RADIATION THERAPY FOR HEAD AND NECK NEOPLASMS

INDICATIONS, TECHNIQUES, AND RESULTS

Second Edition

C. C. Wang

SECOND EDITION

RADIATION THERAPY FOR HEAD AND NECK NEOPLASMS: Indications, Techniques, and Results

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RADIATION THERAPY FOR HEAD AND NECK NEOPLASMS: Indications, Techniques, and Results

In loving memory of my parents, Rev. and Mrs. Tsung-tong Wang, who inspired me to be a physician and educator.

PREFACE

The second edition of this text brings to critical revision every chapter, with many needed changes. The applied anatomy and treatment techniques have been expanded to reflect better understanding and management of the disease processes that may lead to improved patient care and eventually to higher locoregional control and minimal radiation complications.

Outdated material has been replaced with current information and new illustrations. The results of once-daily radiation therapy have been updated to the recent past. This text also includes a chapter on the principles and practice of altered fractionation and results of treatment of the major head and neck cancers.

I wish to thank the members of the staff of the Department of Radiation Medicine for their cooperation and advice. Special gratitude is due my secretary, Patricia McNamara, for her untiring efforts in preparing and typing the manuscript. The cooperation of Year Book Medical Publishers, Inc., is also acknowledged.

C. C. Wang, M.D.
1990

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Chapter 1

General Concepts of Radiation Therapy for Cancer of Head and Neck

Cancer of the head and neck constitutes a major anatomic group of tumors with respect to morbidity and mortality: approximately 85,500 new patients, or 8.6% of all newly diagnosed cases annually, and 14,250 deaths or 2.8% of all cancer mortalities in the United States in 1988.[1]

Head and neck cancer is considered one of the most productive fields of management in terms of cure rate. Many of these tumors can be readily seen, palpated, and evaluated, and biopsy is relatively simple. Because there is seldom a second chance to effect a cure, the choice of initial treatment must be correct and made after careful consideration of all clinical features in each individual patient. This clearly requires that surgeons, radiation therapists, and chemotherapists know the strengths and weaknesses of their opposing disciplines and be thoroughly informed of the limitations of their chosen specialty. The welfare of patients with malignant disease rests on the complementary and cooperative efforts of this team. Although tremendous strides in the management of human cancers in general are attributable to chemotherapy, its role in the treatment of head and neck carcinomas is primarily palliative and adjuvant.

Carcinomas originating from the mucous membrane of the upper aerodigestive tract are predominately squamous cell carcinoma of various degrees of differentiation ranging from in situ carcinoma to verrucous carcinoma to poorly differentiated carcinoma, including so-called lymphoepithelioma. The early mucosal lesion may appear as an indurated nodule or as a shallow ulcer with poorly defined margins. These areas are poorly endowed with pain fibers; thus pain is not an early symptom. Most patients present with unilateral sore throat or canker sore in the mouth; unilateral otitis media, frequently of several weeks duration; odynophagia; or hoarseness as the only symptoms of extensive disease. These tumors may be exophytic or infiltrative and may extend rapidly into the underlying muscle and cause fixation with resultant difficulty in speech and swallowing, or hoarseness, and in the advanced stage impairment of hearing, trismus of the jaw, cranial nerve paralysis, and difficulty in breathing. Metastatic disease usually occurs in the homolateral cervical lymph nodes,

although bilateral or contralateral metastases commonly develop from midline lesions. Distant metastases below the clavicle are not common, but do occur late in the disease or with extensive cervical metastasis.

Carcinomas of the head and neck commonly are diseases of middle and old age, occurring especially in patients with long-standing habits of cigarette smoking, alcoholism, and poor oral hygiene. Men are more often affected, although the incidence of women is rapidly increasing due to changing life-styles of American women. Tumors of the salivary gland, thyroid gland, lymph nodes, bone, and soft tissue also occur in the head and neck regions. These tumors are less common, and their management often calls for combined efforts of various medical specialists for optimum local control and survival.

