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IMRT For Head And Neck Cancer

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Introduction

Historical Overview

Radiation therapy is a principal modality in the treatment of head and neck cancer. Its capabilities have steadily progressed with the increase in clinical knowledge and technological development. From its humble beginnings with treatment on orthovoltage units, we learned that tumors could be eradicated but that major acute and late side effects were often part of the results. Even with the availability of deeply penetrating teletherapy units (Cobalt-60) and linear accelerators (linacs), two-dimensional (2-D) treatment planning, and the cone down approach, the therapeutic ratio was still a major concern. The incorporation of a brachytherapy boost often improved the dose distribution between the tumor and the surrounding normal tissue. However, this

approach is not suitable for many head and neck tumors due to anatomical, medical, or technological considerations.

Over the past two decades, there have been several major advances in the treatment of cancers of the head and neck. Effective chemotherapeutic agents have been developed for squamous cell carcinoma of the head and neck and are increasingly used sequentially or concurrently with radiation to treat unresectable cases or to promote larynx preservation (Fu 1997; Lefebvre et al. 1996; Vokes et al. 1993; Pfister et al. 1992; Bourhis and Pignon 1999; Brizel et al. 1998; Pignon et al. 2000). In response to the findings that local control was dependent on the overall duration of treatment, accelerated fractionation schemes have been devised to decrease the repopulation by tumor clonogens (Withers, Taylor, and Maciejewski 1988). Preliminary results from a recent randomized study (Fu et al. 2000) showed improved two-year local-regional control and disease-free survival using accelerated fractionation with a delayed concomitant boost compared to standard fractionation. Advances in computer and linac technology have also significantly impacted treatment of head and neck cancers by improving our ability to maximize tumor dose while minimizing the dose to adjacent normal critical structures. Image-based treatment planning and multileaf collimators have both been widely implemented, facilitating both the planning and delivery of three-dimensional conformal radiation therapy (3DCRT). More recently, the development of inverse planning systems and methods for delivering non-uniform radiation intensities have ushered in the era of intensity-modulated radiation therapy (IMRT), representing the state of the art in the treatment of many head and neck cancers (Blanco and Chao 2002).

Rationale for the Use of IMRT in Head and Neck Tumors

Based on studies comparing IMRT and other treatment approaches, IMRT appears to be clinically justifiable for cancers in the nasopharynx, sinonasal region, parotid gland, tonsil, buccal mucosa, gingiva, and thyroid as well as in tumor tracking along the cranial nerves. IMRT may also be useful in the re-treatment of previously irradiated head and neck cancers, due to its ability to spare adjacent normal tissues with acceptable target dose uniformity. Although technically superior, IMRT is costly, and its cost-effectiveness requires due consideration as the technology evolves. Only as clinical data establishing the therapeutic ratio, local-regional control, side effects, and survival with IMRT become available, will the efficacy of IMRT be established.

To date, a small number of investigators have reported on the use of IMRT for head and neck cancer. Although earlier efforts were primarily treatment planning studies, clinical studies, primarily retrospective reviews with limited patient populations and heterogenous diagnoses, have recently been reported. In one treatment planning study, Boyer et al. (1997) examined the use of IMRT in three patients with nasopharyngeal, vocal cord, and ethmoid sinus tumors. They found that IMRT was capable of producing dose distributions with invaginations, bifurcations, and internal voids, thus exhibiting significant potential for normal organ sparing.

In another treatment planning study, van Dieren et al. (2000) evaluated whether IMRT could spare parotid and submandibular glands without compromising target coverage. Thirty patients (15 with T2 tumors of the tonsillar fossa with extension into the soft palate, 15 with T3 tumors of the supraglottic larynx) were treated with lateral opposed portals. For each patient, an IMRT plan was developed retrospectively that included a parotid sparing approach. Compared to the distribution from lateral opposed portals, IMRT improved the target dose distribution. For the supraglottic larynx carcinomas, the volume receiving a biologically equivalent dose greater than 40 Gy decreased by 23% in the parotid and 7% in the submandibular gland. With tonsillar fossa cancers, the decrease in volume was 31% in the parotid and 7% in the submandibular gland.

Verellan et al. (1997) reviewed their implementation of IMRT in the treatment of nine patients with head and neck cancer using the MIMiC device (NOMOS Corporation, Sewickley, PA). Relative and absolute dosimetric measurements in anthropomorphic phantoms using a variety of detectors

demonstrated excellent agreement between the measured and calculated dose distribution. For immobilization, a noninvasive system capable of achieving a setup uncertainty standard deviation of 0.3 cm (translations) and 2.0 degrees (rotations) was used in conjunction with a verification protocol capable of detecting errors as small as 0.1 cm and 1 degree. To achieve the higher degree of precision in target localization that may be necessary for IMRT treatment, the authors stated that daily on-line verification and implanted fiducial markers may be necessary.

Eisbruch et al. (1998) reported on their use of IMRT in 15 patients with stage III/IV head and neck cancer requiring bilateral neck irradiation. The minimum primary planning target volume (PTV) dose in the IMRT plans was higher than that in the standard plans (95.2% and 91% of the prescribed dose, respectively); coverage of the ipsilateral jugular nodes was also improved, but coverage of the contralateral jugular or posterior neck nodes was similar to conventional treatment. With respect to the normal critical structures, both the magnitude of dose and the volume in the high-dose regions decreased with IMRT. The mean dose to all major salivary glands, particularly the contralateral parotid gland, was much lower. It was noted that despite the normal tissue sparing, the tumor target coverage was not compromised.

Preliminary results of a retrospective study on the first 28 head and neck cancer patients treated with IMRT at Baylor College of Medicine was reported by Kuppersmith et al. (1999). The histopathologies included squamous cell carcinoma, adenoid cystic carcinoma, paraganglioma, and angiofibroma. Patients received doses from 14 to 71 Gy in daily fractions of 1.55 to 4 Gy. With respect to the normal tissue doses, the parotid gland received less than 30 Gy for midline tumors. Their incidence of acute toxicity was much lower than with conventional radiotherapy. They noted that with only a portion of an organ irradiated, the tolerance dose was likely to increase. The article highlighted the following clinical capabilities of IMRT: (1) decreased normal tissue doses during re-irradiation of previously treated patients; (2) cranial nerves could be traced to the base of skull while minimizing the dose to the parotid glands and other surrounding structures; varying doses could be administered to the primary site as opposed to the cranial nerves; (3) multiple targets could be treated simultaneously with an accelerated course and once-a-day fractionation while minimizing doses to adjacent normal structures. This technique was referred to as Simultaneous Modulated Accelerated Radiation Therapy (SMART).

The SMART technique was used between January 1996 and December 1997 on 28 patients to treat various primary head and neck sites including oropharynx, nasopharynx, larynx, oral cavity, and sphenoid sinus (Butler et al. 1999). All patients were immobilized with an invasive calvarial screw technique to yield a patient position reproducibility of better than 2 mm. The dose to the primary target was 60 Gy in 2.4 Gy fractions, while sites at risk for microscopic disease received 50 Gy in 2 Gy fractions. All targets were treated once a day, 5 days per week and were completed in 5 weeks. Sixteen of 20 patients (80%) completed the treatment in 40 days. Sixteen patients (80%) had RTOG (Radiation Therapy Oncology Group) toxicity grade III mucositis and ten patients (50%) had grade III pharyngitis. Three patients (15%) had greater than 10% weight loss. Nine patients (45%) experienced moderate acute xerostomia that significantly improved within 6 months. Nineteen patients (95%) achieved a complete response and one patient had a partial response. The mean doses to the primary and secondary targets were 64.4 Gy and 54.4 Gy, respectively. On average, 8.9% of the primary target and 11.6% of the secondary target received a dose less than that prescribed. Adjacent normal critical structure doses were as follows: 30 Gy, mandible; 17 Gy, spinal cord; 23 Gy, ipsilateral parotid; 21 Gy, contralateral parotid. The conclusion of the study was that this IMRT technique yielded encouraging initial tumor responses with acceptable morbidity.

Chao et al. (2000) implemented tomotherapy-based IMRT in patients with squamous carcinoma of the head and neck. Seven nasopharyngeal carcinoma, seven oral pharyngeal carcinoma, one supraglottic larynx carcinoma, and two patients with metastatic disease to the upper and mid cervical nodes from an unknown primary were treated with the MIMiC device. Eight patients (six

nasopharyngeal carcinomas, two tonsillar carcinomas) with primary disease and one patient with recurrent nasopharyngeal carcinoma were treated with concurrent cisplatin chemotherapy. Six patients were postoperative and received radiation alone. Using IMRT, different doses were delivered to different targets simultaneously in each fraction. Acute side effects were similar to those seen with traditional radiation therapy. With IMRT, an average of 27%±8% of the parotid gland volumes received more than 30 Gy and an average of 3.3%±0.6% of the target volume received less than 95% of the prescribed dose. The authors concluded that the use of IMRT led to a high degree of target conformity and that the initial results on tumor control were promising with no severe adverse acute side effects.

Sultanem et al. (2000) reviewed the experience with IMRT in the treatment of nasopharyngeal carcinoma at the University of California, San Francisco. Thirty-five patients were treated: 4 (12%) with stage I, 6 (17%) with stage II, 11 (32%) with stage III, and 14 (40%) with stage IV disease. The target for IMRT treatment included the nasopharynx and retropharyngeal nodes but avoided the other regional lymphatics that were treated with conventional techniques. Sixty-five to 70 Gy was prescribed to the gross target volume (GTV) and positive neck nodes, 60 Gy to the clinical target volume (CTV) and 50 to 60 Gy to the clinically negative neck nodes. Eleven patients (32%) underwent a fractionated high dose rate intracavitary brachytherapy boost to the primary tumor one to two weeks following completion of external radiation therapy. Thirty-two patients (91%) were given concomitant cisplatin chemotherapy and adjuvant post-treatment cisplatin and 5FU (5-Fluorouracil) chemotherapy. With a median followup of 21.8 months, the locoregional progression free rate was 100%. At 4 years, overall survival was 94% and the distant metastasis free rate was 57%. The acute toxicity percentages were as follows: 16 patients (46%) with grade II, 18 patients (51%) with grade III, 1 patient (3%) with grade IV. Fifteen patients (43%) had grade I, 13 patients (37%) had grade II, and 5 patients (14%) had grade III late toxicity. The xerostomia evaluation at 24 months post-treatment showed 50% of the evaluated patients had grade 0, 50% had grade I, and none had grade II xerostomia. The GTV received a mean dose of 75.8 Gy while the CTV received 71.2 Gy. All normal tissue received acceptable doses including the parotid glands, which received an average dose of 43.2 Gy to 50% of the volume. The authors concluded that IMRT improved the target coverage, increased GTV dose, and improved sparing of the adjacent normal critical structures. Locoregional control for patients receiving concurrent chemotherapy was excellent.

IMRT Treatment Of Primary Head And Neck Cancer At MSKCC

The above discussion indicates that there are many situations where IMRT may improve the dose distributions for primary head and neck cancers. However, whether this improvement will prove clinically significant can only be answered on a site-by-site basis as outcome data become available. The potential improvement afforded by IMRT must also be considered in the context of its complexity and cost relative to 3DCRT or 2-D planning and treatment.

