1 General Concepts in Head and Neck Radiotherapy

Murat Beyzadeoglu, Omer Sager, and Ferrat Dincoglan

Overview

Although accounting for approximately 4 % of all carcinomas, an important group of tumors both numerically and epidemiologically arise in the head and neck region with diverging disease courses that may pose formidable challenges in therapeutic management. This relatively small region of the body contains critical parts associated with basic physiologic functions including respiration, nutrition, and expression. Debilitating consequences may occur as a result of head and neck cancers depending on location, size, and spread pattern of the tumors. Structural disfiguration and functional impairments may considerably compromise social integration and quality of life. Moreover, treatment of the disease may induce additional mutilations and dysfunctions with the potential to further aggravate quality-of-life impairment.

A multidisciplinary team approach is needed for optimal management of patients with head and neck cancers, and mortality should not simply be regarded as the sole measure for survival with the understanding that these cancers may induce substantial morbidity. Maintaining functionality and decreasing the structural deformities are critical aspects of management. In this context, decisions to achieve maximal cure and functionality with minimal morbidity, and maintaining the capability to salvage recurrent disease should be addressed at the very outset. Initial assessment and designation of individualized treatment algorithm should involve active participation from the multidisciplinary team of experts. Likewise, prevention and management of treatment-related sequelae warrant the involvement of specialists with

M. Beyzadeoglu, MD (✉) • O. Sager, MD • F. Dincoglan, MD
Department of Radiation Oncology, Gulhane Military Medical School,
Etlik, Ankara, Turkey
e-mail: mbeyzadeoglu@yahoo.com

M. Beyzadeoglu et al. (eds.), *Radiation Therapy for Head and Neck Cancers: A Case-Based Review*, DOI 10.1007/978-3-319-10413-3_1

expertise in their field. Treatment of patients within this wide spectrum of the disease may be satisfactory but also disappointing since treatment-induced morbidity may be hazardous even when substantial regression of large tumors is achieved. Patients with acute treatment-related morbidity are usually hardly manageable in the course of their treatment due to poor nutrition and performance status. With the recent technological advances in radiation oncology discipline, factors of maintaining the quality of life, preservation of structure, functionality, and cosmesis have become indispensable management goals to be considered. Improved imaging capabilities may allow earlier diagnosis which may translate into preserved voice and swallowing functions. Optimal selection of treatment modality based on meticulous staging workup is necessary. In this aspect, detailed knowledge of fundamental oncological principles along with thorough patient evaluation is mandatory. Interdisciplinary collaboration of radiation oncologists, surgical oncologists, and medical oncologists is crucial with the inevitable support of dental oncologists, maxillofacial prosthodontists, pathologists, radiologists, nutritionists, reconstructive surgeons, neurosurgeons, oncology nurses, psychiatrists, social workers, physical medicine and rehabilitation physicians, speech and swallowing therapists, neurology service, and other health care personnel involved in management and rehabilitation of head and neck cancer patients. Coordination among the disciplines may offer the best chance of cure with optimal functional and cosmetic outcomes. Nevertheless, the patient's active involvement is another important aspect of successful management. Whichever individualized treatment algorithm is recommended, the patient may prefer a therapeutic approach that offers better functional or cosmetic outcomes at the cost of a lower probability of tumor control. That is why active participation of the patients in decision making process is important.

1 Natural History

Head and neck cancers mostly follow an orderly and predictable spread pattern. Approximately two thirds of the patients have locally advanced disease at presentation. A tendency towards local or regional spread is common in head and neck cancers. Regional involvement is frequently concerned with the primary tumor's anatomic location and extent. Despite the increased risk of hematogenous spread in the presence of enlargement and extracapsular extension of the involved neck nodes, distant metastasis constitutes an infrequent pattern of failure, which allows potential cure by optimal management strategies. Nevertheless, head and neck tumor sites of the nasopharynx and hypopharynx have a relatively higher likelihood for distant spread. The most common site of distant failure is the lungs

Table 1.1 Head and neck lymphatics

Level	Lymphatics
Ia	Submental lymphatics
Ib	Submandibular lymphatics
II	Upper jugular lymph nodes
III	Middle jugular lymph nodes
IV	Lower jugular lymph nodes (transverse cervical)
V	Spinal accessory chain lymph nodes (posterior triangle)
VI	Prelaryngeal, pretracheal, paratracheal lymph nodes

followed by the bones, mediastinal lymphatics, liver, and brain secondaries. However, atypical distant involvement of cutaneous and subcutaneous tissues may occur in patients with radical neck dissection or previous radiotherapy. Due to the risk of nerve invasion for some head and neck tumors, particularly for parotid cancers, nerve traces should meticulously be considered in the treatment planning process.