For an adequate evaluation of the extent of the lesion, careful inspection and palpation of the primary site and neck areas are mandatory whenever possible. Indirect laryngoscopy is extremely informative in evaluating the extent of the lesion and the mobility of the involved parts. Direct laryngoscopy and multiple biopsies to define mucosal and submucosal extension of tumor or to rule out a second primary cancer should be carried out before defining the therapeutic program. Appropriate x-ray examinations (e.g., soft-tissue films and xerograms of the lateral pharynx or larynx, nasopharynx, and base of the tongue) are extremely useful in identifying various anatomic structures (Fig 1–1) and are indicated to assess the extent of the lesion. Computed tomography (CT) scans and polytomes have been useful in obtaining information, such as bone and muscle invasion, which otherwise may not be shown with conventional radiography. As part of the medical workup, a general physical examination, chest radiographs, and a basic liver profile are necessary. Since the hemoglobin level may affect local control of head and neck tumors,[2,3] anemia should be corrected.

Cancers arising from various anatomic sites of the head and neck possess different tumor characteristics. Each has its own natural history, biological behavior, and mode of tumor growth and spread. The therapeutic management and results may differ greatly depending on these factors.

These cancers are described and discussed according to anatomic region: (1) skin, (2) oral cavity, (3) oropharynx, (4) hypopharynx, (5) larynx, (6) nasopharynx, (7) nasal cavity and paranasal sinuses, (8) salivary gland, (9) temporal bone, (10) eye and orbit, and (11) miscellaneous sites, among others. Some clearly defined anatomic regions are shown in Figure 1–2.

The use of radiation therapy in the management of squamous cell carcinoma of the head and neck is based on the following principles[4]:

1. Squamous cell carcinomas are usually radioresponsive, and in early stages highly radiocurable.
2. The more differentiated the tumor the less rapid the radiation response and resolution and the higher the radiation dose required.
3. Exophytic and well-oxygenated tumors are more radioresponsive than deeply ulcerative and infiltrative hypoxic tumors.
4. Squamous cell carcinomas, when limited to the mucosa, are highly radiocurable.

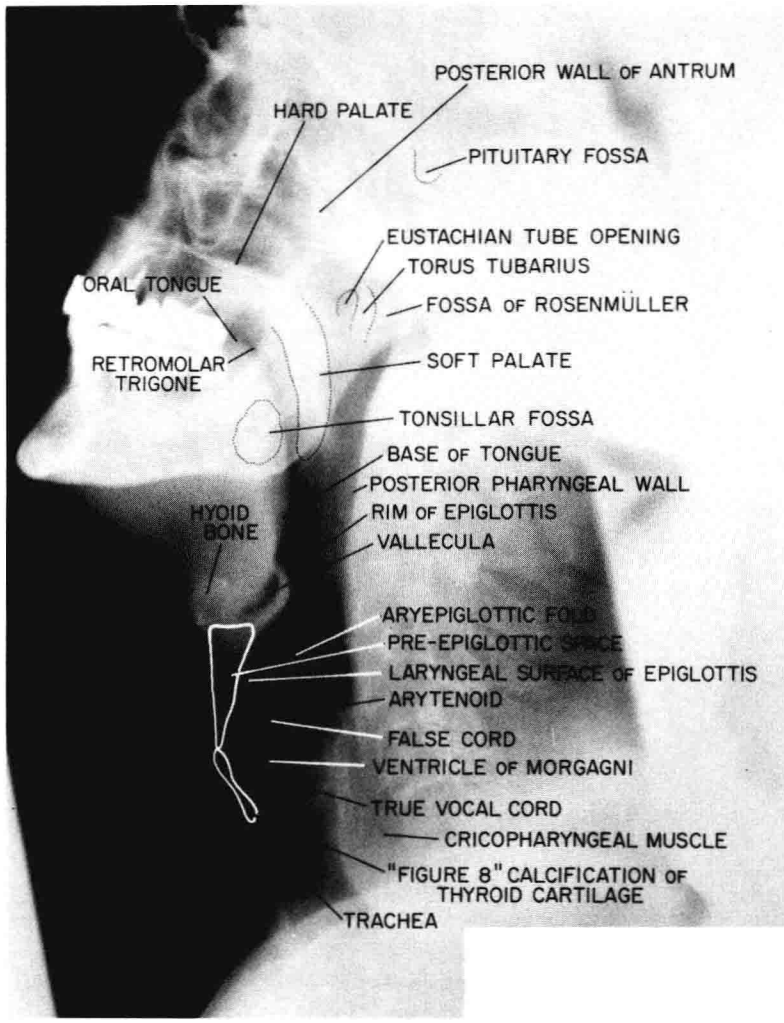

FIG 1–1.
Radiograph of lateral neck showing various anatomic structures and their locations, useful to radiation therapist for placement of treatment portals.