IMRT has been used routinely in the treatment of head and neck cancers at Memorial Sloan-Kettering Cancer Center (MSKCC) since May 1998. Thus far, our primary emphasis has been on the development of techniques for primary nasopharynx cancer, thyroid carcinomas, and recurrent head and neck tumors. A brief description of the technical approaches is given below, followed by a description of the planning process for one site, primary nasopharynx cancer.

Primary Nasopharyngeal Carcinoma

The MSKCC approach to the treatment of nasopharyngeal cancers with 3DCRT was described by Leibel et al. (1991). In this study, 3-D and 2-D treatment plans were compared for 10 previously untreated patients who received 3DCRT for the boost phase of treatment, and 5 others with locally recurrent disease who received 3DCRT for the entire course. 3DCRT improved the dose distribution,

with a ~13% increase in tumor dose and decreased doses to the adjacent normal structures. Unfortunately, the use of a 3DCRT boost did not improve local control relative to traditional treatment (Wolden et al. 2001). It was hypothesized that this was due to the use of the 3-D plan only during the boost phase of treatment since its dose distribution was not appropriate for the entire treatment course. IMRT, on the other hand, can be used to deliver the entire treatment as shown by Hunt et al. (2001). In this study, IMRT, 3DCRT, and 2-D plans were compared for six patients, two each with negative, unilateral, and bilateral neck disease. All six patients were treated using IMRT and retrospectively planned with 3DCRT and 2-D techniques, designed to deliver 70 Gy to sites of gross disease (PTV_{gr}) and 54 Gy to the electively irradiated nodal regions (PTV_{el}). A summary of the beam arrangements and techniques employed for the three plans is given in table 10–1.

The dose distributions produced by the three techniques for a patient with N2 disease are compared in figure 10–1. The 3-D and IMRT dose distributions are similar in shape but the dose conformality, normal tissue doses and target dose uniformity are superior with IMRT. PTV coverage with the traditional parallel opposed 6 MV plan was inadequate particularly in the retropharyngeal area, base of skull, and medial aspects of bulky neck nodes.

Doses to all normal tissues improved using IMRT (table 10–2). The average maximum spinal cord dose was approximately 35, 45, and 50 Gy with the IMRT, 3-D conformal, and traditional plans, respectively. For both the mandible and temporal lobes, the volume irradiated to the higher dose levels was significantly lower with IMRT. Since no attempt was made to spare the parotid glands in this study, the dose to the parotid glands improved with IMRT but not to a level expected to preserve meaningful salivary function. The mean PTV dose increased from 68 Gy for the traditional plan to 76 Gy for IMRT, a 12% increase and *de facto* dose escalation even though the prescription dose was the same.

Thyroid Cancer

Like nasopharynx tumors, thyroid cancer is ideally suited for treatment with IMRT because of the concave shape of the target surrounding the normal critical structures, including the spinal cord and brachial plexus. Patients with unresectable thyroid cancer or those at high risk for postoperative local-regional recurrence are treated with IMRT at MSKCC. Treatment planning is image-based using fused computed tomography (CT) and FDG-PET (fluorodeoxyglucose

Table 10–1. Summary of IMRT, 3-D Conformal, and Traditional Treatment Plans

Plan Name	Field Arrangement	PTVs Included	Delivered Dose (Gy)	Cumulative Dose (Gy)
Traditional	Opposed Laterals 6 MVX	PTV_{el} PTV_{gr}	45	45
	Opposed Laterals with Cord Block Bilateral 9 MeV E^- Strips	PTV_{el} PTV_{gr}	9	54
	Opposed Lateral Cone Down, Involved Neck 9 MeV E^- Strips	PTV_{gr}	16	70
3-D Conformal	Opposed Lateral 6 MVX	PTV_{el} PTV_{gr}	36	36
	Seven Field Conformal Plan	PTV_{el} PTV_{gr}	18	54
	Seven Field Conformal Plan	PTV_{gr}	16	70
IMRT	Seven Field IMRT Plan	PTV_{el} PTV_{gr}	54	54
	Seven Field IMRT Plan	PTV_{gr}	16	70

PTV_{el} = Nasopharynx and electively irradiated nodal regions.
PTV_{gr} = Sites of gross disease in the nasopharynx and nodal regions.

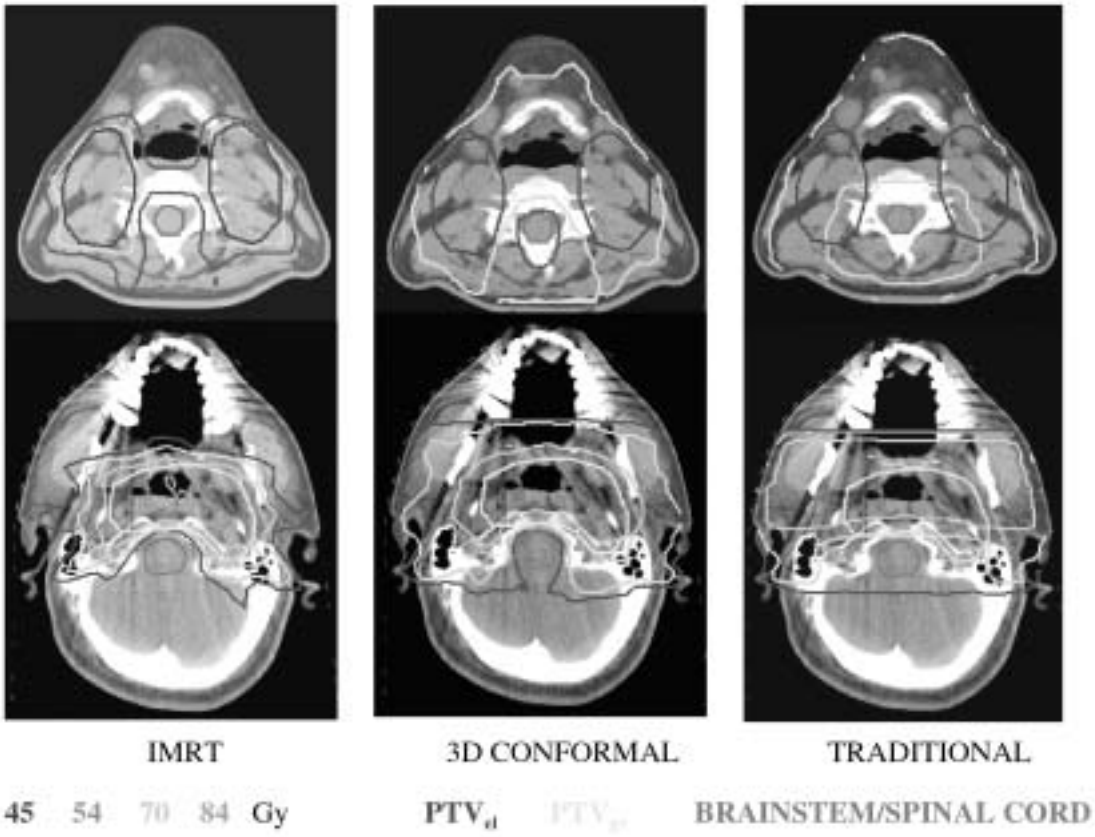


FIGURE 10–1. Comparison of IMRT, 3-D conformal and traditional parallel-opposed field plans for the treatment of primary nasopharynx tumors. See COLOR PLATE 21.

radiolabeled with ^{18}F-positron emission tomography) images to localize metabolically active disease. The target volume includes the gross thyroid mass or thyroid bed, gross adenopathy, and regional lymph nodes (retropharyngeal, cervical, supraclavicular, and superior mediastinal nodes).

For papillary and follicular cancers, 50 to 54 Gy are administered to the elective nodal areas and 63 to 70 Gy to the gross disease. Anaplastic thyroid cancers are generally unresectable and

Table 10–2. Dose Volume Statistics Comparing IMRT, 3-D Conformal And Traditional Treatment Plans

Structure	Statistic	IMRT	3-D Conf.	Traditional
	Max. Dose (D_{05})	81.8 Gy (3.3)	80.2 Gy (1.0)	74.2 Gy (2.5)
PTV_{gr}	Min. Dose (D_{95})	69.4 Gy (6.2)	65.7 Gy (5.0)	54.6 Gy (1.7)
	Mean Dose	77.3 Gy (2.4)	74.6 Gy (2.2)	67.9 Gy (1.3)
Spinal Cord	Max. Dose (D_{05})	34.5 Gy (5.5)	44.2 Gy (1.7)	49.1 Gy (0.9)
Brain stem	Max. Dose (D_{05})	33.1 Gy (5.0)	43.3 Gy (2.7)	56.2 Gy (7.0)
Mandible	Max. Dose (D_{05})	69.3 Gy (7.4)	73.9 Gy (5.3)	74.6 Gy (0.9)
	V_{66Gy} (%)	9.7 % (5.9)	18.6 % (11.7)	26.8 % (13.9)
Temporal Lobes	Max. Dose (D_{05})	58.7 Gy (12.5)	59.4 Gy (11.1)	67.0 Gy (3.5)
	V_{60Gy} (%)	6.3% (7.1)	9.2% (13.1)	17.3% (8.8)
Parotid Gland	Mean Dose	60.5 Gy (8.9)	67.1 Gy (7.0)	67.0 Gy (4.7)
	V_{50Gy} (%)	78.4% (21.2)	97.5% (2.9)	99.9% (0.1)

are administered low dose Adriamycin (10 mg/m^2) once weekly, 1.5 hours prior to the first radiotherapy fraction of the week. The radiotherapy is administered in 1.6 Gy fractions twice a day separated by 6 hours on 3 consecutive days of the week to a total dose of 57.6 Gy.

Happersett et al. (2000) compared IMRT and 3-D treatment plans for five thyroid cancer patients and determined that IMRT improved PTV dose uniformity and normal tissue doses particularly for the lung and spinal cord. As shown in figure 10–2, the IMRT technique consisted of six fields directed anteriorly, posteriorly, and obliquely. On average, the PTV dose uniformity improved by 10% and the volume of the PTV receiving at least 63 Gy increased from 37% with 3DCRT to 96% with IMRT.

Clinical Approach To IMRT Treatment For Head And Neck Cancer Patients

Over 250 patients have been treated to date, roughly half of these with primary nasopharynx cancers and the other half with thyroid carcinomas or recurrent tumors. The IMRT planning and treatment process for a typical patient with primary nasopharynx cancer is discussed below.

Consultation And Evaluation

A head and neck cancer patient is initially seen in consultation by the surgeon and radiation oncologist, and often by the medical oncologist. Consultation and evaluation for patients who will undergo treatment using IMRT is similar to that for other head and neck patients and should include the following:

1. History and physical examination of the head and neck region including indirect laryngoscopy and fiberoptic nasopharyngolaryngoscopy.
2. An illustration of the physical findings demonstrating the primary tumor extent and adenopathy.
3. Review of existing imaging studies and further workup as necessary.
4. Pretreatment dental consultation for the extraction of unsalvageable teeth in poor condition, the construction of mouth guards for patients with moderate to extensive tooth fillings, and the initiation of prophylactic fluoride therapy.
5. Pretreatment ophthalmology and audiology consultations for patients in whom the radiation may affect the orbital structures or ear.
6. Baseline thyroid function tests (T3, T4, TSH).