Head and neck tumors accounting for approximately 4 % of cancers may present with diverse natural histories that make their management more complex. They are named according to their locations and subsites in the head and neck region [1]. Head and neck cancers are usually seen in patients over 40 years of age, while salivary gland and nasopharyngeal cancers may occur at earlier ages. Women are more frequently affected compared to men. Certain types are more commonly observed in certain geographic locations (e.g., nasopharyngeal cancer in Far East Asia). Smoking, tobacco, and alcohol are considered as major risk factors for head and neck cancers. Chewing tobacco and tobacco-like substances have been associated with increased risk of oral cavity cancers [2].

Other risk factors for head and neck cancers include genetic predisposition, previous head or neck cancer, history of cancer in the immediate family members, exposure to ionizing radiation as well as to sun (ultraviolet radiation), nutritional disorders and habits, vitamin deficiencies, iron-deficiency anemia, poor oral hygiene, use of inappropriate prostheses, chronic infections, gastroesophageal reflux, and specific viral infections (EBV, HPV) [3, 4]. Head and neck cancers may occur simultaneously or metachronously in multiple locations in the same individual [5]. Exposure to radiation may occur through several ways, such as prior radiotherapy directed at the head and neck area or radioactive contamination from nuclear reactor accidents (e.g., Chernobyl) or nuclear weapons (e.g., Hiroshima and Nagasaki). Human papillomavirus infection (HPV) has been shown to have a role in the development of particularly oropharyngeal cancers [6, 7].

There is a rich lymphatic network in the head and neck area (Table 1.1). Level I lymphatics include the submental and submandibular area. Levels II, III, and IV include upper internal jugular, middle internal jugular, and lower internal jugular lymph nodes, respectively. Level V includes posterior triangle, and level VI includes prelaryngeal, pretracheal, and paratracheal lymph nodes.

This lymphatic network is divided into sublevels for purposes of neck dissection or radiotherapy (Fig. 1.1).

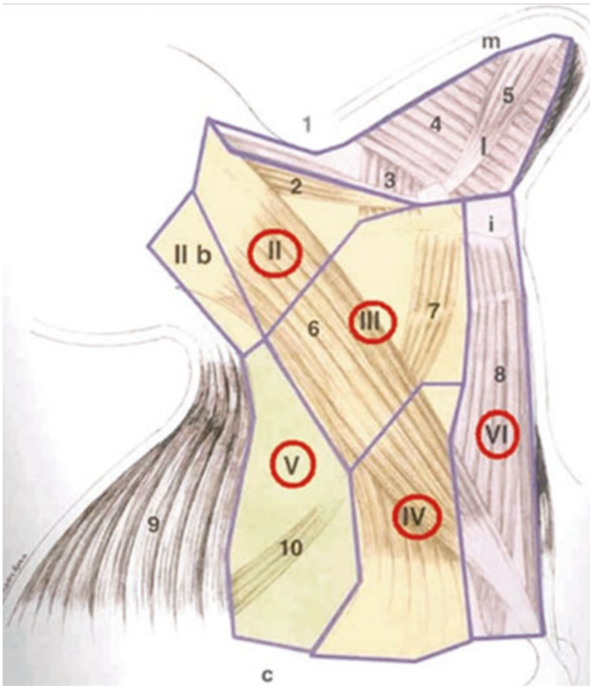

Fig. 1.1 Lymphatic levels of the neck for head and neck cancers

Over 30 % of all head–neck cancer cases show clinical lymph node positivity (Table 1.2) [1, 9]:
Pharyngeal wall cancer: 50 %
Pyriform sinus cancer: 49 %
Supraglottic laryngeal cancer: 39 %
Head–neck cancers with clinical neck lymph node (−) but pathological lymph node (+) (Table 1.2) [9]:
Pyriform sinus cancer: 59 %
Pharyngeal wall cancer: 37 %
Tongue cancer: 33 %
Supraglottic laryngeal cancer: 26 %
Floor of mouth cancer: 21 %
Glottic laryngeal cancer: 15 %

Table 1.2 Lymphatic involvement ratios in various head–neck cancers (%) [1, 8]

