

PRONTO: An evaluative commissioning study to investigate the role of adjuvant proton beam radiotherapy in patients with localised parotid carcinoma

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Background

Malignant parotid tumours are rare, accounting for 3-6% of head and neck cancers. Adjuvant radiotherapy is indicated in patients with high-risk localised disease. Although 5-year cancer control and survival rates are good, treatment is associated with significant toxicity, with >70% of patients receiving photon therapy experiencing significant dysgeusia (altered or impaired taste). Dysgeusia is a common and persistent side effect of photon irradiation to the parotid bed, contributing to weight loss, reduced appetite, xerostomia, and poorer quality of life (QoL).

PRONTO is the first Evaluative Commissioning in Protons (ECIP) programme study. This multi-centre, single-arm study aims to assess the clinical benefit of Proton Beam Therapy (PBT) in the adjuvant treatment of localised malignant parotid cancer. The primary objective is to evaluate whether PBT reduces taste dysfunction compared to historical photon radiotherapy data from COSTAR, a UK Phase III RCT. Secondary endpoints include toxicity, hearing outcomes, trismus, QoL, oncological outcomes, feasibility, health economics, and dosimetric parameters.

Methods

PRONTO is a non-randomised, multicentre prospective study conducted at the two NHS PBT centres (The Christie and UCLH). Adults with histologically confirmed malignant parotid tumours requiring adjuvant radiotherapy to the parotid bed (≥60 Gy equivalent), with or without elective neck irradiation, are eligible for referral. 97 patients will be recruited and treated with PBT over 2-3 years.

The primary objective is to evaluate whether PBT offers a clinically meaningful reduction in taste dysfunction for patients receiving adjuvant radiation for localised malignant parotid cancers (as assessed by the EORTC-QLQ-H&N43). Comparison will be made with historical photon radiotherapy data from COSTAR, a UK Phase III RCT.

Data collection, facilitated by research radiographers at both PBT centres, will occur at different timepoints:

- Baseline
- Weekly during treatment
- 6 weeks post-PBT,
- 3, 6, 12, and 24 months post-PBT.

Data analysis will be led by Christie Proton Clinical Outcomes Unit (PCOU).

