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It is with great pleasure and excitement that I introduce the first edition of *Radiation Oncology Self-Assessment Guide*. This handbook was specifically designed to help facilitate one’s understanding and knowledge of the natural history, epidemiology, diagnosis, staging, treatment options, and treatment-related side effects of the various diseases encountered in radiation oncology practice by using a “flash card” format. The contributors to this guide are faculty and residents of the Department of Radiation Oncology at the Cleveland Clinic Taussig Cancer Institute. To help reinforce the reader’s knowledge of each area, including key studies and treatment recommendations, each answer has key reference(s) that can be reviewed.

This handbook covers the various disease sites, including head and neck cancers, central nervous system tumors, breast cancers, thoracic cancers, gastrointestinal cancers, genitourinary cancers, gynecologic cancers, lymphomas, and pediatric cancers. Each disease site is further subdivided into specific diseases or tumor types to help facilitate further self-assessment and reinforce one’s knowledge. This Guide uses an evidence-based approach when discussing treatment recommendations.

My sincere hope is that this self-assessment guide will provide a convenient and efficient method to enhance the understanding of radiation oncology, which is a dynamic and evolving medical specialty. By providing this unique “flash card” approach with citations of key references, I believe that *Radiation Oncology Self-Assessment Guide* will provide educational, actionable, and practical information that will enhance one’s ability to provide evidence-based, high-quality patient care. I wish to thank my many colleagues in the Department of Radiation Oncology at the Cleveland Clinic Taussig Cancer Institute whose valuable contributions made this learning resource possible and the many patients who inspire me to do better each day.

John Suh, MD
# HEAD AND NECK CANCERS

SHLOMO KOYFMAN AND MONICA SHUKLA

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### GENERAL QUESTIONS

**Question 1**
Is there a benefit to radiation intensification with altered fractionation when treating locally advanced squamous cell cancer of the head and neck (LA-HNSCC) with radiation alone?

---

**Question 2**
Is there a benefit to altered fractionation in the setting of concurrent chemotherapy?

---

**Question 3**
Is there a benefit to treating locally advanced squamous cell cancer of the head and neck (LA-HNSCC) with 6 fractions weekly rather than 5?

*Turn page to see the answers.*
**General Questions**

| Answer 1 | A significant benefit in local control (LC) for hyperfractionated radiotherapy (HRT) or accelerated concomitant boost (ACB) radiotherapy was shown in RTOG 90-03, a 4 arm phase III randomized trial that demonstrated ~10% improvement for either HRT (81.6 Gy/68 fx at 1.2 Gy BID) or ACB (72 Gy/42 fx at 1.8 Gy QD with an additional 1.5 Gy fx in the PM for the last 12 treatment days) compared to either standard RT (70 Gy/35 fx) or split course accelerated hyperfractionated radiotherapy (AHF-RT 67.2 Gy/42 fx at 1.6 Gy BID with a 2-week break after 38.4 Gy). Locoregional control (LRC) was ~55% in the former two groups compared to ~45% in the latter two groups. The MARCH meta-analysis also demonstrated a significant LRC advantage (7%) to both hyperfractionation and concomitant boost RT. While there was a modest survival advantage overall, hyperfractionated regimens produced an 8% OS advantage and outperformed other altered fractionation regimens (2%).


| Answer 2 | No. The RTOG 0129 protocol randomized patients with locally advanced HNC to standard fractionation (70 Gy/35 fx) with 3 cycles of cisplatin (d 1, 22, 43) vs ACB-RT (72 Gy in 42 fx) with 2 cycles of cisplatin (d 1, 22). There were no significant differences between the arms in terms of LRC or OS. Some hypothesize that a 3rd cycle of cisplatin offers similar benefit to hyperfractionation in this setting.


| Answer 3 | Yes. The phase III DAHANCA-6/7 trial randomized patients to 6 fractions a week (either an extra fraction on Saturday/Sunday, or a BID fraction given on Thursday or Friday of weeks 2–6) vs 5 fractions weekly, and demonstrated a LRC (70% vs 60%) and DFS advantage to this regimen. This forms the basis for the current RTOG standard accelerated regimen of 70 Gy in 35 fx/6 weeks with a BID fraction delivered on Thurs/Fri of weeks 2–6 being used in the RTOG 1016 trial. Of note, the DAHANCA-6/7 trial treated to 66–68 Gy with concurrent Nimorazole, and did not use concurrent chemotherapy.

| Question 4 | What are the indications to add systemic chemotherapy to definitive radiotherapy in head and neck cancer? |
| Question 5 | What induction chemotherapy regimen produces superior results to conventional cisplatin and 5-fluorouracil (PF) chemotherapy? |
| Question 6 | How is cetuximab dosed when used concurrently with radiotherapy, and what is the evidence supporting its use? |
| Question 7 | What structures are removed in a radical neck dissection?  
Modified radical neck dissection?  
Selective neck dissection? |
### Answer 4
Chemotherapy is indicated in stage III/IV disease based on several prospective randomized trials that demonstrated LRC, DFS and OS advantages with the addition of concurrent chemotherapy. This benefit was seen compared to standard fractionated RT (Adelstein) as well as hyperfractionated RT (Brizel). The MACH-NC meta-analysis also demonstrated a 4% 5-yr OS advantage overall, with the highest advantage seen in the setting of concurrent chemotherapy (35% vs 27%).