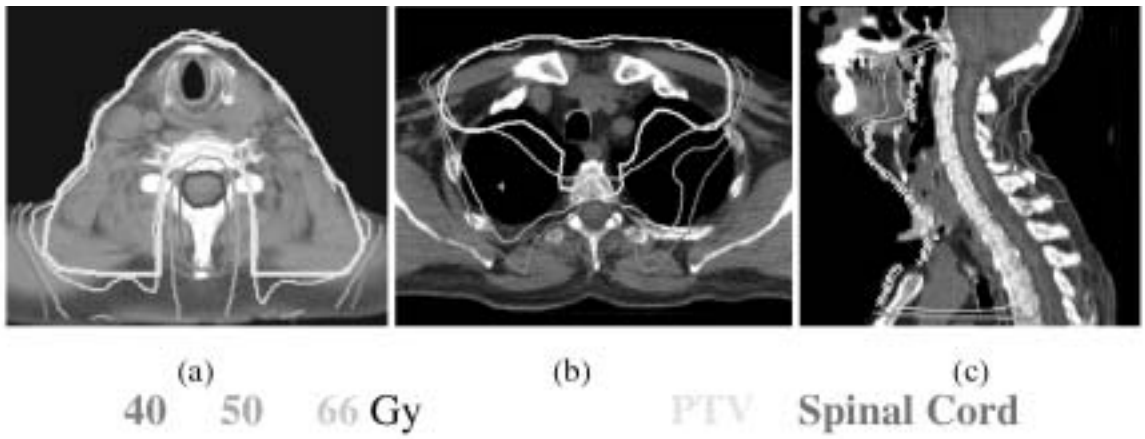


FIGURE 10–2. Axial and sagittal IMRT dose distributions for thyroid carcinoma designed using a six-field plan. See COLOR PLATE 22.

Simulation

Patients treated with IMRT must undergo CT-guided simulation, i.e., either conventional simulation followed by a CT in the treatment position or CT simulation. At MSKCC, all patients treated with IMRT undergo CT simulation. The patient is immobilized in the supine position, typically with the neck hyper-extended using a head rest and custom thermoplastic mold. When appropriate, a bite block is used to separate the mandible and tongue from the upper oral cavity, thereby facilitating a decrease in the irradiation of these structures and a decrease in side effects. A shoulder pull board is employed to bring the shoulders toward the feet, minimizing the amount of shoulder within the lateral or oblique fields. Palpable masses and incisional scars are outlined with radio-opaque material for later radiographic visualization.

For the CT study, intravenous contrast is used as needed to differentiate vasculature from masses or lymphadenopathy. CT images are acquired at 3 mm spacing from the vertex to a level approximately 5 cm inferior to the treatment volume. Accurate calculation of dose volume histograms (DVHs) and biological indices (e.g., normal tissue complication probability) mandate the inclusion of the entire extent of the relevant structures within the image set. The isocenter for the IMRT fields is positioned approximately in the center of the treatment volume and, if the supraclavicular nodes will be treated with separate fields, a second isocenter is placed midline at the inferior border of the IMRT fields.

Image Registration And Structure Delineation

In selected cases, other imaging studies, specifically, FDG-PET or magnetic resonance (MR), are obtained after the planning CT with the patient in the treatment position. They are registered with the planning CT and used in target and/or normal tissue delineation. The FDG-PET images can potentially improve tumor delineation over that with CT imaging alone (Jabour et al. 1993; Anzai et al. 1996; Chen et al. 1990). One limitation in the current use of PET data for treatment planning is the potentially large inaccuracy of the registration process, due to the relatively poor resolution of the PET emission and transmission images that sometimes may occur. Recently, combination PET-CT units have become available. These units provide both diagnostic quality CT and PET images without moving the patient between studies, improving the accuracy of the registration process.

MR studies are also often useful in the head and neck region, both for target and normal tissue localization. MR images may show the tumor extent much better than the CT scan alone.

It is imperative that the radiation oncologist be trained in the interpretation of all images used for structure localization. Consultation with neuroradiologists and nuclear medicine physicians may be necessary to accurately identify structures in the head and neck region or interpret PET-positive regions. An excellent reference with respect to the CT anatomy of the head and neck is the study by Nowak et al. (1999) who correlated borders of the surgical levels in the neck (I–VI) with structures seen on a CT scan, defining the six potential cervical lymph node regions and noting reproducible landmarks on the CT images. Wijers et al. (1999) developed a simplified protocol for delineating cervical target volume based on CT scans, and noted that target coverage and sparing of the major salivary glands were comparable to the more complex contouring guidelines of the above Nowak protocol. Chao et al. (2002) presented guidelines for target volume determination of head and neck lymph nodes. This was based on their analysis of nodal failure in IMRT-treated patients. The detailed and complex anatomy of the cranial nerve pathways is another important area of knowledge for the radiation oncologist. The gross anatomic information and associated axial CT images depicting these pathways are explicitly presented in the reference text by Leblanc (1995).

As mentioned previously, both MR and FDG-PET images are used in combination with CT for target and structure localization for selected head and neck cases at MSKCC including nasopharynx and thyroid cancers. The fusion of the magnetic resonance imaging (MRI) and/or

PET images with CT can aid in tumor localization for both the initial and cone down planning target volumes. Image fusion can also help ensure a minimum amount of normal tissue is treated, which is particularly important for patients undergoing high-dose irradiation with concurrent chemotherapy. Figure 10–3 depicts registered CT, MR, and PET-FDG images for a patient with advanced nasopharyngeal cancer. The treatment planning CT scan shows a very large area of abnormality that could represent either tumor or post-obstruction sinus/nasal changes depending on the area. The PET image reveals increased uptake in the bilateral retropharyngeal lymph nodes, indicating gross involvement at this level in contrast to the remaining cervical nodes. The MRI was superior to CT for evaluating the intracranial extension, due to its superior soft tissue resolution. The use of MR in this setting increases the certainty of covering the full extent of tumor, while minimizing exposure to healthy brain tissue.

Registered CT and PET images for a patient with thyroid cancer are shown in figure 10–4. This illustrates the significant extent of the thyroid carcinoma that is depicted as white areas of abnormality on the PET scan. It should be noted that normal structures may also show up as white

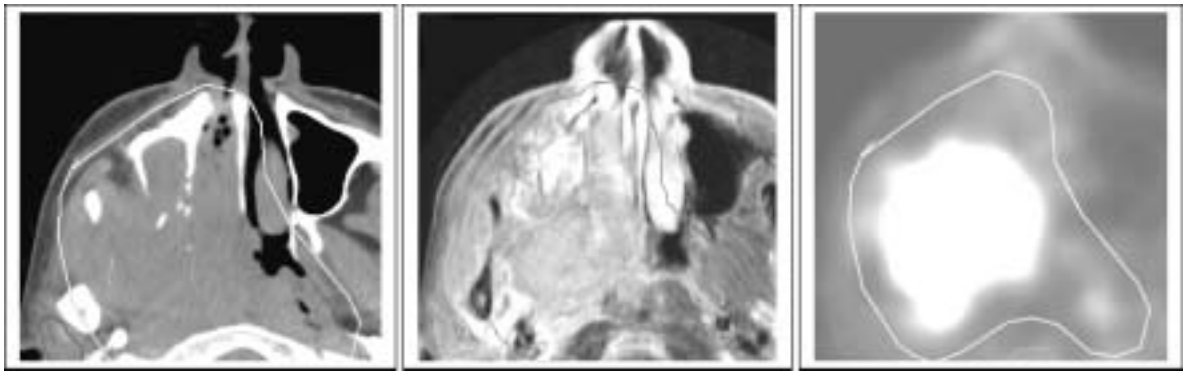


FIGURE 10–3. CT, MR, and FDG-PET images for a patient with primary nasopharynx cancer.

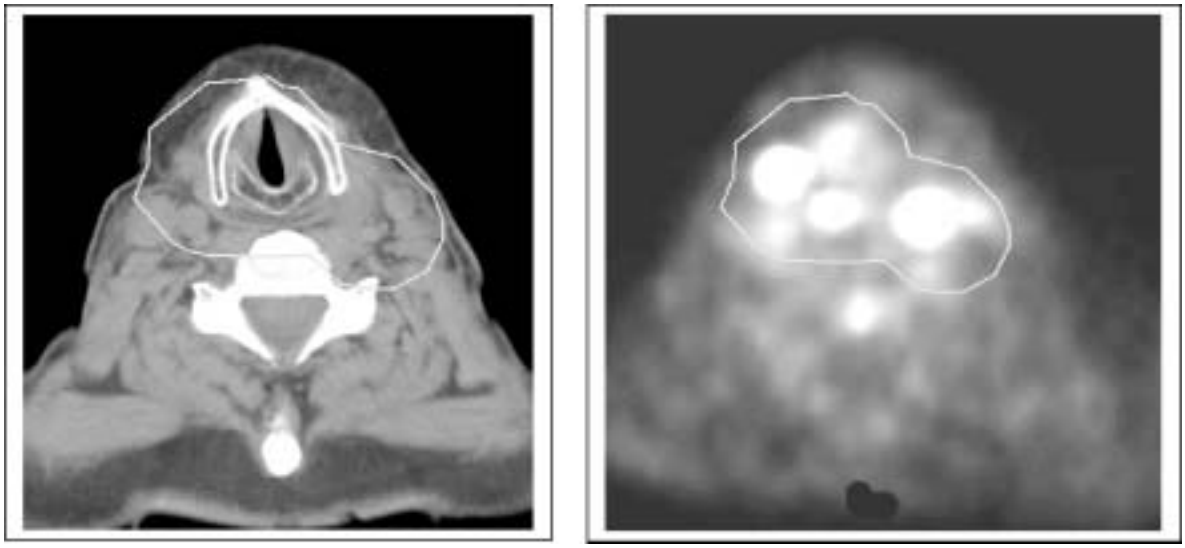


FIGURE 10–4. FDG-PET and CT images for a patient with thyroid carcinoma. The images were obtained with the patient in the treatment position, registered, and then used for localization of the target volume.

areas as is seen in the spinal cord in this slice and is not included in the PTV contours. Particularly in postoperative cases, the normal anatomy may be changed and it is quite difficult to distinguish tumor from normal structures. However, the fusion of the planning CT and PET images can allow one to more accurately contour the PTV. This approach is particularly effective in determining the cone down PTV, especially if high doses are to be administered.

Once all image sets needed for planning are acquired and registered, the target volumes (PTV) are defined by the physician. For nasopharyngeal carcinoma, two volumes are defined. PTV_{el} includes the entire nasopharynx and the elective nodal regions (CTV_{el}) with a uniform 0.5 cm margin. PTV_{gr} includes sites of gross disease in the nasopharynx and nodal regions (GTV) with a 1 cm margin everywhere except posteriorly along the skull, where a 0.5 cm margin is used. Normal tissues including the spinal cord, brainstem, bilateral parotid glands and cochlea, optical structures, and pituitary gland are also delineated as appropriate.