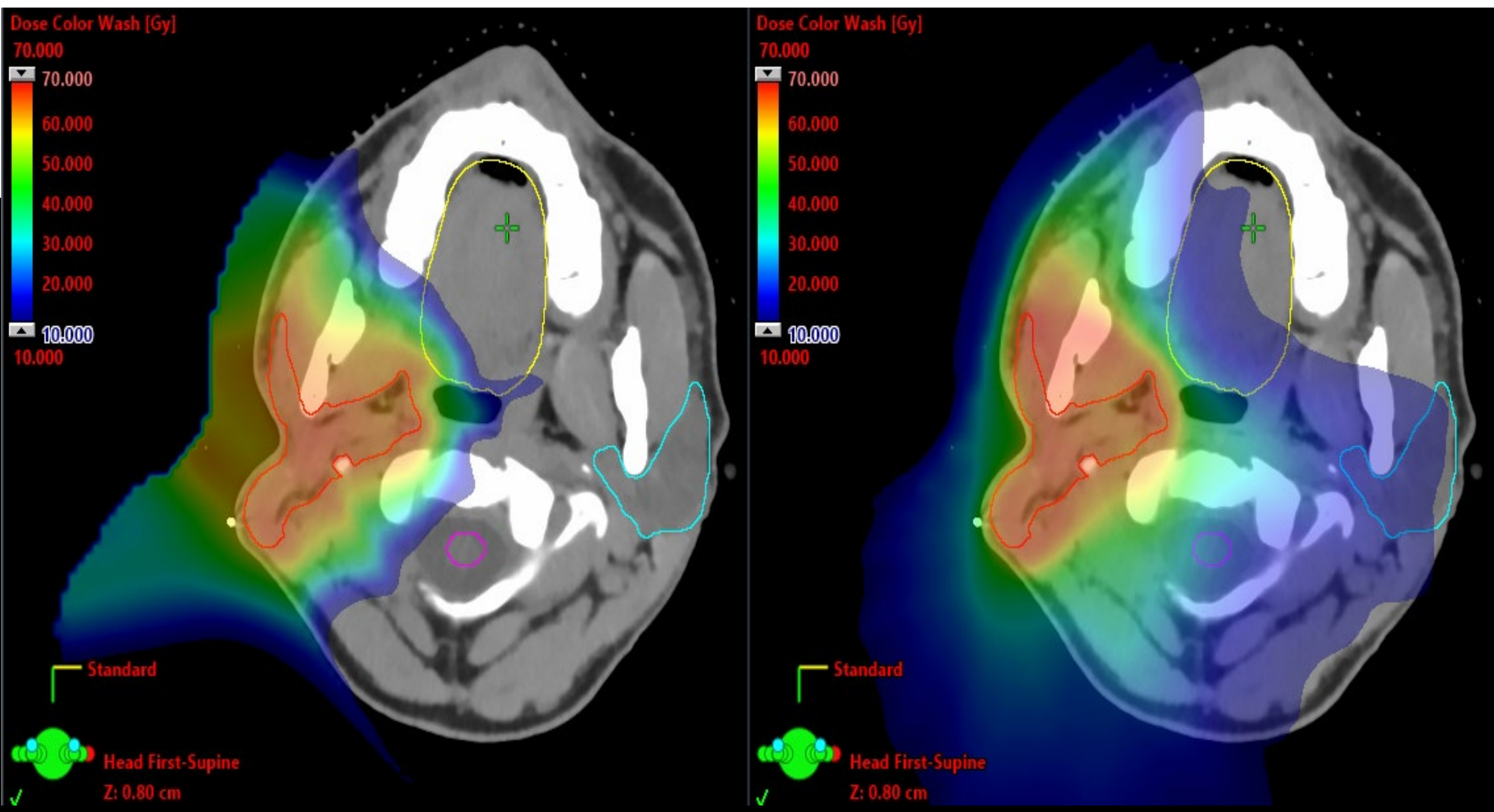


Figure 1: Comparison of PBT (left) and photon-intensity-modulated radiotherapy (IMRT) plan (right) for a patient receiving adjuvant radiotherapy to the right parotid region and associated ipsilateral lymph nodes. The colour wash highlights tissues receiving doses above 10Gy. Note the sparing across healthy tissues, including oral cavity, with PBT compared with photons. Selected regions of interest are outlined, including: high dose target region (red), oral cavity (yellow), contralateral thyroid gland (blue), spinal cord (yellow).