5. Bone and muscle involvement by carcinomas adversely alters radioresponsiveness and subsequently decreases radiocurability.
6. The early small metastases can be controlled with radiation therapy alone. Advanced cervical metastatic lymph nodes are better treated with combined surgery and radiation therapy.

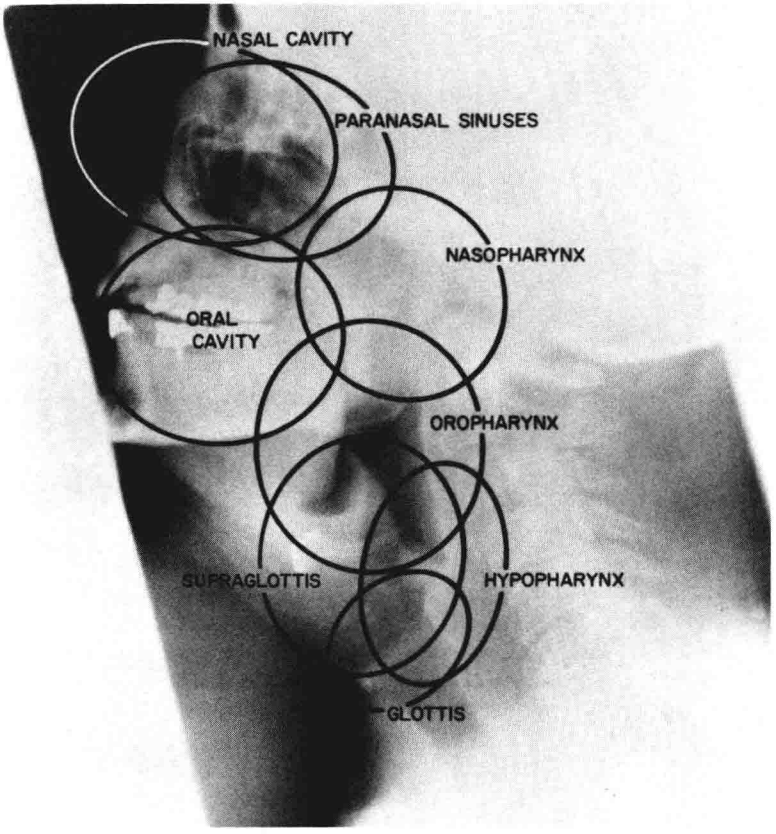

FIG 1–2.
Radiograph of lateral neck showing various anatomic grouping of head and neck carcinomas.

Therapies available for the management of cancers of the head and neck include surgical resection, laser excision, radiation therapy, and chemotherapy. Immunotherapy and cryotherapy have been tried, but results were disappointing and these treatments are now used primarily for palliation. The choice of treatment method depends on factors such as (1) cell type and degree of differentiation, (2) site and extent of the primary lesions, (3) metastatic nodal status, (4) gross characteristics of the tumor (e.g., exophytic, superficial vs. endophytic, infiltrative), (5) presence and extent of bone and muscle involvement, (6) likelihood of complete surgical resection, (7) possibility of preservation of speech or swallowing mechanisms, (8) physical condition, social status, and occupation of the patient, (9) experience and skill of both the surgeon and the radiotherapist; and (10) cooperation and wishes of the patient.

The radiation dosage is determined by (1) tumor site, (2) size of the lesion, (3)

irradiated volume, (4) number of fractions of treatment, (5) total elapsed time of the treatment course, (6) various techniques of delivery of radiation, (7) tolerance level of the patient, and (8) response of the tumor. In general, a dose of 50 to 55 Gy over 5 to 6 weeks is considered adequate for sterilization of microscopic or occult diseases,[5] and 65 to 70 Gy over 7 weeks for control of gross squamous cell carcinoma. The initial dose is usually 50 Gy wide-field irradiation, including the primary lesion and the first echelon regional lymph node drainage areas. A further dose to the primary site is given via reduced portal toward completion. However, although dose-response curves demonstrate the importance of adequate dosage for tumor control, these same curves cannot show convincingly that higher doses (> 75 Gy) produce substantial improvement in cure rates. Such high doses do carry a substantially higher risk for severe complications such as painful fibrosis of the subcutaneous tissues of the neck, osteoradionecrosis of the mandible, orocutaneous fistulas, and severe problems with wound healing if salvage surgery is necessary after radiotherapy failure.