Region	Level I		Level II		Level III		Level IV		Level V		RPLN	
	N–	N+	N–	N+	N–	N+	N–	N+	N–	N+	N–	N+
Nasopharynx											40	86
Tongue	14	39	19	73	16	27	3	11	0	0	–	–
Base of tongue	4	19	30	89	22	22	7	10	0	18	0	6
Retromolar trigone	25	38	19	84	6	25	5	10	1	4	–	–
Tonsil	0	8	19	74	14	31	9	14	5	12	4	12
Pharyngeal wall	0	11	9	84	18	72	0	40	0	20	16	21
Pyriform sinus	0	2	15	77	8	57	0	23	0	22	0	9
Supraglottic larynx	6	2	18	70	18	48	9	17	2	16	0	4
Glottic larynx	0	9	21	42	29	71	7	24	7	2	–	

RPLN retropharyngeal lymph nodes

2 Pathology

Most cancers arising from the upper aerodigestive mucosa are squamous cell carcinomas (SCC) or one of its variants including lymphoepithelioma, spindle cell carcinoma, verrucous carcinoma, and undifferentiated carcinoma. Adenocarcinoma, mucoepidermoid carcinoma, and adenoid cystic carcinoma are seen in the major salivary glands including the parotid, submandibular and sublingual glands, as well as the minor salivary glands. Merkel cell carcinoma most frequently arises on the head and neck skin and is among the cutaneous neuroendocrine neoplasms. Merkel cell tumors follow an aggressive disease course with common locoregional and distant failure. Lymphomas, solitary plasmocytomas, soft tissue sarcomas, melanomas, and other malignant and benign neoplasms represent the remaining cases.

3 Workup

A meticulous physical examination including the palpation of the head and neck lymph node regions, direct or indirect visualization of the primary site by mirror, or fiberoptiscopic examination is an important part of initial patient assessment. Imaging studies include computed tomography (CT) and/or magnetic resonance imaging (MRI) of the head and neck region and X-ray examinations of the skull, sinuses, and soft tissue. Barium swallow may be suggested for symptomatic patients, along with chest radiograph and bone scan to exclude metastatic disease. Integrated positron emission tomography (PET)/CT imaging may assist in precise definition of locoregional disease and distant metastases. It may also aid in locating occult tumors in the setting of an unknown primary and may be beneficial for detecting recurrent disease after treatment. Viral titers may be elevated in some patients, anti-Epstein–Barr virus antibody titers may be used to assist in the diagnosis of nasopharyngeal cancers in some cases. Laryngoscopy, bronchoscopy, and esophagoscopy may be considered in the setting of suspected synchronous aerodigestive primary.

Staging of head and neck cancers is mostly based on clinical diagnostic information about the tumor size, extension, and presence of involved lymph nodes. Decision making for adjuvant treatment warrants accurate surgical–pathological classification.

4 Radiation Therapy Planning and Treatment Procedure

Radiation therapy process for head and neck cancers generally include the following steps:

- Positioning for treatment, immobilization, and imaging for treatment planning
- Contouring of treatment volumes and organs at risk (OARs)
- Dose prescription
- Forward planning (3-dimensional conformal radiation therapy, 3DCRT) or inverse planning (intensity-modulated radiation therapy, IMRT)
- Plan assessment and improvement
- Implementation of plan and treatment verification

5 Patient Preparation and Immobilization

Positioning of the patient for treatment may depend on the specific cancer type being treated and the objectives of the treating physician concerning the tumor volume and normal tissue sparing. Patient lies supine in the majority of cases with the neck extended and the head on headrest. Surgical scars and palpable nodes may be wired. The patient should be immobile during therapy. Movements may cause changes in the treatment area and increase side effects, thus affecting treatment success. The patient should be positioned in the most comfortable, easily reproducible way suitable for the irradiated region of interest.

Optimum immobilization is a major component of radiotherapy management in head and neck cancers. The importance of setup reproducibility is becoming more important with the need for tighter margins and steep dose gradients in the modern radiotherapy era.

Thermoplastic face mask is frequently used for immobilization of patients with head and neck cancers (Fig. 1.2).

Such a mask should not only be tight but also there should be no space between the patient's skin and the mask. The mask should be checked during every setup