For target delineation using image fusion, the spatially registered image sets are displayed side by side in a split screen representation on the treatment planning computer. As the target or normal tissue is contoured in one screen, the corresponding regions are outlined automatically on the other screen. The radiation oncologist then discusses the case with the treatment planner, communicating pertinent information such as brief clinical findings, location of the primary tumor, adenopathy, high risk regions, adjacent critical structures, and the minimum dose to the tumor and maximum dose to critical structures.

Treatment Planning

The treatment planning process will be discussed in detail for one specific site, nasopharynx cancer. A similar process is used for other sites although the beam arrangements, clinical dose limits, and algorithm constraints are modified as needed.

1. IMRT Treatment Approach

   Patients with primary nasopharynx cancers are treated using seven coplanar 6 MV intensity-modulated (IM) fields, positioned every 30° from the posterior and lateral directions (figure 10–5), delivered with dynamic multileaf collimation (DMLC) (Spirou and Chui 1994).

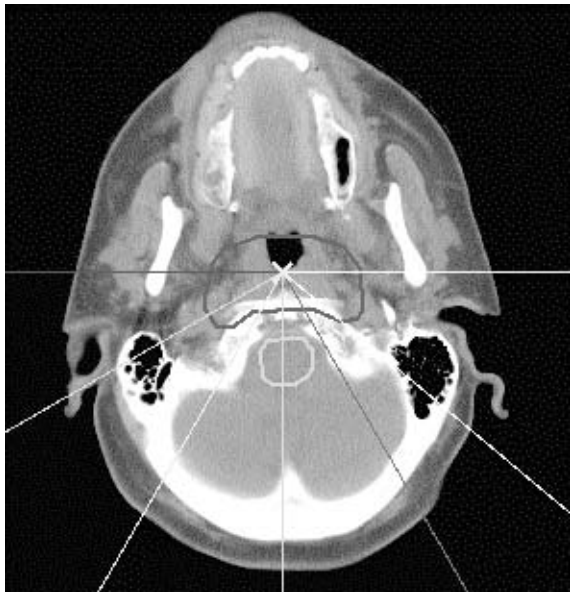


FIGURE 10–5. Beam directions for the MSKCC IMRT nasopharynx technique. Typically, ten treatment fields directed from seven gantry angles are used.

A prescription dose of 70 Gy is delivered to gross disease (PTV_{gr}) in the nasopharynx and neck, and 54 Gy to the elective nodal regions (PTV_{el}). The supraclavicular nodes are treated with a single anterior lower neck field, the superior edge of which is matched to the IMRT fields. Patients receive 1.8 Gy per fraction for the first 20 fractions (36 Gy) and thereafter, 1.8 Gy and 1.6 Gy in 2 daily fractions separated by a minimum of 6 hours for a total of 40 fractions. PTV_{el}, as defined above, is treated during the 1.8 Gy fractions, while treatment is limited to PTV_{gr} for the 1.6 Gy fractions.

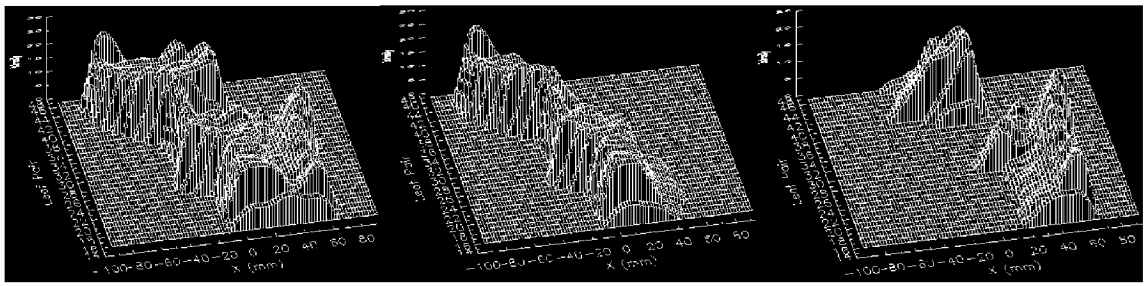
2. Optimization and DMLC fields

The MSKCC inverse planning algorithm is based upon a conjugate gradient minimization method and least-squares objective function developed by Spirou and Chui (1998) that is discussed extensively in chapter 2 on optimization. During optimization, the desired dose distribution is specified in terms of optimization parameters, i.e., dose constraints for targets, dose and/or dose-volume constraints for normal tissues, and penalties that define the relative importance of each constraint. During the development of the IMRT technique for primary nasopharynx cancer, criteria for PTV dose uniformity and normal tissue doses were established by the clinicians (table 10–3). Subsequently, a set of optimization parameters were determined that produce acceptable dose distributions for most patients. This constraint template (table 10–3) serves as the starting point for planning, although, invariably, the constraints are manipulated to improve the dose distribution for individual patients.

The intensity profile derived for each IM beam is translated into a leaf-sequence file for DMLC delivery. Due to a limitation on DMLC field size on the Varian equipment, any IM fields with widths > ~14.5 cm are divided into two subfields that overlap by 1 to 2 cm. The total intensity required in the overlap is distributed between the two subfields, creating a "feathered" region. For most patients, the three most posterior fields (figure 10–5) are split, for a total of 10 DMLC fields delivered from seven gantry directions. Intensity profiles for an IM field, approximately 16 cm wide, and its "split" subfields are illustrated in figure 10–6. Note that the "split" occurs in the low-intensity region that overlies the spinal cord and brain

Table 10–3. MSKCC Clinical Dose Limits and Inverse Planning Algorithm Constraints for Primary Nasopharynx Tumors

		Inverse Planning Algorithm Constraint Template			
Structure	Clinical Dose Limits	Prescription Dose (%)	Maximum Dose (%) /Penalty	Minimum Dose (%) /Penalty	Dose (%)–%Volume Constraint/Penalty
PTV_{el}	D_{95} ≥50 Gy (95% of 54 Gy) Max.Dose ≤64.8 Gy (120% of 54 Gy)	54 Gy (77%)	56.7 Gy (81%)/50	51.3 Gy (73%)/50	NA
PTV_{gr}	D_{95} ≥70 Gy (100% of 70 Gy) Max.Dose ≤84 Gy (120% of 70 Gy)	70 Gy (100%)	66.5 Gy (105%)/50	73.5 Gy (95%)/50	NA
Spinal Cord	Max.Dose ≤45 Gy		28 Gy (40%)/50		NA
Brainstem	Max.Dose ≤50 Gy		35 Gy (50%)/50		NA
Parotid Gland	Mean Dose ≤26 Gy		68 Gy (98%)/50		≥21 Gy (30%) to ≤30% Volume/50
Cochlea	Max. Dose ≤60 Gy		56 Gy (80%)/50		NA



(a) (b) (c)

FIGURE 10–6. Intensity profiles for a left lateral nasopharynx field before (a) and after (b and c) field splitting to overcome the DMLC maximum field width limitation.

stem. This feature and the "feathering" in the overlap region help to minimize the potential dosimetric uncertainty due to field matching.

3. Plan Evaluation And Quality Assurance (QA)
   The dose distributions and DVHs through the center of the nasopharynx and neck nodes for a typical patient with N0 disease are shown in figure 10–7. PTV_{gr} and PTV_{el} are well-covered by the 70 and 54 Gy prescription isodose levels while the spinal cord and brain stem receive approximately 45 Gy. The average mean dose to the parotid glands is 27 Gy and the cochleae receive an average maximum dose of 64 Gy.

For each beam of a completed IMRT plan, digitally reconstructed radiographs (DRRs) are generated displaying the so-called "DMLC aperture," corresponding to the complete irradiated area (figure 10–8). These DRRs are compared with portal images obtained with the DMLC aperture when the patient comes for treatment.

Prior to treatment, all IMRT plans undergo the following QA checks. A complete review of the plan is done by a physicist, including an evaluation of the dose distributions and DVHs and a review of all data used for patient treatment including the leaf motion files. The leaf motion files and intensity profiles are evaluated for unusual intensity peaks that might either limit treatment delivery or introduce dosimetric problems due to patient intra-fractional motion. An independent verification of the monitor unit setting for each treatment field is performed using a computer program specifically designed for this purpose. Discrepancies in excess of 2% warrant further investigation including film or ionization chamber dosimetry.

Daily Treatment with IMRT

Prior to the first treatment, the patient is positioned on the linear accelerator and images of each portal are obtained. Using the VARiS Treatment and Vision software, the DMLC aperture is automatically created, the portal images are acquired and then carefully compared against the DRRs.

IMRT for head and neck cancer patients requires precision and care on the part of the radiation therapist in every phase of the patient's daily setup and treatment procedure. Accuracy and reproducibility are vital if the tumor is to receive the proper dosage and overdosage to the normal critical structures avoided. The patient must be motivated and capable of fully cooperating with the setup and treatment procedure. Body motion must be kept to a minimum. Proper patient immobilization is absolutely essential (Chao et al. 2000). Close communication between the radiation oncologist and radiation therapist must be maintained throughout the course of treatment regarding any patient setup abnormality, problems, or difficulty. Weekly port films will

