

CLINICAL INVESTIGATION

Head and Neck

PROSPECTIVE STUDY OF INNER EAR RADIATION DOSE AND HEARING LOSS IN HEAD-AND-NECK CANCER PATIENTS

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Purpose: To determine the relationship between the radiation dose to the inner ear and long-term hearing loss. **Methods and Materials:** Eligible patients included those receiving curative radiotherapy (RT) for head-and-neck cancer. After enrollment, patients underwent three-dimensional conformal RT planning and delivery (180–200 cGy/fraction) appropriate for their disease site and stage. The inner ear was contoured on axial CT planning images. Dose–volume histograms, as well as the mean and maximal dose for each structure, were calculated. Patients underwent pure tone audiometry at baseline (before treatment) and 1, 6, 12, 24, and 36 months after RT. The threshold level (the greater the value, the more hearing loss) in decibels was recorded for 250, 500, 1000, 2000, 4000, and 8000 Hz. For patients receiving predominantly unilateral RT, the contralateral ear served as the *de facto* control. The differences in threshold level between the ipsilateral and contralateral ears were calculated, and the temporal pattern and dose–response relation of hearing loss were analyzed using statistical methods that take into account the correlation between two ears in the same subject and repeated, sequential measurements of each subject.

Results: Of the 40 patients enrolled in this study, 35 qualified for analysis. Four patients who received concurrent chemotherapy and RT were analyzed separately. The 31 unilaterally treated patients received a median dose of 47.4 Gy (range, 14.1–68.8 Gy) to the ipsilateral inner ear and 4.2 Gy (range, 0.5–31.3 Gy) to the contralateral inner ear. Hearing loss was associated with the radiation dose received by the inner ear (loss of 210 dB was observed in ears receiving ≥ 45 Gy) and was most appreciable in the higher frequencies (≥ 2000 Hz). For a 60-year-old patient with no previous hearing loss in either ear, after receiving 45 Gy, the ipsilateral ear, according to our clinical model, would have a 19.3-dB (95% confidence interval [CI], 15.5–23.0) and 5.4-dB (95% CI, 3.5–7.5) hearing decrement compared with the contralateral ear for 8000 Hz and 1000 Hz, respectively. Age and an initial hearing difference within an ear pair also affected hearing loss. The baseline hearing threshold was inversely related to radiation-induced hearing loss. The degree of hearing loss was dependent on the frequency tested, age, baseline hearing, and baseline difference in hearing between a patient's two ears.

Conclusion: High-frequency (≥ 2000 Hz) hearing acuity worsens significantly after RT in a dose-dependent fashion. A larger number of patients needs to be studied to validate these results. This knowledge can be applied to create guidelines regarding future dose limits to the auditory apparatus for patients undergoing head-and-neck RT. © 2005 Elsevier Inc.

Hearing, Inner ear, Radiotherapy, Head-and-neck cancer.

INTRODUCTION

Intensity-modulated radiotherapy (RT) has allowed for better dose conformation, improving dose escalation to the target and sparing of more normal tissue. To best use these capabilities, one needs a thorough understanding of the relationship between the normal tissue damage and the radiation dose to make rational decisions regarding the tradeoffs between the dose to the target and the sparing of normal tissue. For head-and-neck tumors, many normal tissue structures coexist in this region, but our understand-

ing of their response to RT varies by structure. Sensorineural hearing loss (SNHL) as a result of RT to the inner ear and cochlea is a radiation dose-limiting toxicity that needs additional investigation.

Approximately 24,000 patients each year present with malignancy of the nasopharynx, parotid gland, paranasal sinuses, or brain (1). The inner ear is often included in the radiation field for treatment of these patients, and a substantial number of these patients will develop transient serous otitis media during or immediately after RT. More importantly, permanent SNHL due to radiation effects on the

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cochlea will also develop in many of these patients. SNHL has been shown to result in significant cognitive impairment, depression, and reduction in functional status (2).

The incidence of post-RT sensorineural deficit has been reported to range from 0% to 50% (3–5). Retrospective reports have also reported radiation-induced hearing loss to begin anywhere from 30 Gy to >65 Gy (6, 7). The influence of confounding variables such as concurrent chemotherapy and other comorbidities that predispose to hearing loss has been unclear in many of these studies. Also, with these historical studies, a reliable dose estimation for the cochlea was often difficult because CT planning might not have been used. Therefore, because hearing loss is an especially morbid sequelae of head-and-neck RT, we sought to determine the relationship between the radiation dose to the inner ear and the development of hearing loss in head-and-neck patients treated at our institution with three-dimensional conformal RT.