Fig. 1.2 Thermoplastic mask

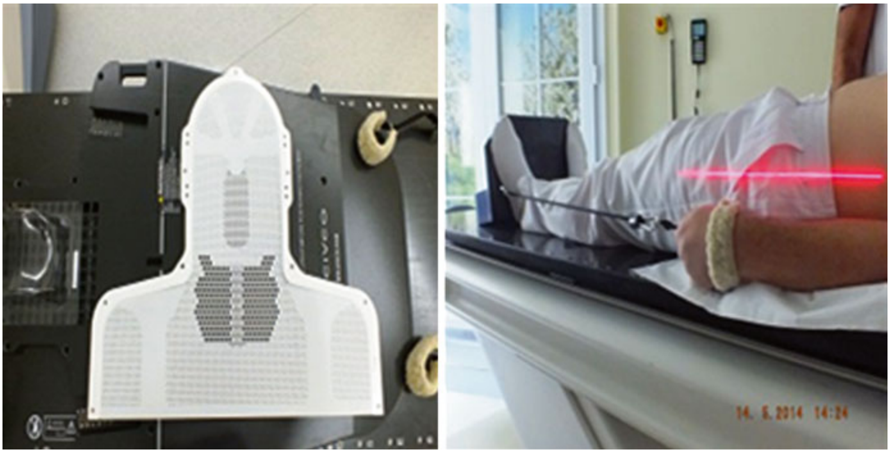

Fig. 1.3 Immobilization mask and shoulder retractor (Courtesy of Gulhane Military Medical Academy)

procedure for tightness or looseness (due to edema or weight loss) and should be remade adaptively if necessary.

Immobilization of patients for irradiation of the head and neck region is usually provided by means of a support under the head with aquaplast cast for facial fixation (with or without shoulder inclusion), both attached to a baseplate on top of the treatment couch. Shoulder retractors may be used to remove shoulders from the treatment field to allow appropriate low-neck irradiation (Fig. 1.3).

Bite-block is frequently used in oral tongue radiation treatments. A small hole can be made in the mask if a bite-block or nasogastric tube is being used. An effective tongue blade with a cork attached to one end may displace the tongue out of the treatment volume, and mucosal sparing of the hard palate may also be achieved by displacing the palate.

Inadequate immobilization may result in inaccuracies. Erroneous alignment of treatment fields causes interfraction errors. Intrafraction errors may occur if the patients and/or tumor volumes move during treatment delivery as a consequence of incorrect immobilization or physiologic activity. Accounting for these uncertainties in the treatment planning and delivery processes poses a formidable challenge and is an area of active investigation.

6 Simulation

Simulation is defined as radiotherapy field determination using a diagnostic X-ray machine (conventional or CT based) with similar physical and geometrical features to the actual teletherapy machine. The patient is immobilized before simulation, and then the tumor is localized either in a direct scopy X-ray machine or in serial CT slices. The simulation can be done by CT, MRI, or rarely by PET/CT.

Determination of the patient's treatment position and construction of the immobilization device are typically performed in a dedicated radiation therapy CT-simulator room including a diagnostic quality CT scanner, laser patient positioning/marking system, virtual simulation 3D treatment planning software, and various digital display systems for viewing the digitally reconstructed radiographs (DRRs) [10–12].

The mask and other required equipment are made on the day of CT simulation by the radiotherapist, under the supervision of the radiation oncologist, for the patient who is to receive radiotherapy (Fig. 1.4).

The patient is sent to the nurse for an IV route before CT simulation if an IV contrast material is to be used. Then, the patient is positioned on the CT couch, and the mask, knee support, alpha cradle, or any other similar device is fitted on the CT couch if required. The lasers are turned on, and they are positioned at the midline according to the region of interest. Reference points are determined by radiopaque markers located at the cross sections of the lasers (Fig. 1.5).

Reference points are predetermined locations for each region of the body. There are three reference points: one is craniocaudal, and the others are on the right and left lateral sides.

Contrast material is given intravenously by the nurse, if required. Adequate measures should be taken for any possible anaphylactic reactions. Any required adjustments are performed by the CT technician in the CT command room (Fig. 1.6).

The region of interest (that for which serial CT slices are to be taken) is determined by the radiation oncologist. The slice thickness is also determined. All of these data are transferred to the CT computer. After the region of interest has been verified on screen, serial slices are taken.

Initially, CT topograms are generated and reviewed before the acquisition of the planning scan to verify patient alignment, and relevant adjustments are performed if required. Radiopaque markers may be placed both on the aquaplast and at three levels on the patient's skin. These serve as the fiducial marks which aid in relevant coordinate transformation. Treatment planning CT is acquired using a slice thickness of 2–5 mm and should typically include the entire supraclavicular region with an approximate number of 50–200 slices totally. In some circumstances, however,

Fig. 1.4 Immobilization and simulation procedures (Courtesy of Gulhane Military Medical Academy)