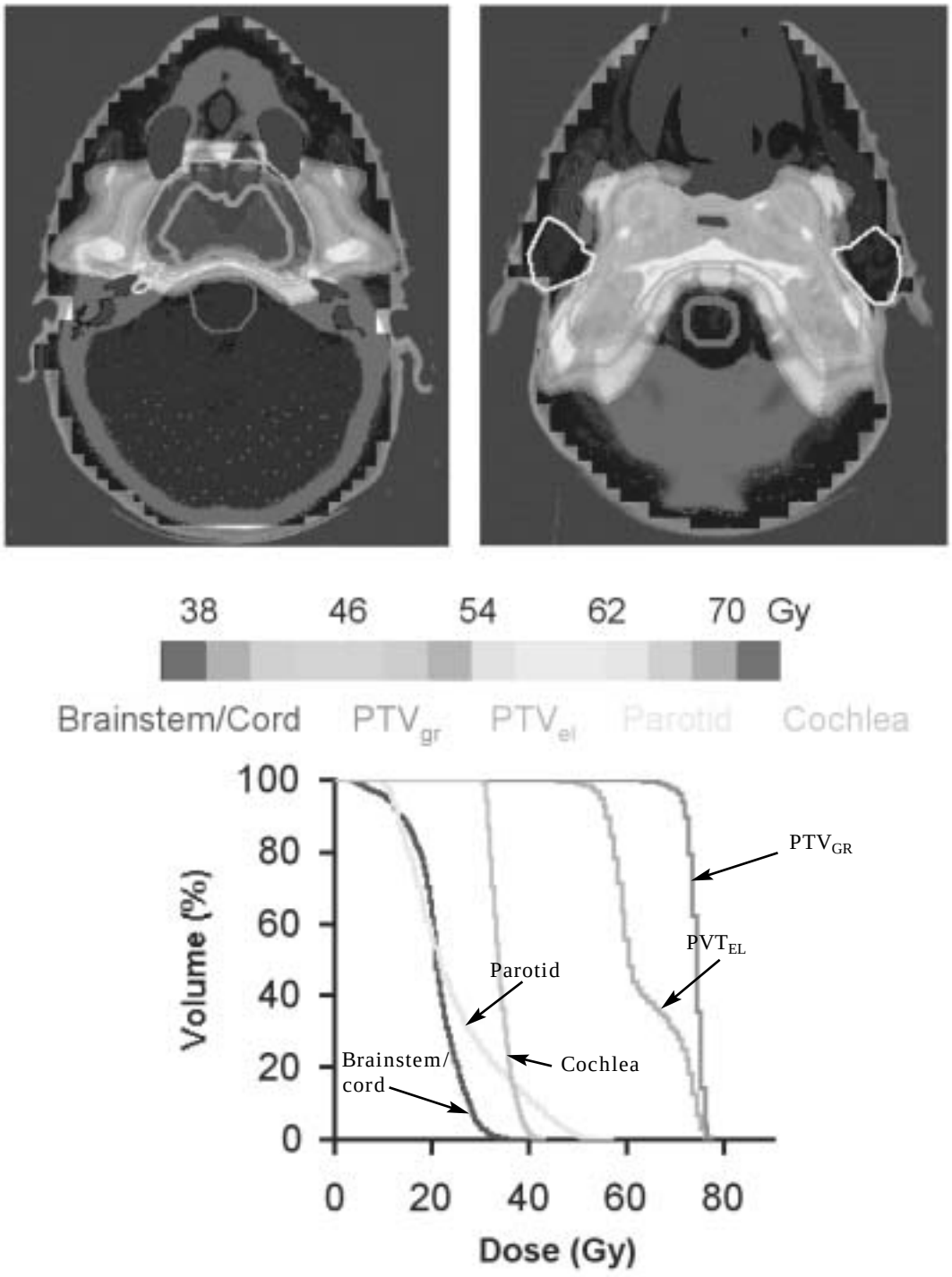


FIGURE 10–7. Axial dose distributions through the nasopharynx and neck for a seven-field IMRT plan.

be compared with the DRRs throughout the treatment course. Development of facial edema and significant weight loss may adversely affect the snug fit of the face mask and cause problems with patient immobilization and setup. Conservative modification of the mask, and on rare occasions, creation of a new mask and repeat CT simulation and treatment planning may be necessary.

Clinical Care During Radiation Therapy

The medical care of head and neck patients undergoing IMRT is the same as that required for those treated with conventional radiation therapy. For patients treated with a multi-modality approach including chemotherapy with cisplatin or carboplatin and 5FU, placement of a percutaneous endoscopic gastrostomy tube should be considered prior to initiation of treatment, particularly for elderly or frail patients, those who have lost a considerable amount of weight, or those with problems of dysphasia or odynophagia at the outset.

Weekly status evaluations are mandatory, with some patients requiring more frequent evaluations as treatment progresses. During these visits, an interval history is obtained reviewing the development of skin symptomology, a sore mouth or throat, xerostomia, decreased or abnormal taste, hoarseness, or dysphagia. A pertinent examination will note the status of the portal skin; the location and size of the primary tumor; the location, size, mobility, tenderness, and texture of lymphadenopathy; the presence of mucositis and of oral Candida. Routine measurement of the patient's weight and complete blood counts will be obtained.

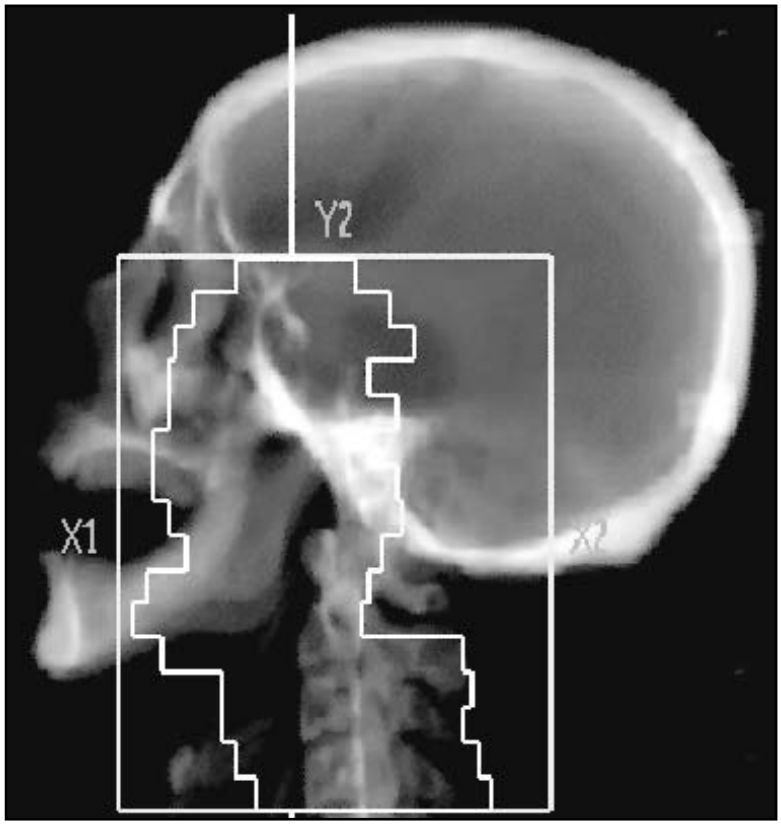


FIGURE 10–8. Digitally-reconstructed radiograph (DRR) of a left lateral IMRT field for primary nasopharynx cancer. The aperture indicates the initial and final positions of the MLC leaves used for the dynamic delivery.

Occasionally, a patient will develop acute parotitis within the first 12 hours after commencement of therapy when the treatment volume includes the parotid gland. The symptoms include swelling in the parotid regions associated with localized pain and occasionally a low-grade temperature. Although parotitis generally resolves on its own, we would prescribe a non-steroidal anti-inflammatory drug and reassure the patient should this occur.

Tumoritis can develop at ~20 Gy and is characterized by a mucosal inflammation that represents the true extent of the tumor and may necessitate subsequent modification of the portal (Wang 1997). As the primary tumor is followed during the course of treatment, those lesions that show progression or minimal regression should be reevaluated by all the physicians on the case. This may be a situation where surgery is indicated.

As patients develop the acute side effects of xerostomia, decreased or abnormal taste, and mucositis, appropriate supportive medical intervention is mandatory. Narcotic analgesics should be considered and modified as necessary to provide adequate pain relief. This may involve the use of long-acting morphine sulphate or a fentanyl patch as well as immediate-release morphine sulphate for any break-through pain. Intravenous hydration is sometimes indicated for patients who have become dehydrated due to poor oral intake or who have difficulties with their percutaneous endoscopic gastrostomy tube. A fair percentage of patients may develop oral Candida which may be asymptomatic, present with acute development or exacerbation of a sore mouth or throat or even perhaps an abnormal taste. Initiation of an antifungal medication will usually resolve the problem rapidly.

The head and neck cancer patients that we have treated with IMRT do not appear to have responses that differ from that of patients undergoing conventional treatment. Our clinical observation has been that these patients have similar acute reactions and can be managed quite adequately as presented above.

Post-Treatment Follow-up

Immediately upon completion of radiation therapy, routine follow-up evaluations should be scheduled. If the patient is elderly, frail, or having a particularly difficult time with acute mucositis, esophagitis, and weight loss, we will see this patient weekly until sufficient recovery has occurred which generally takes 3 to 4 weeks. The patients in better condition are seen monthly for 2 months and every 1 to 3 months thereafter, alternating with the other physicians on the case unless we are monitoring the response of a mass. Baseline imaging studies are considered 2 to 3 months post treatment and may include a CT or MRI of the head and neck or and/or a PET scan.

Serial endocrine screening will be important for patients who have had irradiation of these organs, including the pituitary gland and thyroid gland. Thyroid function tests, including a TSH, are obtained every 6 months post treatment for up to 5 years. Clinical hypothyroidism has been seen in ~5% of adults and a higher percentage in children whose thyroids have been irradiated. There is a 20% to 25% risk of chemical hypothyroidism overall, but this increases to 66% in patients who have also undergone a hemithyroidectomy. In patients who are found to have a significant elevation of the TSH, thyroid hormone replacement therapy is initiated irrespective of the T3 and T4 values, which oftentimes may be within normal limits. Patients who have their pituitary gland irradiated should periodically undergo irradiated screening every 1 to 2 years post irradiation. These tests should evaluate LH, FSH Serum cortisol, prolactin, TSH, free T4, and GH. For male patients, a testosterone level is also included.

Patients who have received radiation to the oral cavity or oropharynx should be seen routinely by the dental service for an indefinite period of time. Fluoride prophylaxis, initiated at the start of treatment, should be continued. These patients are advised that their dentist should be fully informed of their radiation therapy as well as the potential risk for osteoradionecrosis that may result from subsequent dental surgery.

Occasionally, a patient will develop Lhermitte's syndrome, a benign, transient myelopathy presumably due to radiation-induced demyelination in the cervical spinal cord. This can begin 1 to 3 months post therapy and last an average of 3 to 4 months and as long as 9 to 12 months. This is characterized by the development of a symmetrical, instantaneous, shooting, electrical sensation that radiates down the spine and extremities upon flexation of the neck, but it does not progress and requires no treatment.

High-dose irradiation, especially when combined with chemotherapy, can lead to late effects of the soft tissues. Particular attention should be directed towards the development of trismus as well as the decreased range of motion of the tongue, mandible, neck, and shoulders. Physical therapy should be considered as it may decrease or prevent these post treatment functional deficits resulting from fibrosis and scarring.

Some patients may develop dysphagia during treatment that could become chronic and significant. Post treatment dysphagia may be due to dysfunction of the pharyngeal muscles, the development of an esophageal stricture, or even possibly the presence of a tumor. We have observed in some patients whose pharyngeal muscles received high-dose radiation therapy, particularly in conjunction with chemotherapy, significant swallowing problems long after completion of treatment. Appropriate medical evaluation must be performed for diagnosis and appropriate therapeutic intervention.

Effect Of Setup Uncertainty

Several studies evaluating setup uncertainty specifically for head and neck patients (Rabinowitz et al. 1985; Verellen et al. 1997; Hunt et al. 1993) have measured standard deviations of systematic and random uncertainties of approximately 2 to 3 mm. Hunt et al. compared the impact of setup errors on target coverage, spinal cord, and brainstem dose for 3-D and parallel opposed dose distributions. Systematic setup errors led to target underdosage and normal tissue overdosage with both techniques, but the 3-D distributions were more susceptible to the effects of both random and systematic errors because of the increased conformality. Although, studies evaluating the effect of setup uncertainty specifically for IMRT head and neck distributions have not yet been done, the impact may be even more significant because of their exquisite conformality and the presence of steep dose gradients.