INTENT OF RADIATION THERAPY

The intent of radiation therapy can be divided into three categories: cure, palliation, and as combination therapy with surgery.

Radical radiation therapy with intent to cure is not without morbidity and should be performed with care and justification. In curative radiation therapy, the total tumor dose is high and the treatment course is usually prolonged and physically taxing. Painful radiation reactions in the oropharyngeal mucosa may be severe, resulting in dysphagia and impairment of nutrition. In fact, the discomfort suffered by the patient from curative radiation therapy is no less than, and is sometimes more than, that from radical surgery. It is generally observed that elderly or alcoholic patients tolerate radical surgical procedures (e.g., partial glossectomy or total laryngectomy for advanced disease) far better than they tolerate a radical course of radiation therapy extending for 6 to 7 weeks or with interstitial implant.

Massive primary tumor or extensive cervical lymph node metastases are rarely curable, and the intent of radiation therapy is symptomatic relief. Pain, bleeding, ulceration, and oropharyngeal obstruction may be alleviated with radiation therapy, but for effective palliation of most squamous cell carcinomas of the head and neck the dose of radiation is necessarily high—45 to 50 Gy or more over 5 to 6 weeks—if lasting benefits are to be obtained. This palliative radiation dose may produce symptomatic reactions. Therefore, for patients with terminal but relatively asymptomtic lesions the best treatment is human kindness, morphine, and good nursing care.

Radiation therapy is frequently used as an adjuvant procedure either before or after surgery for advanced cancer of the head and neck. The rationale, aims, and treatment concepts are discussed in Chapter 3.

CARE OF PATIENTS

Before Radiation Therapy

After radiation therapy is elected, treatment should be carefully planned and executed. In the modern practice of radiation therapy, treatment planning is based on the nature, size, and location of the tumor; the volume of tissue to be encompassed; the normal organs to be spared; and intent of treatment (curative or palliative), and is carried out with the aid of a dedicated simulator and computer prior to actual treatment. The treatment planning procedure for radiation therapy must be as thorough as the preparation of a patient for radical surgery. All workups should be complete, and the extent of the primary lesion and its lymph node status should be known and, if possible, staged according to the recommended staging system (e.g., TNM). The patients must be apprised of the treatment goal, side effects, potential radiation complications, and if possible, the percentage or probability of benefits from the proposed therapies. Other options, including surgery and chemotherapy, should also be discussed. When the patient agrees to the proposed radiation therapy, informed consent must be obtained prior to initiation of treatment.

In patients with lymphoma arising primarily from the head and neck regions (e.g., Waldeyer's ring, paranasal sinuses), pretreatment evaluation should include a complete lymphoma workup, including bone marrow biopsy and a CT scan of the abdomen or bipedal lymphogram to exclude the presence of enlarged retroperitoneal lymph nodes. Extent of tumor is staged according to the Ann Arbor Classification.[6]

During Radiation Therapy

While receiving radiation therapy, mucosal reaction and tumor regression should be carefully monitored. With lesions in the pharynx and larynx, indirect laryngoscopy should be done at least once a week (more often if complications are pending) to assess tumor response and to detect development of edema of the laryngeal structures. Our experience has shown that examination of the oral cavity, oropharynx, and larynx after a dose of approximately 20 Gy over 2 weeks with 1.8 to 2 Gy per fraction may clearly delineate the true extent of the tumor by the development of tumoritis. This is a golden opportunity to evaluate the superficial spread of the tumor and its margins (Fig 1–3). Such an earlier differential reaction is probably due to the difference in response to radiation of normal and diseased tissues. Once the radiation therapy dose reaches 40 Gy, the confluent mucositis and tumoritis make such distinction impossible.