Fig. 1.5 Fiducial marks and patient simulation

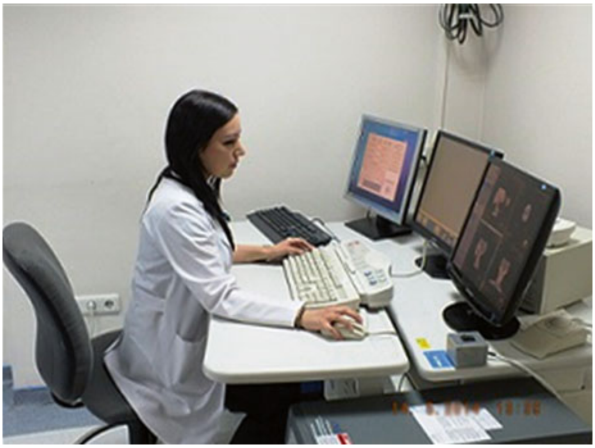

Fig. 1.6 A command room for computerized tomography simulator

slice thicknesses of 1 mm may be required for contouring of fairly small volumes like the optic nerves and chiasm. Treatment volumes and relevant critical structures are outlined on consecutive slices to generate the structure set. Planning CT data allows for the generation of a three-dimensional anatomic model of the patient and provides electron density information to be used in the calculation of three-dimensional dose distribution. Administration of intravenous contrast may improve the visualization of the parotids and may assist in contouring of primary tumor and nodal disease.

7 Treatment Planning

IMRT warrants precise definition of treatment volumes and OARs. Uncertainties in the definition of tumor extensions and target volumes may directly affect treatment outcomes. The treatment planning process typically starts with contouring of treatment volumes and OARs. The recent report ICRU 83 has updated the definitions of volumes [13] with the consideration that volumes are more relevant in IMRT. Three types of tissue is included in the volumes which are (a) malignant lesion, (b) otherwise normal tissue close to the tumor which is already or likely to be infiltrated by microscopic disease, and (c) more distant normal tissue and organs [13].

Contouring of CTV requires clinical experience. An important difference in IMRT applications includes the quantitative definition of treatment volumes and critical structures. The use of complementary information from multimodality imaging may facilitate this process by providing additional data about disease extent. Also, contouring atlases may assist in delineation (Fig. 1.7).

Normal structures typically included in the structure set are the spinal cord, brainstem, parotid glands, skin, mandible, oral cavity, submandibular glands, lacrimal glands, glottis, brachial plexus, optic pathway, retina, lenses, lips, and inner and middle ears.

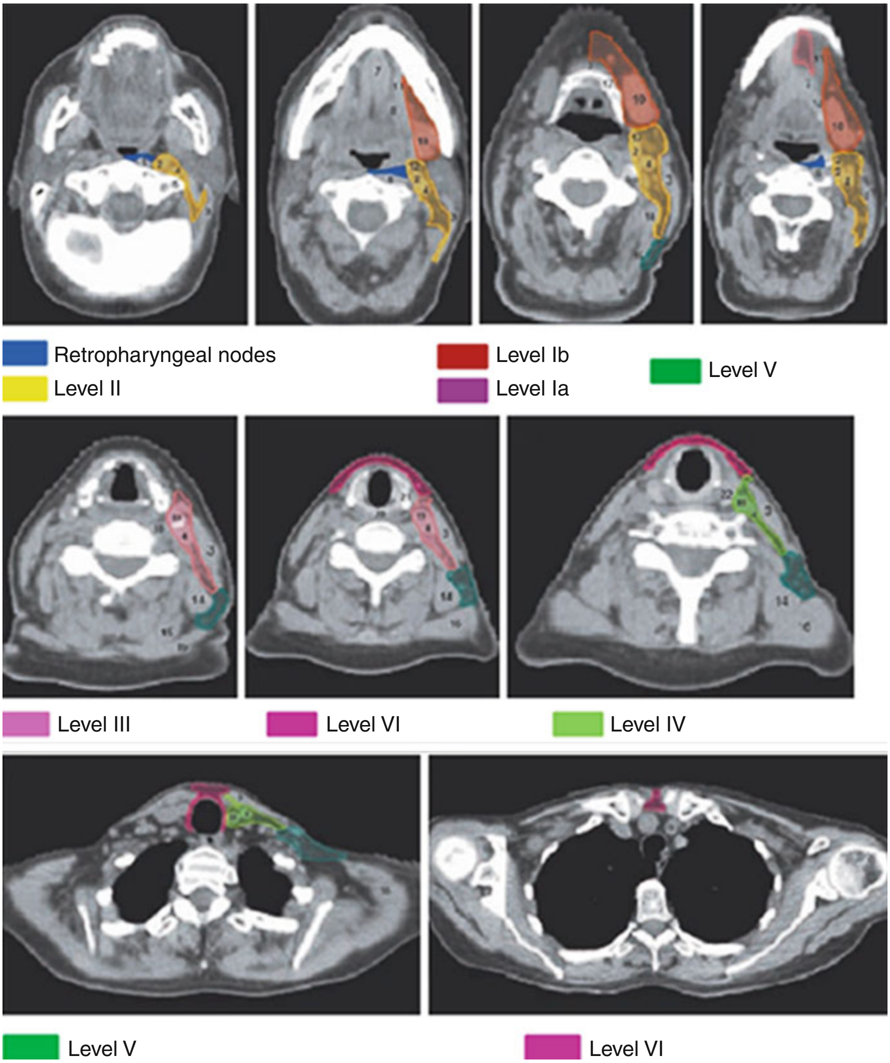

Fig. 1.7 Consensus guidelines for the delineation of N0 (elective) neck nodes [1, 14]