In a preliminary evaluation for nasopharynx cancer, we have modeled the effects of random and systematic setup uncertainty on IMRT dose distributions for selected patients using the following technique. Briefly, the random treatment uncertainty is modeled by convolving the planned dose distribution with a normal frequency distribution with a standard deviation of 2 mm, a technique developed by Chui, Kutcher, and LoSasso (1992). After blurring the dose distribution to show the effect of random uncertainty, systematic uncertainty is modeled using a Monte Carlo simulation. A normal frequency distribution with a standard deviation of 2 mm in each direction is sampled 500 times. For each iteration the dose distribution corrected for random uncertainty is shifted according to the sampled systematic error and the doses to the targets and normal tissues are recalculated. Confidence limit DVHs, i.e., the DVHs expected with a given statistical confidence for a population of patients, can then be calculated and analyzed. The 2 mm standard deviations of random and systematic setup uncertainty were estimated from our own analysis of setup for head and neck patients (Hunt et al. 1993). The planned, 95%, and 5% confidence limit DVHs for the PTV, brain stem, and cochlea are shown in figure 10–9 for a patient planned with the IMRT dose painting technique described below **(IMRT Dose Painting and Dose Escalation for Primary Nasopharyngeal Carcinoma).** The tight conformality of the dose distribution and, in particular, the manner in which the high-dose region surrounds the spinal cord and brainstem is responsible for the observed increase in normal tissue dose and degradation in target coverage. Based on this preliminary analysis, we currently limit the spinal cord and

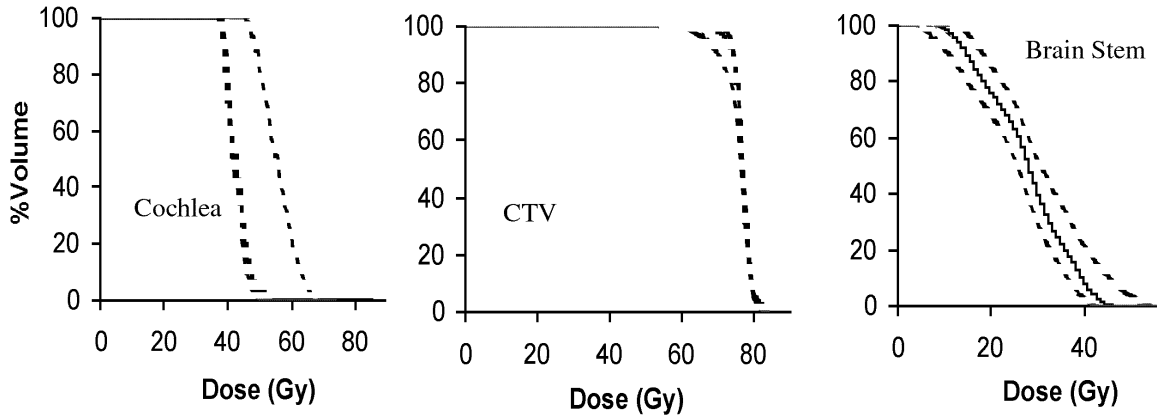


FIGURE 10–9. Dose-volume histograms for an IMRT dose painting simultaneous boost technique incorporating the effects of random and systematic setup uncertainties, each with a 2 mm standard deviation. For each structure, the planned DVH is indicated by the solid line. The 5% and 95% confidence limit DVHs are indicated by the dashed lines.

brainstem to 45 and 50 Gy, respectively, approximately 5 Gy less than what would be accepted with a less conformal distribution.

Vital Organ Sparing

Much research has been reported on the sparing of the parotid gland with IMRT. This organ is responsible for 60% to 65% of the saliva produced and xerostomia is a major acute and late side effect that can have a significant negative impact on a patient's quality of life. Salivary output may begin to decrease within 24 hours after the first fraction of 2.25 Gy (Mira et al. 1981), fall by 50% or more by the seventh day (Dreizen et al. 1977; Franzen et al. 1992; Eneroth, Herikson, and Jakobson 1972) and be barely measurable by the end of treatment (Dreizen et al. 1977; Franzen et al. 1992; Mossman 1986). Six months post treatment, the stimulated salivary flow is reduced exponentially for each parotid gland at a rate of approximately 4% per Gy of mean parotid dose (Chao et al. 2001). However, the patient's subjective evaluation of their xerostomia may not reliably correlate with objective salivary flow measurements.

Patients note a dry mouth secondary to decreased salivary output and a very thick and viscous saliva. These problems may or may not improve after completion of treatment. Recovery may be observed in some patients for the first 2 to 3 years post treatment, depending on their age, the volume of gland irradiated, the dose per fraction, and the total dose. If more than 50% of the gland was spared from radiation, the probability for some recovery is increased (Cooper et al. 1995).

The use of IMRT for head and neck cancer can reduce the parotid volume treated to high doses and result in an improved salivary status (van Dieren et al. 2000; Kuppersmith et al. 1999; Chao et al. 2001; Eisbruch et al. 1999, 2001; Wu et al. 2000). Wu et al. (2000) noted that IMRT plans were more conformal than 3DCRT plans and that the dose to the parotid glands could be reduced with an equivalent coverage of the primary tumor and regional lymph nodes. Eisbruch et al. (2001) reported that the sparing of major salivary glands by IMRT increased late salivary flow rates, and improved xerostomia. They also noted that sparing of minor salivary glands in the oral cavity was a significant independent predictor of xerostomia. An analysis of dose, volume, and function relationships in the parotid glands after IMRT suggested that a mean parotid dose of ≤26 Gy was necessary for substantial sparing of the gland (Eisbruch et al. 1999).

Butler et al. (1999) noted in a review of 20 IMRT patients with primary head and neck cancer that the mean dose to the ipsilateral parotid gland was 23 Gy and to the contralateral gland, 21 Gy. Chao et al. (2000) reported that the mean parotid dose in their series was approximately 20 Gy. They also noted that 3%±1.4% of the primary target received less than 95% of the prescribed dose due to proximity of the target volume to the critical structures such as the parotid gland. The steep dose gradient commonly noted in head and neck IMRT plans in which the tumors are in very close proximity to the parotid gland means that part of the primary target volume may be underdosed. Further research is necessary to determine whether this is of clinical importance.

At MSKCC, we attempt to limit the mean dose to at least one parotid gland to ≤26 Gy, without compromising target coverage. For patients with nasopharyngeal cancer, mean parotid doses of ≤26 Gy are usually achievable in patients with negative or unilateral neck disease for the gland on the side without neck disease. In the presence of gross adenopathy, mean parotid doses of ~35 Gy are typical. To ensure adequate target coverage in the presence of a parotid sparing technique, we require that at least 95% of the electively irradiated and gross disease PTVs receive 50 Gy and 70 Gy, respectively. Our experience indicates that, as a consequence of parotid sparing, the dose to the oral cavity and the submandibular glands may increase and therefore should be carefully evaluated. Dose distributions and DVHs derived from inverse planning with and without an attempt to spare the parotid glands are compared in figure 10–10 for a patient with a negative neck. A small section of the electively irradiated PTV receives less than 54 Gy in order to achieve a mean parotid dose of 26 Gy.

Radiation therapy may also lead to sensorineural hearing loss, particularly when the radiation is delivered in combination with chemotherapy. As discussed by Choi et al. (2000), hearing loss occurs more frequently in patients whose cochlea received ≥70 Gy. Unfortunately, the cochleae are often within or adjacent to the high dose target in the nasopharynx and could easily receive doses in excess of 70 Gy. Grau et al. (1991) demonstrated that doses of 50 to 70 Gy to the cochlea may lead to hearing loss within 18 months, but that the probability and severity of the loss was correlated with dose and the sound frequency. IMRT can be used to spare the cochlea, but similar to parotid sparing attempts, may lead to compromised target coverage (figure 10–11). A retrospective analysis of 20 of our nasopharynx patients indicated that the cochleae straddle or lie within the PTV_{gr} in approximately three-fourths of all patients and that their position greatly affects the dose they receive. At MSKCC, we currently limit the dose to the cochlea for nasopharynx patients to ≤60 Gy when possible given the target constraints outlined in table 10–3. To further guard against tumor underdosing, an additional constraint requiring ≥99% of the GTV to receive ≥70 Gy is used. IMRT dose painting and the simultaneous boost technique, as discussed in the next section, may facilitate lower cochlear doses without compromising target coverage. Figure 10–12 shows dose distributions and DVHs for a patient planned with the IMRT dose painting simultaneous boost technique according to the target criteria in table 10–3 and the additional GTV coverage criteria. The cochleae receive a maximum dose of 30 Gy.

In addition to the structures already discussed, other important normal structures to consider when planning head and neck tumors with IMRT include the orbital structures, optic nerves, optic chiasm, brain, and mandible. Generally, the dose limits for these structures can easily be achieved with IMRT except in patients with extensive superior disease or cranial extension.

IMRT Dose Painting And Dose Escalation For Primary Nasopharyngeal Carcinoma

The use of IMRT to plan non-uniform dose distributions within the target volume for head and neck patients has been described recently by Wu et al. (2000). The advantages of this technique include the delivery of a biologically higher dose to the gross disease and the simplification of

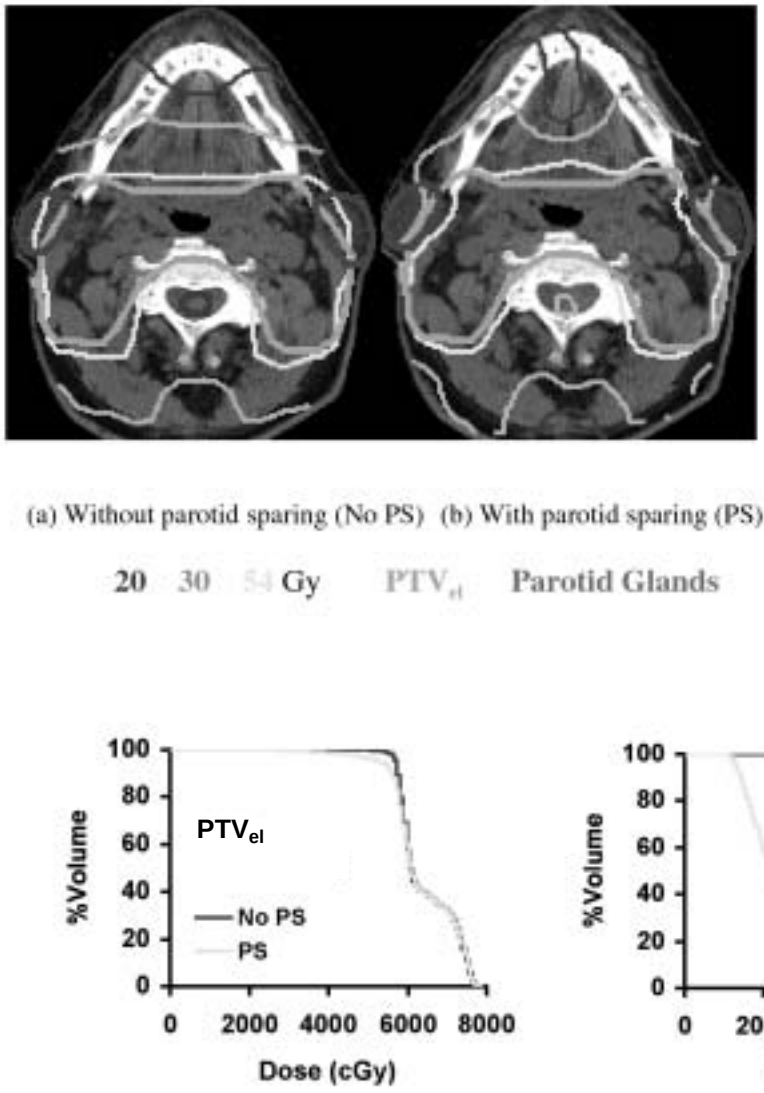


FIGURE 10–10. Axial dose distributions and DVHs for the PTV_{el} and parotid glands with and without an IMRT parotid sparing technique for a patient with N0 disease. See COLOR PLATE 23.

the planning and treatment processes since only one plan is designed and used for the entire treatment course. The study by Wu examined the potential of this *concomitant* or *simultaneous integrated* boost technique for a variety of head and neck tumors and concluded that, using IMRT, they could achieve distributions similar to conventional fractionation in terms of target coverage and normal tissue doses. The technique being considered at MSKCC would deliver 70.2 Gy to the nasopharynx in 30 fractions (2.34 Gy/fraction) while concomitantly treating the neck to 54 Gy (1.8 Gy/fraction). Typical dose distributions and DVHs comparing this technique with our standard two-phase technique are shown in figure 10–13. Coverage of the PTV_{gr} is very similar to that achieved with a conventional treatment strategy and IMRT, although the mean dose to PTV_{el} is slightly less.

