

Mitochondrial changes induced by melatonin lead to a metabolic switch in cancer cells inducing cellular death but doesn't affect normal tissues.

Ortiz F, et al. *J Pineal Res* 2015; 58: 34-49

Escames G, et al. *Hum Genetics* 2012; 131:161-173

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PO-091 Intensity modulated radiotherapy (IMRT) in nasopharyngeal cancer – a dosimetric and QoL analysis

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Purpose or Objective

Intensity modulated radiation therapy (IMRT) as a treatment technique has become the standard of care in treatment of nasopharyngeal carcinoma. The dosimetry of the modality with respect to parotid and other normal organ sparing and other clinical outcomes are presented in our study.

Material and Methods

The medical records of 32 patients with histologically proven primary nasopharyngeal carcinoma treated with IMRT were retrospectively reviewed. The majority of patients showed advanced clinical staging. IMRT was performed in step-and-shoot technique using an integrated boost concept. The boost volume covered the primary tumor and involved nodes with doses of 66-70.4 Gy (single dose 2.2 Gy) and uninvolved regional nodal areas were covered with doses of 54-59.4 Gy (median single dose 1.8 Gy). The dose constraints were optimized and normal organs at risk (OARs) spared. Dosimetric analysis was done and quality of life was assessed at initial stage and later during follow up at 3 and 6 months. The survival analysis was evaluated.

Results

The median follow-up for the entire cohort was 24 months. Radiation therapy was completed without interruption in all patients. Four local recurrences have been observed, transferring into 1-, 3-, and 5-year Local Control (LC) rates of 95%, 90% and 90%. Two patients developed regional nodal recurrence, resulting in 1-, 3-, and 5-year Regional Control (RC) rates of 95%. All locoregional failures were located inside the radiation fields. Distant metastases were found in three patients, transferring into 1-, 3-, and 5-year Distant Control (DC) rates of 90%, 84% and 82%. Progression free survival (PFS) rates after 1, 3 and 5 years were 85%, 72% and 65% and 1-, 3- and 5-year Overall Survival (OS) rates were 90%, 85% and 80%. Acute and chronic toxicities were assessed as per EORTC grading scale and found to be better with IMRT and under acceptable tolerance levels.

Conclusion

IMRT with an integrated boost concept yielded good disease control, good OARs sparing, better quality of life outcomes and overall survival in patients suffering from primary nasopharyngeal cancer with acceptable acute side effects and limited rates of late toxicity.

PO-092 Dosimetric comparison of conformal and intensity modulated radiotherapy for locally recurrent NPC

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Purpose or Objective

Locally recurrent nasopharyngeal carcinoma (NPC) can be salvaged by reirradiation with a substantial degree of radiation related complications.

The aim of this study was to evaluate the dosimetric

advantage of intensity modulated radiotherapy (IMRT) in treating locally recurrent NPC.

Material and Methods

Between January 2014 and september 2016, six patients with no metastatic locally recurrent NPC were re-irradiated with concomitant chemotherapy. The median prescribed dose was 60 Gy with 2 Gy per fraction. Treatment planning of each patient was performed for two techniques: Three dimensional Conformal radiotherapy (3D CRT) and Intensity modulated radiotherapy (IMRT). The minimum dose (Dmin), the maximum dose (Dmax) and the volume that received 95% of the dose prescribed (D95%) of the planning target volume (PTV) and doses to the organs at risk (Spinal cord and brainstem) were calculated and compared for the two techniques.

Results

All two techniques delivered adequate doses to the PTV. The average Dmin was 48Gy for the two techniques, the average Dmax was 67,5 Gy vs 64,2 Gy respectively for IMRT and 3D CRT (p=0,41) and D95% was 96%. Concerning the organs at risk, the Dmax for the brainstem was significantly higher for 3D CRT (22 Gy vs 14 Gy, p=0,003). This finding was similar for the spinal cord (20Gy vs 7,8 Gy). But, the difference was not statistically significant (p=0,12).

Conclusion

Based on the dosimetric comparison, IMRT was optimal by delivering a conformal and homogenous dose to the PTV with significant better sparing of critical organs than 3D CRT.

In this regard, re-irradiation using IMRT may be a very attractive technique for locally recurrent NPC.

PO-093 COSTAR trial results: 3-D Conformal Radiotherapy vs Cochlea-Sparing IMRT in parotid cancer patients

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Purpose or Objective

30-50% of patients receiving post-operative radiotherapy (RT) for parotid cancer experience ipsilateral hearing loss. IMRT can reduce radiation dose to the cochlea. COSTAR (CRUK/08/004) investigated the role of IMRT in reducing hearing loss in these patients.