Physical and imaging findings are used in the delineation of gross primary tumor, nodal disease, and high-risk subclinical disease. Contouring of treatment volumes and OARs on the volumetric planning CT images is typically done by the radiation oncologist and the medical dosimetrist working as a team. OARs with distinct boundaries such as the skin and lungs may be autocontoured and slightly edited if needed. However, delineation of some critical structures such as the brachial plexus requires active participation of the radiation oncologist in the contouring process. The planning CT data set is typically transferred to treatment planning system (TPS) via the computer network.

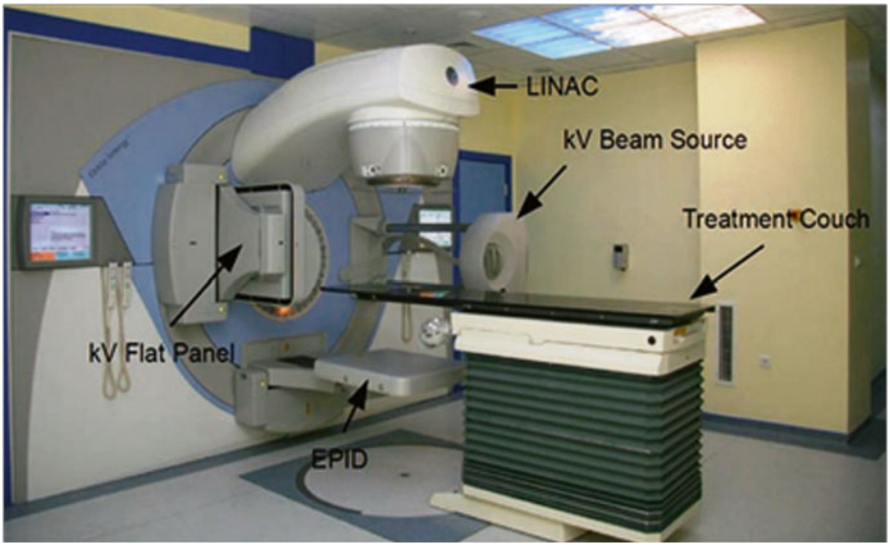

Fig. 1.8 Image-guided radiotherapy unit (Courtesy of Gulhane Military Medical Academy)

Contemporary anatomic imaging modalities including CT and MRI allow for constructing three-dimensional patient anatomy. Structure sets including target volumes and organs at risk (OAR) are defined in consecutive image slices frequently by using additional information from complementary functional imaging such as positron emission tomography (PET). Improved imaging technologies aid in the precise identification of target volumes and their relationship with critical normal tissues. With the availability of computer-controlled multileaf collimator (MLC) systems and development of linear accelerators integrated with advanced volumetric imaging systems, accurate modification and positioning of dose distributions have been possible (Fig. 1.8).

Intensity-modulated radiation therapy (IMRT) has emerged as a major technical innovation in the modern era. As a highly developed form of 3DCRT, IMRT provides a highly conformal dose distribution around the target through the use of nonuniform beam intensities. This is achieved through using either static or dynamic segments. The isodose distribution can then be matched closely to the target by modulating the intensity of each subsegment [1, 8]. IMRT may optimize the therapeutic ratio with improved control of dose distributions by manipulation of beam intensities and the incorporation of image-guided techniques for precise target contouring and treatment delivery.