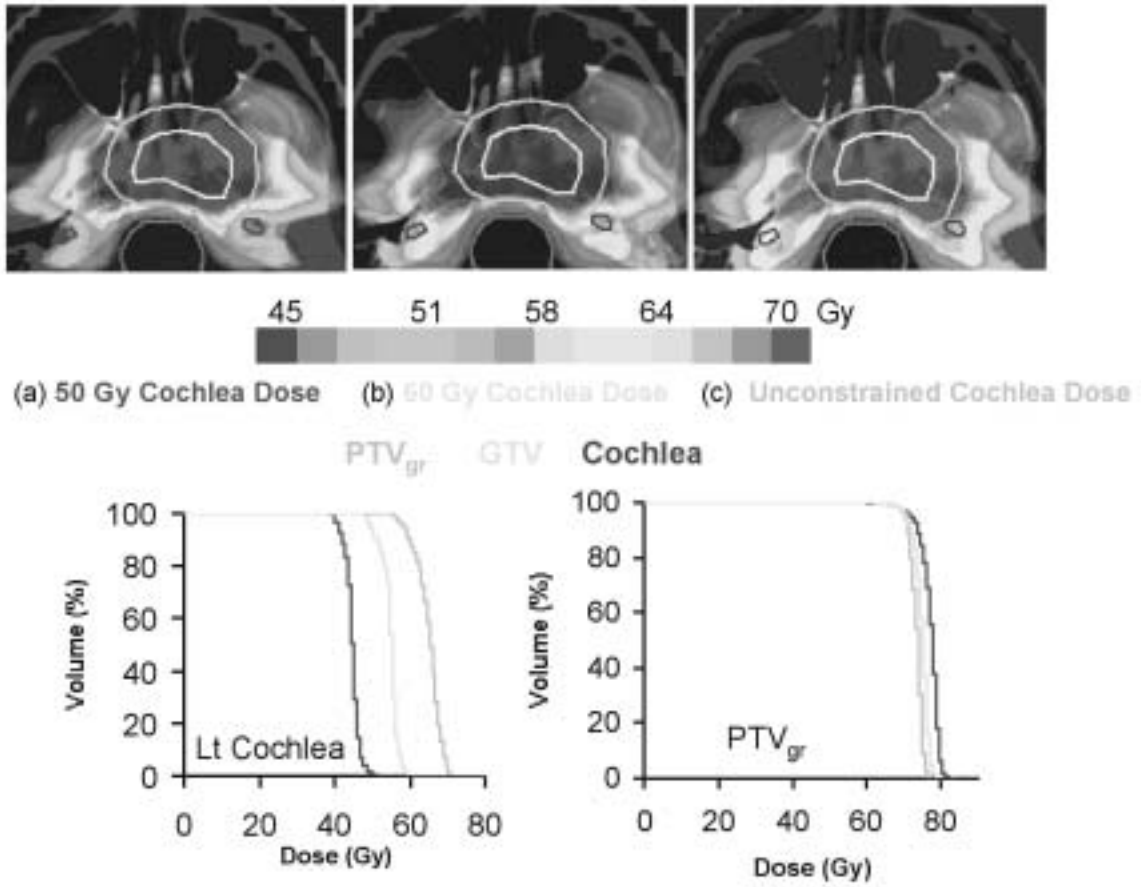


FIGURE 10–11. Dose distributions and DVHs illustrating the effect of cochlear sparing on PTV coverage when the cochleae lie within PTV_{gr}. Results are shown for three plans: unconstrained cochlear dose, 50 Gy, and 70 Gy maximum cochlear dose. See COLOR PLATE 24.

Plans designed with a simultaneous boost technique are inherently more conformal than those using a two-phase technique, leading to lower doses to critical structures in very close proximity to the 70 Gy volume such as the cochlea. Additional dose distributions in the nasopharynx for the current MSKCC two-phase treatment and the simultaneous boost technique are compared in figure 10–14. These distributions were generated with constraints on target coverage and dose uniformity, spinal cord and brainstem maximum dose, and parotid mean dose, but no constraint on the cochlea. The conformity index (Volume (70 Gy)/Volume (PTV)) is significantly improved with the simultaneous boost technique. As a result of this improved conformality, the dose to the cochlea is also less.

Treating Recurrent Head And Neck Tumors With IMRT

The management of head and neck cancer patients with recurrent disease who have previously received radical radiation therapy is a challenge. For these patients, surgery is often the treatment of choice, provided the lesion is resectable, the patient is able to tolerate the procedure, and that

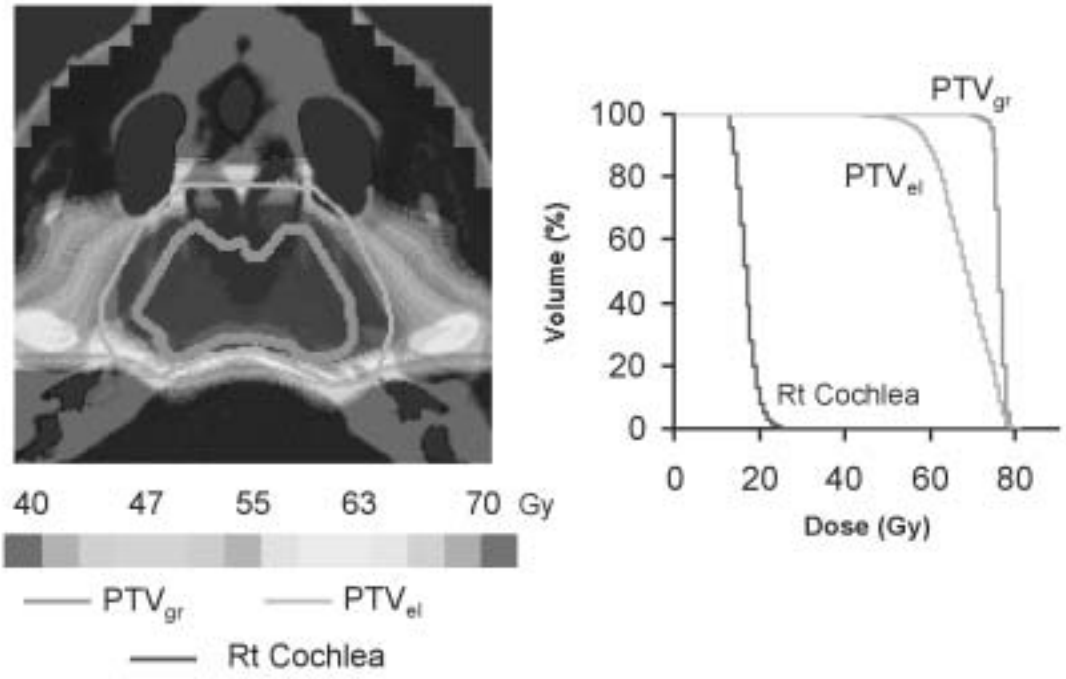


FIGURE 10–12. Dose distribution and DVH of the PTV_{gr} and cochlea for a patient planned with the 70 Gy IMRT dose painting simultaneous boost technique. The cochleae receive a maximum of 30 Gy with acceptable target coverage and dose uniformity.

recovery and rehabilitation are likely. For patients who are not surgical candidates, re-irradiation can be considered. This is a highly select group with true local-regional recurrence rather than persistence of the disease post radiation therapy. Evaluation of the following items is necessary: (1) patient condition; (2) time interval since completion of initial radiation therapy; (3) radiation dosage administered; (4) tolerance of treatment and any complications; (5) anatomic location of recurrence and adjacent normal critical structures; (6) condition of previously irradiated tissues; (7) symptoms related to the recurrence; (8) life expectancy. Relative contraindications to re-irradiation include: (1) poor condition; (2) recurrence less than 6 months from initial radiation therapy; (3) ultra-high radiation doses; (4) massive tumor recurrence equivalent to T3–T4 lesions; (5) location of recurrence in or around the central nervous system. The dose of re-irradiation will need to be in the range of 60 to 65 Gy (De Crevoisier et al. 1998; Stevens, Britsch, and Moss 1994; Wang 1994). Moderate dose re-irradiation of 45 Gy will most likely not be effective and may not even provide sufficient palliation. The more limited the disease, the better the chances for a meaningful therapeutic intervention.

Meticulous treatment planning and careful radiation technique are necessary. At MSKCC, IMRT is often used for re-irradiation cases although brachytherapy as the primary treatment or as a boost is also considered. Conservative margins around the tumor of no more than 1 cm are appropriate. The central nervous system must not be directly re-irradiated by the primary beam. Only patients who understand the high risks involved and exhibit a willingness to accept the possible complications should be considered for re-irradiation.

Re-irradiation of recurrent nasopharyngeal cancer with a stage equivalent to a T1 or T2 lesion has frequently been reported in the literature (Teo et al. 1998; Wang 1993). PET or MR image fusion can aid in localization of the tumor allowing for a limited treatment volume with a high

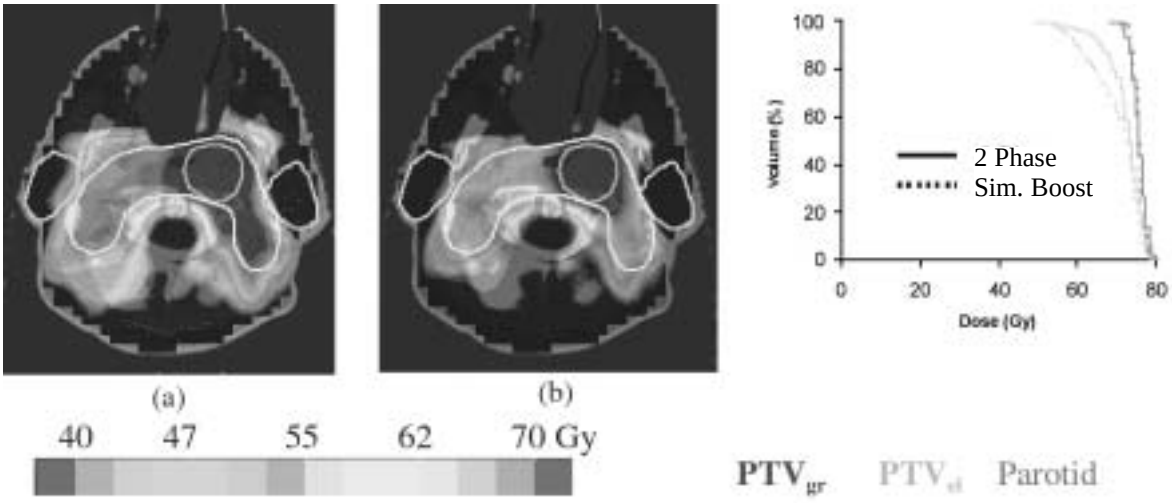


Figure 10–13. Comparison of IMRT nasopharynx dose distributions for a two-phase treatment technique (a) and a simultaneous boost treatment (b). See COLOR PLATE 25.