METHODS AND MATERIALS

Population

This study was an institutional review board-approved prospective study involving 40 patients with head-and-neck tumors undergoing curative RT that was anticipated to involve one or both inner ears in the Department of Radiation Oncology at the University of Michigan. Patients agreed to undergo hearing tests, and all patients provided written informed consent for participation in this prospective study.

Treatment

Each patient underwent three-dimensional planning and treatment as practiced at the Department of Radiation Oncology. Most patients received unilateral neck RT, and the inner ear contralateral to the primary tumor primarily received scatter radiation. All RT was planned using an in-house three-dimensional treatment planning system (UMPlan) (8–10). Each patient underwent CT simulation, using a standard 3-mm slice thickness and interval, except for 5 patients who underwent simulation with a 5-mm slice thickness and interval, all with no gap. One radiation oncologist (C.C.P.) contoured both cochleae for each patient (Fig. 1). Dose-volume data for each cochlea were obtained. Because the cochleae are small (average volume, 0.56 cm³; range, 0.15–0.91), the mean cochlear dose was used in our analysis. The median prescription dose was 64.0 Gy (range, 40.0–70.0 Gy). No modification in the plan or prescribed radiation dose was made due to the patient participation in this study. Most patients were treated primarily with surgery, followed by postoperative RT. Four patients, all with nasopharyngeal cancer, were treated primarily with concurrent, cisplatin-based chemoradiotherapy. The patient characteristics are presented in Table 1.

Hearing tests

Audiologic testing was conducted at baseline (before treatment) and at 1, 6, 12, 24, and 36 months after RT completion. Each test battery consisted of otoscopy, acoustic immittance testing (tympanometry and acoustic reflex), pure-tone audiometry, including air and bone conduction testing, speech reception threshold, and

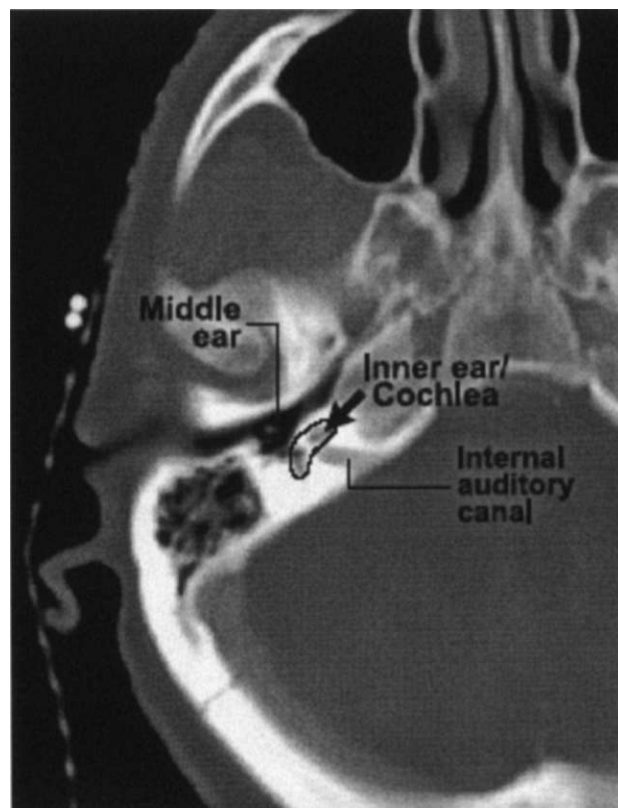


Fig. 1. Computed tomography anatomy of middle and inner ear.

speech recognition determination. A hearing decrement of ≥ 10 dB was considered clinically significant (11).

To avoid contamination of the hearing threshold data by the presence of conductive hearing loss caused by middle ear effusion, bone conduction thresholds were used to establish the changes in hearing for frequencies ≤ 4000 Hz. Bone conduction testing is a routine component of an audiologic assessment and involves the delivery of pure tone stimuli via a bone oscillator placed on the mastoid of the ear to be tested, thus bypassing the conductive mechanism. These measurements, therefore, reflect only sensory hearing loss, when present. Because bone conduction hearing testing is limited to 4000 Hz, measurements >4000 Hz were performed using air conduction testing alone. Sensorineural hearing at high frequencies (8000 Hz) tested by air conduction is unaffected by, and independent of, middle ear effusion.

Audiologic variables

The baseline threshold level (bTL) of an irradiated ear is defined as the hearing threshold level (measured in decibels) obtained at baseline audiologic testing. The difference in the threshold levels (dTL) is defined as the difference between the threshold levels of the irradiated ear and contralateral ear for each patient. The four concurrent chemoradiotherapy patients received significant bilateral inner ear radiation doses, and these patients were analyzed separately.

Statistical analysis

The outcome variable was the dTL between ears for each patient, reflecting the sensory hearing loss associated with an increased radiation dose to the ipsilateral ear. To examine the

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