This most sophisticated form of three-dimensional conformal radiation therapy (3DCRT) has been shown to be useful for decreasing long-term morbidity in nasopharyngeal, oropharyngeal, and paranasal sinus cancers through reducing doses to critical organs including the salivary glands, temporal lobes, and auditory and optic structures without compromising locoregional control [15–21]. Superior dose distributions and reduced critical organ doses in IMRT are achieved by using beamlets of nonuniform intensities delivering nonuniform dose to the target to achieve the desired dose conformality. Thus, an important advantage of IMRT is its capability to achieve higher conformality of dose distributions than those provided by 3DCRT with uniform intensity of beams. Head and neck cancers frequently need concave-shaped treatment volumes to improve sparing of critical structures (the spinal cord, brainstem, etc.) in close vicinity. Even 3DCRT may fail to achieve these fluence dose distributions, but IMRT using inverse planning algorithm in which the desired clinical and dosimetric objectives are stated mathematically may provide excellent dose distributions closely following the shapes and boundaries of target and relevant OARs in 3 dimensions. Another advantage of IMRT is that it allows easier production of nonuniform absorbed dose distributions if needed for treatment of a volume within another defined volume which is also called concomitant boost or simultaneous integrated boost [22–24]. Clearly, this precise treatment technique is more unforgiving for positioning and motion uncertainties, which warrants its use in conjunction with image-guided radiation therapy (IGRT). IGRT may be defined as the integration of various radiological and functional imaging techniques in order to perform high-precision RT. The main aims are to reduce setup and internal margins and to account for target volume changes during RT, such as tumor volume decrease or weight loss (adaptive RT). IGRT is not an IMRT technique; however, it enables various RT techniques, including IMRT, to be delivered more accurately.

Radiation treatment is indicated for most head and neck cancers since tumors in this region are frequently not amenable to optimal surgery. Nevertheless, optimal management may only be achieved through an interdisciplinary approach including experts. Patient preferences, age, performance status, comorbidities, daily habits and lifestyle, and occupation should be taken into consideration.

Preoperative radiation therapy is favored if optimal surgical resection is not feasible initially. With the use of preoperative RT, some unresectable tumors may convert to a resectable status. Also, oxygenation is better in the preoperative setting compared to postoperative setting which makes the application of preoperative RT more favorable when the tumor is more radiosensitive. Preoperative RT may also reduce the extent of normal tissue resection.

Indications of postoperative RT include close or positive surgical margins, tumor extension into soft tissues of the neck or skin, bone or cartilage invasion, perineural and/or vascular space invasion, the presence of neck nodes ≥ 3 cm, involvement in multiple lymph node levels, or nodal extracapsular extension.

Treatment is quite complex for head and neck cancers. Treatment decisions should be based on specific disease site, stage, and pathologic findings. Surgery and radiation therapy (RT) are the major curative treatment modalities for head and neck cancers. Chemotherapy only may not be curative and however is included in combined modality management to exploit the advantages of synergistic effect, particularly for stages III or IV disease. Stage I–II disease may be managed with surgery or RT only. Choice of treatment is dependent on several factors including the location and extension of the primary tumor, differentiation of cancer and cell type, morphologic tumor characteristics, status of nodal disease, the presence or absence of distant metastasis, probability of speech or swallowing function preservation, and patient preference.

Stage at the time of diagnosis is a predictor of survival and aids in decision making for management of head and neck cancers. While stages I or II disease usually define a relatively smaller primary tumor without lymphatic spread, stages III and IV disease include larger tumors with regional nodal involvement and/or invasion of underlying structures. Distant metastasis at presentation is infrequent.

Pre- and Post-radiotherapy Management Pearls

Serious temporary or permanent functional handicaps may occur as a result of high-dose radiation exposure. Appropriate prophylactic pretreatment measures may prevent or reduce the severity of these potential morbidities.

Dental prophylaxis is warranted when the mandible or the salivary glands are at the risk of receiving high-dose irradiation. Assessment of the patient by an expert dentist with special interest in head and neck cancers and the effect of RT on the oral cavity should be performed. Restoration of carious or broken teeth should be performed by a dentist or oral surgeon. Non-restorable teeth should be extracted, and RT should be initiated at least 2 weeks after extraction to allow for adequate healing. Full mouth extraction of restorable teeth should be avoided since it is considered detrimental due to increased risk of oral trauma and osteoradionecrosis. The patients should be instructed to maintain dental hygiene in the course of treatment and afterwards.

Nutritional support before, during, and after treatment is needed for all patients with head and neck cancers. Patients should be instructed to avoid using alcohol and tobacco. The use of hot and acidic fluids during RT should be discouraged. Calorie supplements and blenderized diets should be suggested for maintaining adequate nutrition of the patient.

Patients with head and neck cancers should be encouraged to maintain close contact with the treating physician for meticulous and continued follow-up. Since an overwhelming majority of recurrences occur within the first 2 years of treatment, close and meticulous follow-up is of utmost importance particularly during this time interval. Frequent follow-up of the patient should be considered for dealing with treatment-related morbidities, detecting recurrent disease and second primary cancers at an early stage.