PRONTO Study Design

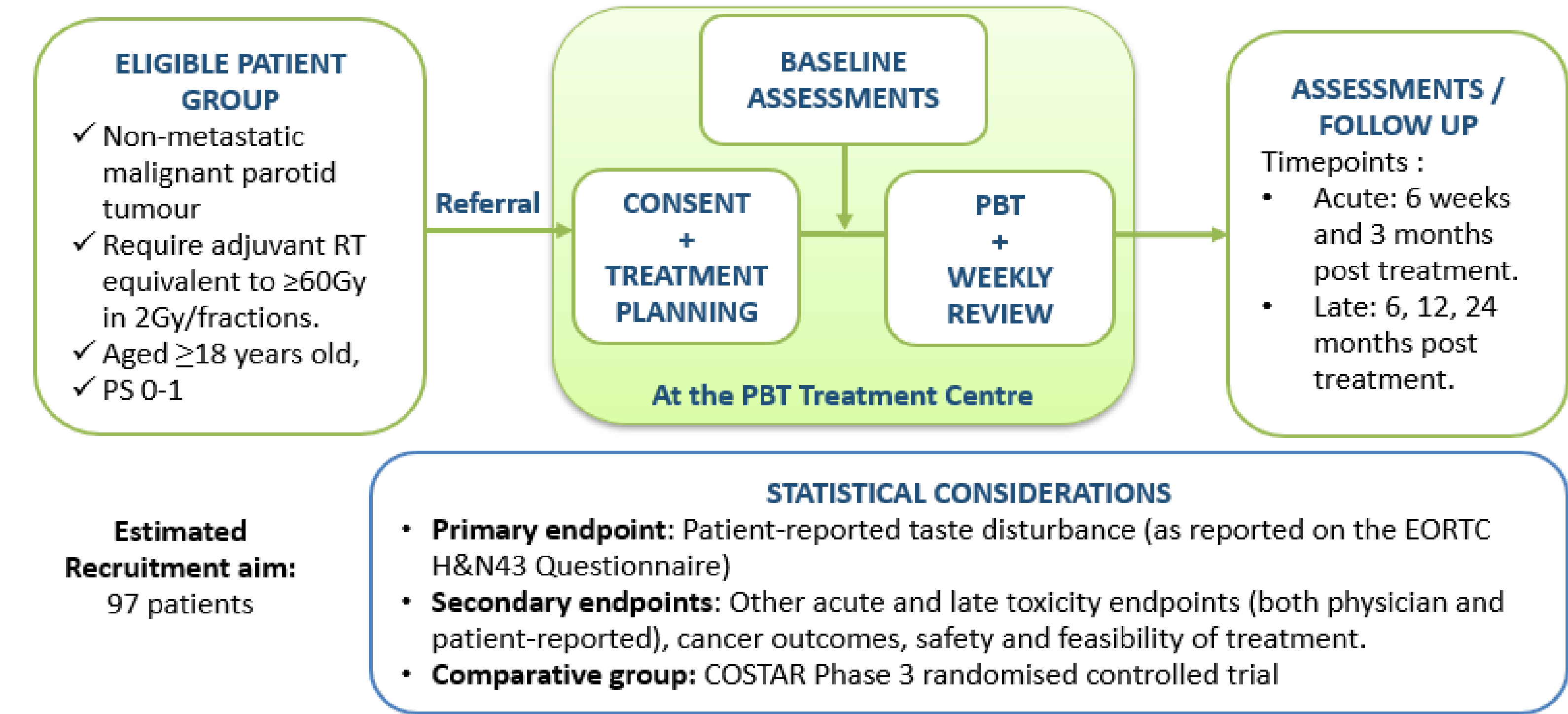


Figure 2: PRONTO study schema

Results

The study opened to recruitment on 5th September 2025. To date, 22 patients have been recruited across three centres (The Christie, UCLH and The Royal Marsden).