Mucosal reactions in the form of mucositis represent acute effects of radiation therapy and equate directly to the extent of tumor response. For successful radiation therapy of squamous cell carcinoma arising from the mucous membrane of the aerodigestive tract, experience shows that it is necessary that radiation mucositis be fully developed, and without it the probability of local control is lessened.[7]

Symptomatic mucosal reactions in the form of pain, sore throat, or dysphagia are often associated with treatment to the nasopharynx, oropharynx, or oral cavity. Symptoms may vary in degree and can be minimized with analgesics and topical anesthetics, such as 0.5% to 1.0% dyclonine hydrochloride (Dyclone) mouthwash, or

by careful adjustment of daily doses of radiation therapy or even a small break in treatment. Silver or gold fillings or dental appliances in the mouth emit secondary electrons when they are in the path of the external radiation beam. These contaminated electrons may produce pinpoint mucosal reactions of the adjacent tongue or buccal mucosa, resulting in localized pain (Fig 1–4) commonly described by patients as "thumbtack" pain. Such localized painful reactions can be completely eliminated by "capping" the teeth fillings with a sheet of 0.5 mm thick tinfoil, which absorbs the symptom-producing electrons from the metals before they reach the adjacent tongue or buccal mucosa during radiation exposure. Most of the exophytic component of

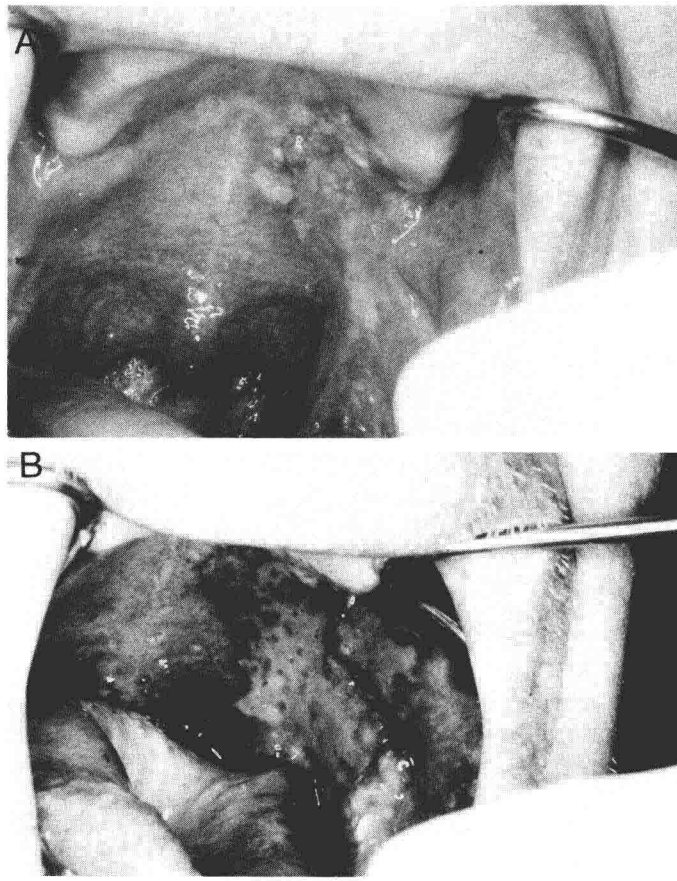

FIG 1–3.
A, photo of a seemingly small, limited carcinoma of the left retromolar trigone and palate before radiation therapy. **B,** photo showing a much more extensive lesion demonstrated by the development of tumoritis after 21 Gy over 2 weeks.