Material and Methods

Patients with histologically confirmed carcinoma of the parotid gland (pT1-4, pN0-3, M0) were randomized 1:1 to receive CT-planned 3-D Conformal RT (3DCRT) or Cochlea Sparing-IMRT (CS-IMRT). 60Gy (R0 resection) or 65Gy (R1-2) in 30 fractions were delivered over 6 weeks. Treatment allocation used minimisation, balancing for centre and planned RT dose. The primary endpoint was proportion of patients with hearing loss in the ipsilateral cochlea of ≥ 10 dB measured by bone conduction at 4000Hz 12 months (m) after RT; compared between randomized groups by an exact test ($\alpha=0.05$). Secondary endpoints ($\alpha=0.01$) included hearing loss at 6 and 24m, vestibular function, acute and late toxicity, patient reported quality of life (including Glasgow Hearing Aid Benefit Profile (GHABP), time to tumour recurrence and survival.

Results

110 patients (54 3DCRT; 56 CS-IMRT) were randomised between 2008 and 2013 from 22 UK centres. 99 (90%) patients were R1-2 (47 3DCRT; 52 CS-IMRT). Mean dose to the ipsilateral cochlea was 56.2Gy for 3DCRT and 35.7Gy for CS-IMRT, ($p<0.001$). 66/110 (60%) patients were evaluable for the primary endpoint; the main reasons for non-evaluability were non-attendance at follow-up audiology and bone conduction assessment not performed. At 12m, a loss of ≥ 10 dB in ipsilateral bone conduction was observed in 14/35 (40%) 3DCRT and 11/31 (36%) CS-IMRT patients ($p=0.80$). No statistically significant differences in bone or air conduction were observed at 6m or 24m after RT nor for any GHABP initial disability or handicap subscales, vestibular function, acute or late toxicity, overall quality of life, time to tumour recurrence or survival.

Conclusion

IMRT reduced the radiation dose below the accepted tolerance of the cochlea, but this did not lead to a statistically significant reduction in the proportion of patients with hearing loss in the ipsilateral ear at 12 months after RT.

PO-094 Radiation induced volume changes in Salivary glands in head and neck cancer patients receiving IMRT
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Purpose or Objective

To evaluate radiation induced volume changes in the parotid glands and submandibular glands in patients with head and neck cancer receiving Intensity Modulated Radiotherapy (IMRT) and correlation with the mean doses received by the glands and assessment of timings of the volume changes during fractionated RT.

Material and Methods

Fourty five patients of Head and Neck Cancers, satisfying the inclusion criteria were included from May 2015 to Dec 2015 and were treated with radical or post-operative Radiotherapy using IMRT with or without Chemotherapy. Radiotherapy planning CT scans were done at pre RT, after 40 Gy and on completion of treatment for each patient. Parotid and submandibular gland volumes were re contoured on each study scan and rechecked with same observer. The volumes (V0 - Volume on initial CT scan) and mean doses to the parotid and submandibular glands were calculated from the Dose-volume histograms (DVHs) of the IMRT plan, done on pre RT scan. The re contoured volumes

of parotid and submandibular glands on the CT after 40 Gy (V1) and on completion (V2) were noted. Volume changes of the glands were assessed and statistical analysis was done to see any correlation between the mean dose and volume changes of the glands.

Results

The total mean dose to the parotid glands in IMRT patients was 24.47 Gy (for the ipsilateral and contralateral parotid glands they were 41.61 Gy and 26.13 Gy, respectively). For IMRT patients, the total mean doses to spared and irradiated submandibular glands were 7.39 Gy and 58.04 Gy, respectively. The average volume loss after 4 weeks of RT, upon completing RT versus before RT were 22.12%, 31.12%, and between 4 th week to completion of RT 11.56% for the parotid glands and 25.26%, 32.93% and between 4 th week to completion of RT 10.28% for the submandibular glands, respectively. The average mean volumes of both parotid glands and submandibular glands after 4 weeks of RT and upon completing RT were significantly smaller than before RT (P value $<.001$). We observed volume loss during RT in the parotid and the submandibular glands. The average rates of volume loss during the first 4 weeks of RT (22.12% and 25.26% respectively) were larger than in the last 2/3 weeks of RT (11.56% and 10.28% respectively). Volume loss at higher doses (>30 Gy) to the glands was significantly larger than at low doses (<30 Gy; $P < .001$).

Conclusion

The parotid and submandibular glands shrunk during RT. These gland volume reductions correlated significantly with the mean dose to the irradiated glands; the spared glands showed few changes.

PO-095 Electrochemotherapy for mucosal head and neck tumours: results from a phase II clinical trial.

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Purpose or Objective

Electrochemotherapy is a local tumour treatment currently used for cutaneous tumours and metastases in a palliative setting. Electric pulses are applied to the exterior of the cells creating a temporary permeability of the cell membrane. During this phase chemotherapy can gain access to the interior of the cell and cause apoptosis. Electrochemotherapy applied on mucosal tumours has only been tested in a few trials. The purpose of this trial was to evaluate electrochemotherapy on recurrent head and neck tumours in a palliative setting.

Material and Methods

ClinicalTrials.gov Identifier: NCT02549742. The study was designed as a phase II, clinical trial, with planned decision to discuss continuation after the first twelve evaluable patients. Patients included had recurrence of carcinoma in the oral cavity, rhino-, oro- or hypopharynx and no further curative treatment options left as determined by multidisciplinary conference (MDT). Electrochemotherapy