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Original Research

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)

Christopher M. Nutting [a,*], James P. Morden [b,1], Matthew Beasley [c], Shreerang Bhide [a], Audrey Cook [d], Emma De Winton [e], Marie Emson [b], Mererid Evans [f], Lydia Fresco [g], Simon Gollins [h], Dorothy Gujral [i,o], Kevin Harrington [a], Mano Joseph [j], Catherine Lemon [k], Linda Luxon [l], Qurrat van den Blink [m], Ruheena Mendes [n], Aisha Miah [i,o], Kate Newbold [a], Robin Prestwich [p], Martin Robinson [q], Paul Sanghera [r], Joanna Simpson [s], Muthiah Sivaramalingam [t], Narayanan Nair Srihari [u], Mark Sydenham [b], Emma Wells [v], Stephanie Witts [b], Emma Hall [b] on behalf of the COSTAR Investigators

[a] *Head and Neck Unit, Royal Marsden Hospital, London, United Kingdom*
[b] *The Institute of Cancer Research Clinical Trials and Statistics Unit, The Institute of Cancer Research, London, United Kingdom*
[c] *Bristol Cancer Institute, Bristol Haematology and Oncology Centre, United Kingdom*
[d] *Gloucestershire Oncology Centre, Cheltenham General Hospital, United Kingdom*
[e] *Department of Oncology, Royal United Hospital, Bath, United Kingdom*
[f] *Clinical Oncology, Velindre NHS Trust, United Kingdom*
[g] *Department of Oncology, University Hospitals of Coventry and Warwickshire, United Kingdom*
[h] *Department of Oncology, Glan Clwyd Hospital, Rhyl, United Kingdom*
[i] *Head and Neck Department, Imperial College Healthcare NHS Trust, United Kingdom*
[j] *Oncology and Haematology Directorate, The Royal Wolverhampton NHS Trust, United Kingdom*
[k] *Department of Oncology, Mount Vernon Hospital, United Kingdom*
[l] *University College London Ear Institute, United Kingdom*
[m] *Department of Oncology, Northampton General Hospital, United Kingdom*
[n] *Department of Oncology, University College Hospital, London, United Kingdom*
[o] *Sarcoma Unit, Royal Marsden Hospital, Sutton, United Kingdom*
[p] *Department of Clinical Oncology, St James's University Hospital, Leeds, United Kingdom*
[q] *Department of Clinical Oncology, Weston Park Hospital, Sheffield, United Kingdom*
[r] *Department of Oncology, University Hospitals Birmingham NHS Foundation Trust, United Kingdom*

* *Corresponding author*: Head & Neck Unit, Royal Marsden Hospital, Fulham Road, London SW3 6JJ, United Kingdom. Fax: +20 7808 2235.
E-mail address: Chris.Nutting@rmh.nhs.uk (C.M. Nutting).
[1] James Morden died in September 2017.

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[s] Department of Oncology, Royal Sussex County Hospital, United Kingdom
[t] Department of Oncology, Royal Preston Hospital, United Kingdom
[u] Department of Oncology, Royal Shrewsbury Hospital, United Kingdom
[v] QA Physics, Royal Marsden Hospital, London, United Kingdom

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KEYWORDS
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Abstract ***Purpose:*** About 40–60% of patients treated with post-operative radiotherapy for parotid cancer experience ipsilateral sensorineural hearing loss. Intensity-modulated radiotherapy (IMRT) can reduce radiation dose to the cochlea. COSTAR, a phase III trial, investigated the role of cochlear-sparing IMRT (CS-IMRT) in reducing hearing loss.
Methods: Patients (pT1-4 N0-3 M0) were randomly assigned (1:1) to 3-dimensional conformal radiotherapy (3DCRT) or CS-IMRT by minimisation, balancing for centre and radiation dose of 60Gy or 65Gy in 30 daily fractions. The primary end-point was proportion of patients with sensorineural hearing loss in the ipsilateral cochlea of ≥10 dB bone conduction at 4000 Hz 12 months after radiotherapy compared using Fisher's exact test. Secondary end-points included hearing loss at 6 and 24 months, balance assessment, acute and late toxicity, patient-reported quality of life, time to recurrence and survival.
Results: From Aug 2008 to Feb 2013, 110 patients (54 3DCRT; 56 CS-IMRT) were enrolled from 22 UK centres. Median doses to the ipsilateral cochlea were 3DCRT: 56.2Gy and CS-IMRT: 35.7Gy ($p < 0.0001$). 67/110 (61%) patients were evaluable for the primary end-point; main reasons for non-evaluability were non-attendance at follow-up or incomplete audiology assessment. At 12 months, 14/36 (39%) 3DCRT and 11/31 (36%) CS-IMRT patients had ≥10 dB loss ($p = 0.81$). No statistically significant differences were observed in hearing loss at 6 or 24 months or in other secondary end-points including patient-reported hearing outcomes.
Conclusion: CS-IMRT reduced the radiation dose below the accepted tolerance of the cochlea, but this did not lead to a reduction in the proportion of patients with clinically relevant hearing loss.
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1. Introduction

Malignant parotid gland tumours represent 3–6% of head and neck cancers. Surgery is the mainstay of treatment [1]. Local recurrences occur in 20–70% of patients [1–4]. Adjuvant, post-operative radiotherapy of 60–65Gy in 30 fractions given over 6 weeks is recommended for patients with high risk of recurrence [5,6].

The ipsilateral cochlea is usually very close to the planning target volume (PTV) and often receives a dose greater than 50Gy [7] with conventional 3-dimensional conformal radiotherapy (3DCRT) techniques. As a consequence, clinically significant high-tone, sensorineural hearing loss (>10 dB) has been described in 40–60% of patients after radiotherapy [8–14], peaking at a frequency around 4000 Hz.

Intensity-modulated radiotherapy (IMRT) produces highly conformal radiation dose distributions. Cochlear-sparing IMRT (CS-IMRT) can reduce the dose to the ipsilateral cochlea, compared with 3DCRT, to below its accepted tolerance dose of 40–45Gy [7,15]. COSTAR aimed to investigate whether CS-IMRT reduces sensorineural hearing loss.

2. Methods

2.1. Study design and participants

COSTAR is a phase III, parallel group, randomised controlled trial. Patients aged ≥18 years, WHO performance status 0–1 with histologically confirmed malignant primary parotid tumours (pT1-4, N0-3, M0) requiring post-operative adjuvant radiotherapy, were eligible. Exclusion criteria included previous head and neck radiotherapy, pre-existing severe hearing loss (hearing level of >60 dB in bone conduction threshold at 4000 Hz in ipsilateral cochlea) and need for chemotherapy. Patients were staged by diagnostic computed tomography (CT) or magnetic resonance imaging of head and neck and chest X-ray or CT of thorax. Resection status was documented from histopathology as R0 (resection margin >5 mm), R1 (1–5 mm) or R2 (<1 mm). Patients were required to attend long-term follow-up including audiograms and provide written informed consent.

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