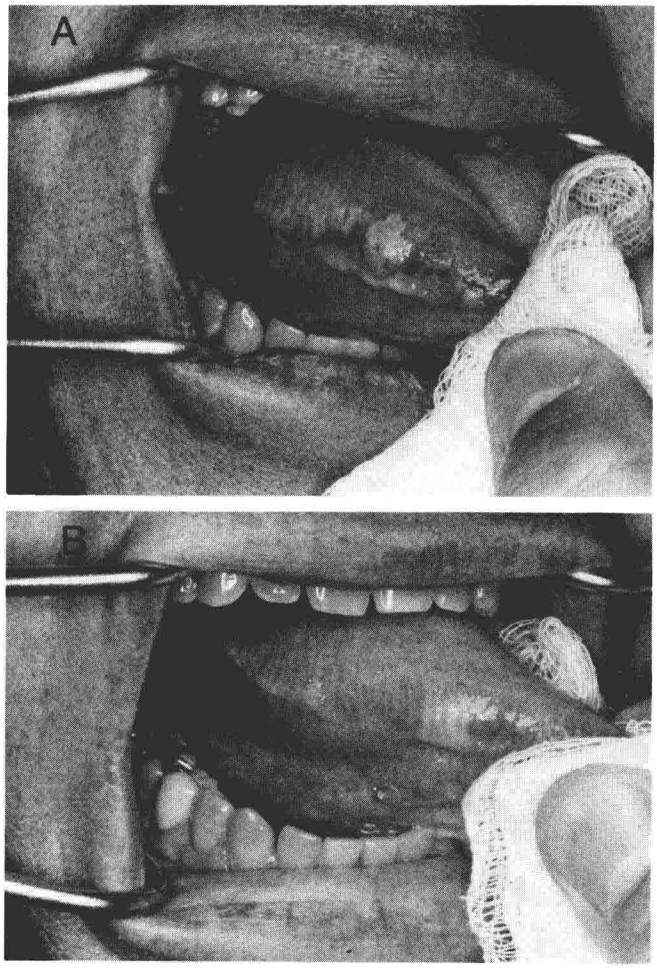

FIG 1–4.
A, photo of lateral border of tongue showing localized pinpoint mucositis from secondary electrons originating from the silver filling in the teeth during irradiation. **B**, photo showing subsidence of localized mucositis, after capping of the teeth with tinfoil, despite continuation of radiation therapy.

the tumor should have regressed by the end of the treatment course. Edema of the irradiated part is minimal.

After Radiation Therapy

Patients should be carefully followed up regularly by both the radiation therapist and the surgeon for evidence of residual disease, recurrence, or complications. The

irradiated part should be smooth and pliable, without granularities, tumefaction, or ulceration. If results of examination are relatively normal, biopsy of the previous tumor site is not advised, because the yield is low and complications frequent. On the other hand, if residual tumor is suspected, a biopsy specimen should be obtained for tissue confirmation, to be followed by appropriate treatment. Most patients with head and neck carcinoma must be followed up regularly for the rest of their life because of the propensity for multiple primary lesions arising from the upper airway and food passages.

MANAGEMENT OF HEAD AND NECK PRIMARY LESION WITH POSITIVE OR OCCULT LYMPH NODE DISEASE

The management of metastasis to the nodes in the neck from a primary lesion arising in the head and neck region depends on the size of the tumor, the number of nodes, bilaterality of disease (N stage), location of the primary lesion, and cell type. Radiation therapy is highly curative for small, metastatic lymph nodes with primary tumors arising from Waldeyer's ring (i.e., nasopharynx, faucial tonsil, and base of the tongue). Therefore the patient with clinically positive lymph nodes should receive radiation therapy to both the primary lesion and the entire ipsilateral neck if lesions are eccentrically situated, and to both sides of the neck if the lesions are in the midline. If the metastatic lymph nodes become nonpalpable after radiation therapy, careful follow-up is justified. On the other hand, if the metastatic lymph nodes persist or reappear, therapeutic radical or functional neck dissection is carried out without jeopardizing ultimate control of the disease. For metastatic lymph nodes with an advanced primary lesion arising from the oral cavity, hypopharynx, and larynx, combined radiation therapy and surgery is the treatment of choice (i.e., radical neck dissection either preceded or followed by radiation therapy). A dose of 45 Gy over 4 weeks as a preoperative procedure and 55 Gy as a postoperative procedure to both sides of the neck should be planned. Such adjuvant radiation therapy not only reduces the incidence of recurrent disease in the dissected neck, but is highly effective in preventing the development of nodal metastases to the opposite side of the neck; thus the necessity for bilateral radical neck dissection is eliminated. For inoperable metastatic lymph nodes in the neck, high-dose radiation therapy is necessary for local control. A dose of 75 to 80 Gy is needed for N2a or N3a disease, but may result in painful fibrosis of the neck.

For lesions having a high risk of occult metastasis (i.e., oral tongue, Waldeyer's ring, or large T3 and T4 primary lesions, each with a 30% to 50% chance of occult metastasis to the lymph nodes), elective irradiation of the neck is indicated. Some studies[5] indicate that 50 Gy over 5 weeks is effective in controlling 90% of occult metastatic disease. These results would argue against the use of "prophylactic" surgical treatment of the neck (i.e., radical or functional neck dissection) after the primary lesion is controlled.