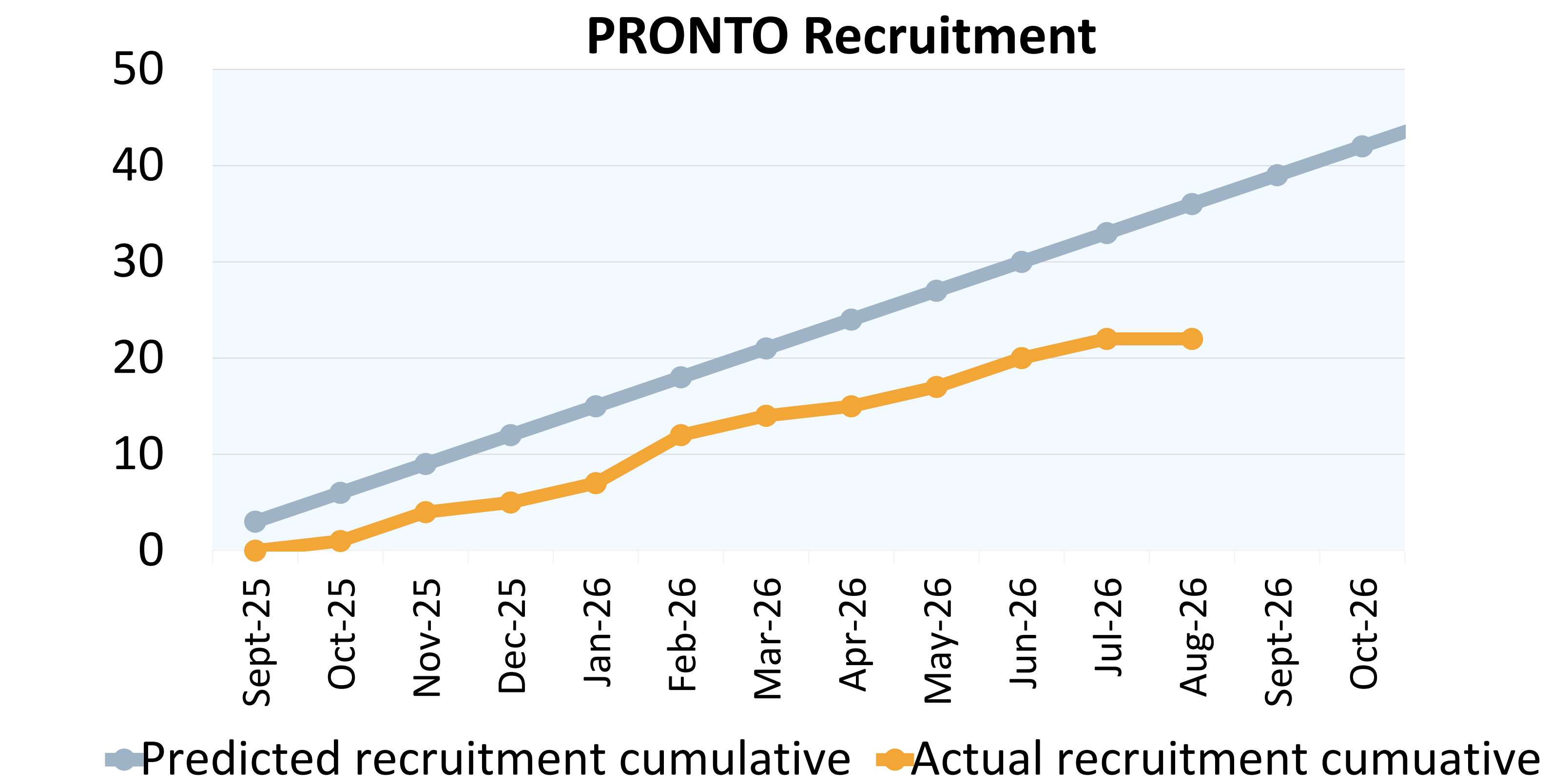


Chart 1: PRONTO recruitment to date

Participant Inclusion Criteria	Participant Exclusion Criteria
- Age ≥18 years - Performance status 0–1 - Histologically confirmed primary malignant tumour of the parotid gland - Indication for post-operative radiotherapy - Radical treatment intent - Suitable for follow-up - Written informed consent	- Previous radiotherapy to the H&N - Primary radiotherapy indication or gross residual disease - Metastatic disease to the parotid - Benign tumours - Significant comorbidity impacting PBT - Chemotherapy planned or ongoing

Table 1: Participant Selection Criteria for PRONTO. All participants must meet all of the inclusion and none of the exclusion criteria at the time of registration.

Conclusion

PRONTO provides a national referral pathway for patients with malignant parotid carcinoma while evaluating whether PBT can reduce treatment-related toxicity, particularly taste dysfunction.

The findings will inform future NHS commissioning of PBT for this rare disease while contributing to high-quality national evidence generation.

Any radiotherapy department in England and Wales can refer patients requiring adjuvant parotid radiotherapy, via the national proton referral portal

<https://protons.protontherapyreferrals.nhs.uk>

Contacts

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References

- Mercante, G. *et al.* Oncological outcome and prognostic factors in malignant parotid tumours. *J. Craniomaxillofac. Surg.* **42**, 59–65 (2014)
- Gunn, L. *et al.* Taste dysfunction following radiotherapy to the head and neck: A systematic review. *Radiother. Oncol.* **157**, 130–140 (2021)
- Romesser, P. B. *et al.* Proton beam radiation therapy results in significantly reduced toxicity compared with intensity-modulated radiation therapy for head and neck tumors that require ipsilateral radiation. *Radiother. Oncol.* **118**, 286–292 (2016).
- Nutting, C. *et al.*, Results of a multicentre randomised controlled trial of cochlear-sparing intensity-modulated radiotherapy versus conventional radiotherapy in patients with parotid cancer (COSTAR; CRUK/08/004). *Eur J Cancer.* **103**, 249–258 (2018)