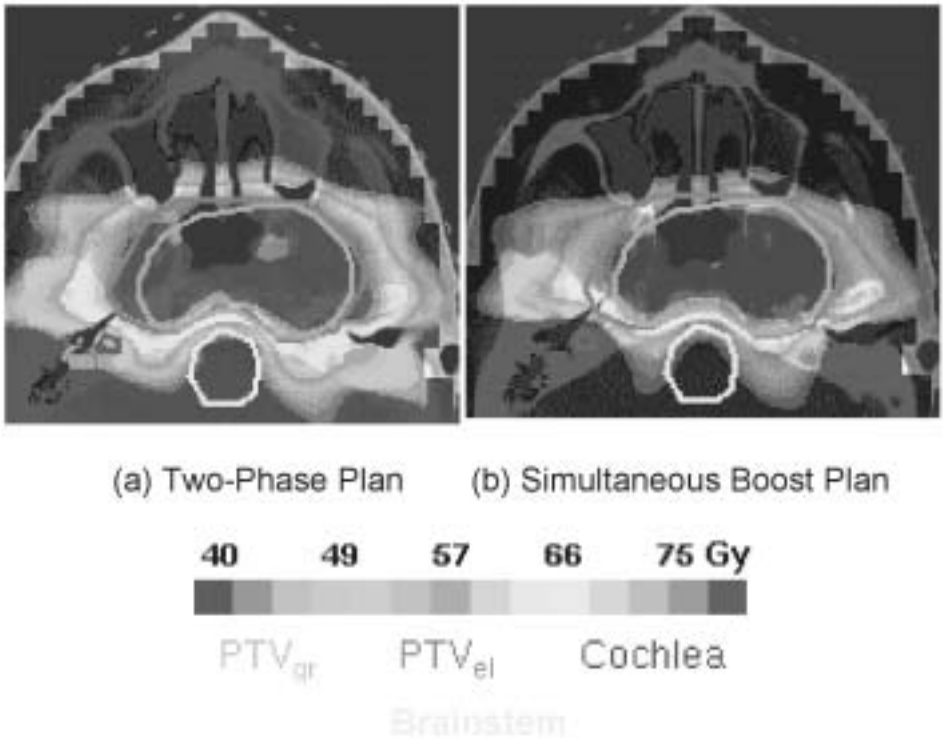


FIGURE 10–14. Comparison of the MSKCC two-phase (a) and simultaneous boost (b) techniques for the treatment of nasopharynx cancer. Using the simultaneous boost technique, the PTV_{gr} receives 70.2 Gy in 30 fractions (2.34 Gy/fraction) while the electively irradiated volume, PTV_{el}, receives 1.8 Gy/fraction to 54 Gy. The 70 Gy conformity index is 2.4 for the two-phase plan and 1.7 for the simultaneous boost. The maximum cochlea doses with the two-phase and simultaneous boost plans are 70 and 63 Gy, respectively. See COLOR PLATE 26.

level of confidence that the disease is contained within the treatment region. Limited volume IMRT with a brachytherapy boost can potentially provide good local control although brachytherapy may not be suitable in some cases because of the size and extent of the tumor. These patients must be treated with IMRT often with concurrent chemotherapy. Special care must be exercised in analyzing the IMRT plan with respect to the central nervous system, orbit, and optic nerve and chiasm doses.

Other regions of the head and neck have been treated with re-irradiation with promising preliminary results. Studies have shown good palliation of symptoms and some have reported long term control with 20% 2-year survivals and 15% to 17% 5-year survivals (DeCrevoisier et al. 1998; Stevens, Britsch, and Moss 1994). The results appear better than those obtained with the use of chemotherapy alone.

The incidence of late toxicity is greater than that noted after primary radical radiation therapy. Several studies have suggested however that these adverse effects were still deemed acceptable (Wang 1994).

Re-irradiation with IMRT at MSKCC

At MSKCC, IMRT is used routinely in the treatment of recurrent cancers, primarily nasopharynx although additional sites including paranasal sinus have been treated. Typically, doses of ~60 Gy are prescribed with dose limits to the spinal cord and brainstem of 10 to 12 Gy. The doses delivered to other normal tissues, particularly optical pathway structures, are determined after consideration of the previous therapy.

Typically, five to nine equally spaced treatment fields are used, including non-coplanar beam arrangements when beneficial. Although PTV constraints similar to those for PTV_{gr} in table 10–3 are used, the individual needs of each patient are considered when defining the normal tissue constraints. IMRT and 3-D conformal plans for recurrent nasopharynx disease, created using seven field beam arrangements, are compared in figure 10–15. IMRT improved the target dose uniformity and led to lower doses to the optical structures. Our experience has been that it is generally not possible to achieve the extremely low normal tissue doses required for these cases with IMRT alone. Conventional cerrobend blocking is combined with dynamic multileaf IMRT when normal tissue doses must be less than approximately 30% of the prescription.

Summary

The concave shape of the target volume and close proximity of normal tissues make head and neck tumors ideal cases for IMRT. Multiple planning studies within the past 5 years have clearly demonstrated the ability of IMRT to improve target coverage and dose uniformity for many head and neck sites. More exciting, perhaps, is the opportunity to impact the significant normal tissue morbidity associated with head and neck radiotherapy and the ability to deliver different fractionation schemes using the SMART technique or IMRT “dose painting.” Clinical results have already established that IMRT can be used to decrease the morbidity associated with the irradiation of the salivary glands. It remains to be seen if similar improvements in hearing loss can be achieved without sacrificing local control.

Head and neck sites have always been among the most challenging, complex and time consuming to plan. Our experience with head and neck IMRT planning has been that the complete planning process can require 10 to 12 hours of a planner’s time, more if image fusion is required. Site-specific class solutions, specifying the clinical criteria for target and normal tissue doses in as much detail as possible, the beam arrangements and constraint templates to use as starting points for planning are mandatory for efficient head and neck IMRT planning. Despite the increased complexity and time required to produce them, IMRT dose distributions offer

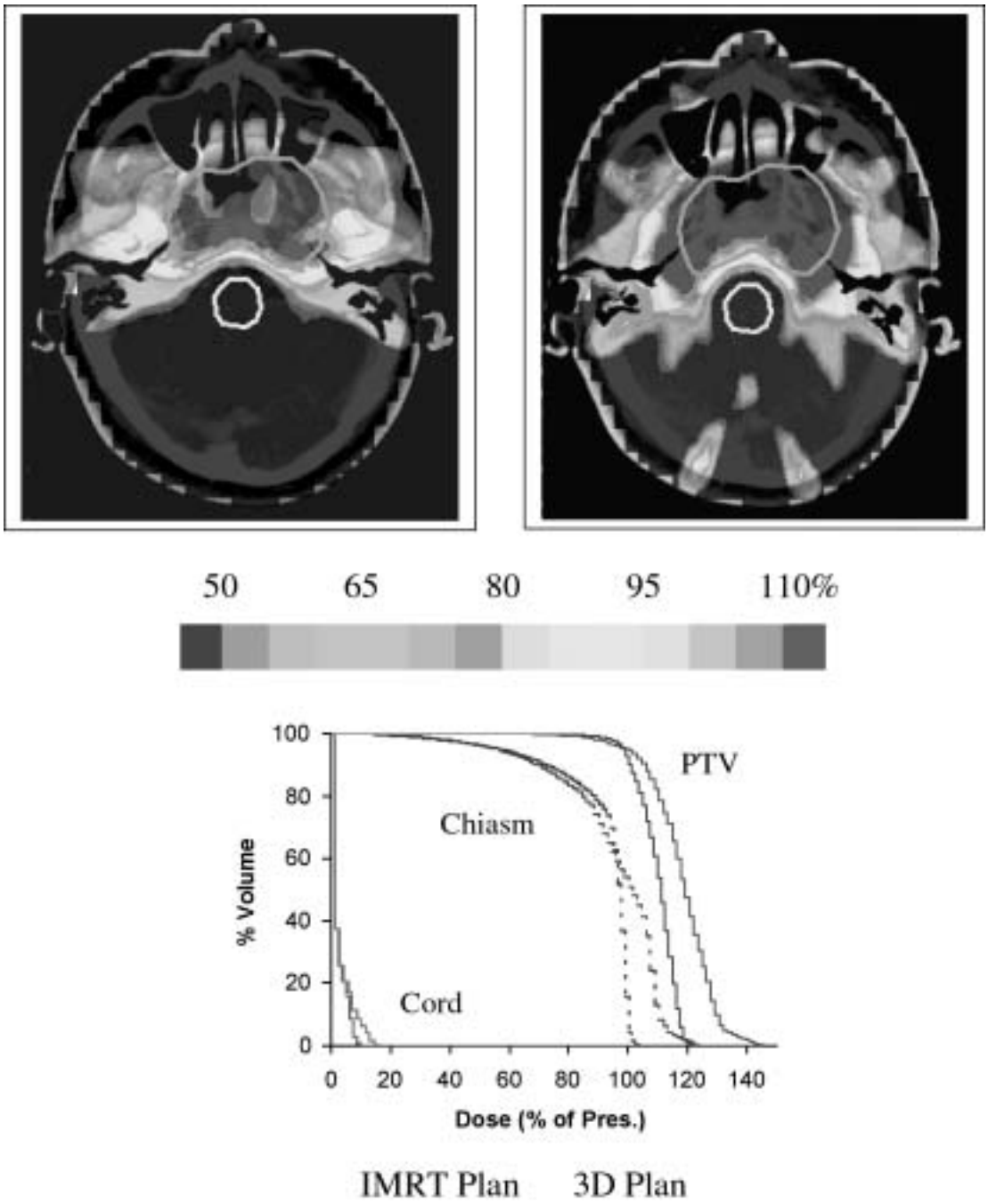


FIGURE 10–15. Dose distributions and DVHs for IMRT (left) and 3-D (right) plans for recurrent nasopharyngeal cancer. Both plans utilize a seven-field beam arrangement as shown in figure 5. For the 3-D plan, wedges and cerrobend blocks over the spinal cord and brainstem are used to create a concave dose distribution. Cerrobend blocks over the cord and brainstem are also used with the IMRT plan to achieve doses of <20% of the prescription to these structures. IMRT significantly improves target dose coverage and uniformity and normal tissue doses compared to the 3-D plan. See COLOR PLATE 27.

significant improvements over 3-D conformal plans. We believe that IMRT will become the standard method of treatment for many head and neck sites.

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