References

1. Beyzadeoglu M, Ozyigit G, Ebruli C (2010) Basic radiation oncology, 1st edn. Springer, Berlin
2. Wannenmacher M, Debus J, Wenz F (2006) Strahlentherapie. Springer, Berlin, pp 344–345
3. Mellin H, Friesland S, Lewensohn R et al (2000) Human papillomavirus (HPV) DNA in tonsillar cancer: clinical correlates, risk of relapse, and survival. Int J Cancer 89:300–304
4. Mendenhall WM, Logan HL (2009) Human papillomavirus and head and neck cancer. Am J Clin Oncol 32:535–539
5. Schwartz LH, Ozsahin M, Xhang GN et al (1994) Synchronous and metachronous head and neck carcinomas. Cancer 74:1933–1938

6. D'Souza G, Kreimer AR, Viscidi R et al (2007) Case–control study of human papillomavirus and oropharyngeal cancer. N Engl J Med 356:1944–1956
7. Gillison ML, Koch WM, Capone RB et al (2000) Evidence for a causal association between human papillomavirus and a subset of head and neck cancers. J Natl Cancer Inst 92:709–720
8. Chao KS, Wippold FJ, Ozyigit G et al (2002) Determination and delineation of nodal target volumes for head-and-neck cancer based on patterns of failure in patients receiving definitive and postoperative IMRT. Int J Radiat Oncol Biol Phys 53(5):1174–1184
9. Lindberg RD (1972) Distribution of cervical lymph node metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. Cancer 29:1446
10. Halperin EC, Wazer DE, Perez CA, Brady LW (2013) Perez and Brady's principles and practice of radiation oncology, 6th edn. Lippincott Williams & Wilkins, Philadelphia, p 207
11. Mutic S, Palta JR, Butker EK et al (2003) Quality assurance for computed-tomography simulators and the computed-tomography-simulation process: report of the AAPM Radiation Therapy Committee Task Group No. 66. Med Phys 30:2762–2792
12. Perez CA, Purdy JA, Harms WB et al (1994) Design of a fully integrated three-dimensional computed tomography simulator and preliminary clinical evaluation. Int J Radiat Oncol Biol Phys 30:887–897
13. ICRU Report 83: prescribing, recording, and reporting intensity modulated photon beam therapy (IMRT) (2010) J ICRU 10
14. www.rtog.org CT-based delineation of lymph node levels in the N0 neck: DAHANCA, EORTC, GORTEC, RTOG consensus guidelines. Accessed Jan 2009
15. Chi A, Nguyen NP, Tse W et al (2013) Intensity modulated radiotherapy for sinonasal malignancies with a focus on optic pathway preservation. J Hematol Oncol 6:4
16. Al-Mamgani A, Van Rooij P, Tans L et al (2013) Toxicity and outcome of intensity-modulated radiotherapy versus 3-dimensional conformal radiotherapy for oropharyngeal cancer: a matched-pair analysis. Technol Cancer Res Treat 12:123–130
17. Kam MKM, Leung S-F, Zee B et al (2007) Prospective randomized study of intensity-modulated radiotherapy on salivary gland function in early-stage nasopharyngeal carcinoma patients. J Clin Oncol 25:4873–4879
18. De Arruda FF, Zhung J, Narayana A et al (2006) Intensity modulated radiation therapy (IMRT) for treatment of oropharyngeal carcinoma: the MSKCC experience. Int J Radiat Oncol Biol Phys 64:363–373
19. Chao KS, Ozyigit G, Blanco AI et al (2004) Intensity-modulated radiation therapy for oropharyngeal carcinoma: impact of tumor volume. Int J Radiat Oncol Biol Phys 59:43–50
20. Lee N, Xia P, Quivey JM et al (2002) Intensity-modulated radiotherapy in the treatment of nasopharyngeal carcinoma: an update of the UCSF experience. Int J Radiat Oncol Biol Phys 53:12–22
21. Eisbruch A, Kim HM, Terrell JE et al (2001) Xerostomia and its predictors following parotid-sparing irradiation of head and neck cancer. Int J Radiat Oncol Biol Phys 50:695–704
22. Franceschini D, Paiar F, Meattini I et al (2013) Simultaneous integrated boost-intensity-modulated radiotherapy in head and neck cancer. Laryngoscope 123:E97–E103
23. Wu B, McNutt T, Zahurak M et al (2012) Fully automated simultaneous integrated boosted-intensity modulated radiation therapy treatment planning is feasible for head-and-neck cancer: a prospective clinical study. Int J Radiat Oncol Biol Phys 84:e647–e653
24. Weeks KJ, Arora VR, Leopold KA et al (1994) Clinical use of a concomitant boost technique using a gypsum compensator. Int J Radiat Oncol Biol Phys 30:693–698