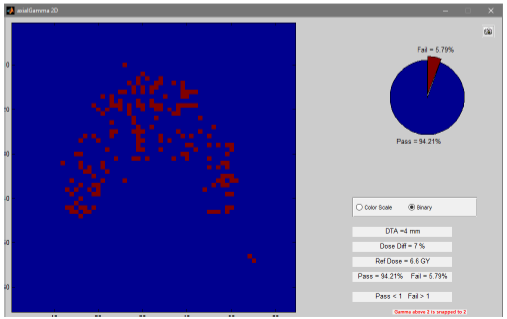



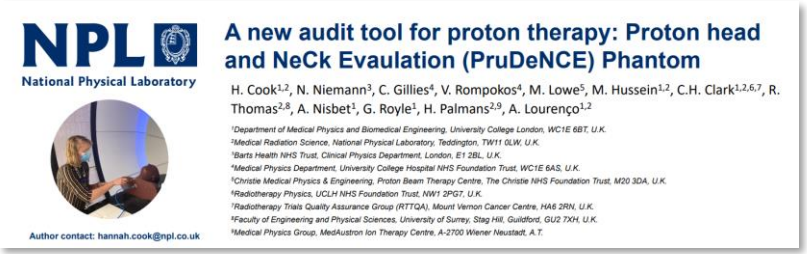



# TORPEDO -Audit

- NPL Audit Tool- Proton head and NeCk Evaluation (PruDeNCE) Phantom- A phantom for end-to-end audits
  - Novel proton imaging and therapeutic proton tissue equivalent plastics
  - Tested at both UK PBT centres
  - Absolute dose measurements with either alanine pellets or ionisation chamber at equivalent points of measurement within tumour and spine region.
  - EBT3 film in coronal plane of the phantom
- Agreement between ionisation chamber and alanine to treatment planning calculations within 2% in the tumour region
- Film analysis showing 95% pass rate for 4%/3 mm global gamma analysis for both centres
- **Dosimetry therefore validated in two ways**


NPL National Physical Laboratory

A new audit tool for proton therapy: Proton head and NeCk Evaulation (PruDeNCE) Phantom

H. Cook[1,2], N. Niemann[3], C. Gillies[4], V. Rompokos[4], M. Lowe[5], M. Hussein[1,2], C.H. Clark[1,2,6,7], R. Thomas[2,8], A. Nisbet[1], G. Royle[1], H. Palmans[2,9], A. Lourenço[1,2]

[1]Department of Medical Physics and Biomedical Engineering, University College London, WC1E 6BT, U.K.
[2]Medical Radiation Science, National Physical Laboratory, Teddington, TW11 0LW, U.K.
[3]Barts Health NHS Trust, Clinical Physics Department, London, E1 2BL, U.K.
[4]Medical Physics Department, University College Hospital NHS Foundation Trust, WC1E 6AS, U.K.
[5]Christie Medical Physics & Engineering, Proton Beam Therapy Centre, The Christie NHS Foundation Trust, M20 3DA, U.K.
[6]Radiotherapy Physics, UCLH NHS Foundation Trust, NW1 2PG7, U.K.
[7]Radiotherapy Trials Quality Assurance Group (RTTQA), Mount Vernon Cancer Centre, HA6 2RN, U.K.
[8]Faculty of Engineering and Physical Sciences, University of Surrey, Stag Hill, Guildford, GU2 7XH, U.K.
[9]Medical Physics Group, MedAustron Ion Therapy Centre, A-2700 Wiener Neustadt, A.T.

Author contact: hannah.cook@npl.co.uk

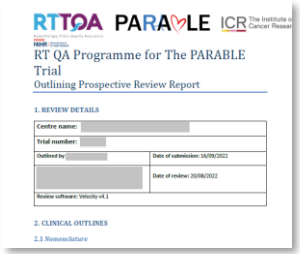
*Courtesy of Hannah Cook- NPL*

# PARAMLE

- Assess whether PBT can reduce mean heart dose without increasing shorter-term side effects, in patients with breast cancer who have increased risk of radiotherapy-induced heart toxicity.
- Second UK Trial- Refined methodology and process
- Pre-trial QA
  - Contouring Benchmark (vs gold standard), detailed contouring guidelines
    - Unless streamlined by a previous trial
  - Planning benchmarks
    - Two cases, one including SIB
    - Centres permitted to submit only case 1 if SIB technique under development
  - Prospective Contouring review for first three cases
  - Prospective plan review for first three IMAT and first five IMPT at each reviewed by peers and RTTQA
  - Timely retrospective plan review at periodic meetings by peers

- As trial was used to set up breast PBT in proton optimal VMAT treatment had to be the comparator

- Detailed planning guidance issued in the form of RT guidelines (for both PBT and conventional)
- Outlining was prospectively reviewed for first three all cases (72 hour turnaround)
- At least the first three IMAT and first five IMPT plans prospectively peer reviewed
- Retrospective peer review is performed between UCLH and the Christie in MDT meetings
- Proton sites already had dosimetry audit from IROC so no further audit was required


RT QA Programme for The PARABLE Trial

Outlining Prospective Review Report

1. REVIEW DETAILS

Centre name:

Trial number:

Outlined by:

Date of submission: 16/09/2022

Date of review: 20/08/2022

Review software: Velocity v4.1

2. CLINICAL OUTLINES

2.1 Nomenclature

# Trials in Active Setup

RTTQA Radiotherapy Trials Quality Assurance

| Trial | Description | Phase | Status/Opening |
|---|---|---|---|
| APPROACH | Analysis of Proton vs. Photon Radiotherapy in Oligodendroglioma and Assessment of Cognitive Health | PH III | QA programme in progress. 7 centres ready to recruit. Q4 2023 intended opening |
| PROTIEUS | A Randomised Phase 2 Trial Comparing Proton versus Photon Based Neoadjuvant Chemoradiation, followed by Adjuvant Immunotherapy, in Oesophageal Cancer | PH II | QA programme ready to implement. Opening date TBC |
| PROTIS | PROTon beam therapy vs IMRT in Sinonasal cancer | PH III | QA programme ready to implement. Q2 2024 intended opening |
| HIT-Meso | Hemithoracic Irradiation with Proton Therapy in Malignant Pleural Mesothelioma | PH III | QA programme in setup. Opening date TBC |

# ECIP Studies

| Trial | Description | Sample Size | Anticipated Start date |
|---|---|---|---|
| SUPERMAN | Selection of patients for proton beam radiotherapy for the management of **abdominal neuroblastoma** in children | 100 (75 PBT/ 25 XRT) | Q1/2 2024 |
| PRONTO | An Evaluative Commissioning Study for the Role of IMPT in the treatment of **Malignant Parotid Tumours** | 100 | Q1/2 2024 |
| PARTNERS | An Evaluative Commissioning Study for the Role of IMPT in the treatment of **Nasopharyngeal Cancers** | 100 | Q1/2 2024 |
| EMPHATIC | Evaluation of Combined Modality Proton and HepAtic Transplantation for **Hilar Cholangiocarcinoma** | 25-30 | Q1/2 2024 |

2 further adult ECIP studies are in development

# Acknowledgements


- NIHR
- RTTQA group
- Hannah Cook
- Romelie Rieu
- Liz Miles
- Catharine Clark


@RTTQA_UK

william.harrison-carey@nhs.net

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