### Answer 5
The addition of docetaxel (T) to the PF backbone was investigated in two phase III randomized studies and demonstrated improved LRC and OS (not DM), compared to PF alone. In the Vermorken study, pts were treated with TPF X 4 cycles followed by RT alone. In the Posner trial, pts were treated with similar induction chemotherapy (3 cycles) followed by RT + concurrent weekly carboplatin.


### Answer 6
400 mg/m² loading dose 1 week prior to RT and 250 mg/m² weekly during RT. It was tested in a phase III study compared to RT alone and demonstrated superior outcomes, including 2-yr LRC (50% vs 41%) and 3-yr OS (55% vs 45%). There was no difference in rates of DM (16% vs 17%). 5-yr results confirmed these findings.


### Answer 7
In these procedures the following is removed:

- Radical neck dissection (RND) – removes levels I–V, sternocleidomastoid muscle (SCM), omohyoid muscle, IJV, EJV, CN XI, submandibular gland.
- Modified RND – removes levels I–V, but does not remove at least one of the following structures: SCM, IJV or CN XI.
- Selective neck dissection – does not remove all of levels I–V. There are several named subtypes of selective neck dissections, including:
  - supraomohyoid neck dissection – removes levels I–III.
  - lateral neck dissection – removes levels II–IV.

### Question 8
In non-nasopharyngeal head and neck IMRT planning, what is the most important planning organ at risk (OAR)?

### Question 9
In IMRT planning, what are the three different target constraints for the parotid glands?

### Question 10
In IMRT planning, what are the PTV coverage constraints generally mandated in RTOG studies?

### Question 11
What is the main benefit to IMRT planning seen in randomized studies compared to 2D/3D-CRT?
### Answer 8
No more than 0.03 cc of the spinal cord planning risk volume (PRV) can receive > 50 Gy. No more than 0.03 cc of the brainstem PRV can receive > 52 Gy. The PRV cord = cord + 5 mm in each dimension. The PRV brainstem = brainstem + 3 mm in each dimension. These supersede PTV coverage.


### Answer 9
> 95% of the PTV should receive prescription dose; no more than 20% of PTV will receive ≥ 110% of prescription dose (V110 ≤ 20%); no more than 5% of PTV will receive ≥ 115% of prescription dose (V115 ≤ 5%)


### Answer 10
Mean dose to at least one gland (contralateral to disease) ≤ 26 Gy; or at least 50% of one gland to < 30 Gy; or at least 20 cc of the combined volume of both parotid glands to < 20 Gy.


### Answer 11
IMRT has been studied in several phase III randomized trials and has been associated with reduced late grade ≥ 2 xerostomia (29%–40% for IMRT vs 80%–83% for 2/3D).


Question 12
What is the mechanism of action for amifostine and its primary side effects?
Is it beneficial in preventing xerostomia in patients treated with RT for H&N cancer?

Question 13
OROPHARYNGEAL CANCER
What is the risk of ipsilateral and bilateral nodal disease for a base of tongue (BOT) cancer?

Question 14
What is the risk of contralateral nodal involvement for a T1-2N0-1 well lateralized tonsil cancer?

Question 15
What are the most common assays to stain for HPV and p16?
Answer 12
Amifostine is a free radical scavenger. It can cause nausea, vomiting, hypotension and allergic reactions. The subcutaneous administration helps reduce these toxicities. It was tested in two phase III studies as an IV formulation. In the Brizel trial (RT vs RT + amifostine at 200 mg/m² 15–30 minutes prior to RT), it significantly reduced the rate of acute (78% vs 51%) and chronic (58% vs 34%) grade ≥ 2 xerostomia. In the Buentezel trial (RT + carboplatin + placebo vs RT + carboplatin + amifostine), there was no advantage to its use. It is FDA approved as a radioprotectant, but is not routinely used in many centers.


Answer 13
About 70% of patients with BOT cancer have ipsilateral LN disease and 20% have contralateral nodal involvement at presentation.


Answer 14
The risk is below 5%. In a retrospective series from PMH in which patients with T1-2N0 tonsil cancers were treated with unilateral irradiation, the incidence of contralateral neck failure was 3.5%


Answer 15
HPV is most often assessed using in situ hybridization techniques, which identifies the HPV DNA, while the p16 protein is most reliably identified through immunohistochemistry. About 20% of tumors that are p16+ are high risk HPV negative, making p16 a more sensitive assay.

Question 16
Which subsite of the H&N is most associated with HPV/p16-related SCC, and what is its prognostic significance?

Question 17
What are some of the epidemiological and tumor related differences between HPV + and HPV – disease?

Question 18
What is the risk of microscopic involvement of level IB and level V in patients with T1/T2, node + SCC-OP with a negative staging CT in these levels?

Question 19
What are the early oncologic and functional results of transoral robotic surgery (TORS) for oropharyngeal cancers?
Answer 16
Oropharyngeal cancers are most heavily associated with HPV/p16+, with 60–70% of these tumors being HPV + and/or p16+. Both HPV + and p16+ status is a powerful prognostic marker, and has been shown on subset analysis of the RTOG 0129 trial to demonstrate the following improved outcomes:

<table>
<thead>
<tr>
<th></th>
<th>3-yr OS</th>
<th>3-yr PFS</th>
<th>3-yr LRF</th>
<th>3-yr DM</th>
<th>2nd Primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPV +</td>
<td>82%</td>
<td>74%</td>
<td>14%</td>
<td>9%</td>
<td>6%</td>
</tr>
<tr>
<td>HPV –</td>
<td>57%</td>
<td>43%</td>
<td>35%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>&lt;.001</td>
<td>.23</td>
<td>.02</td>
</tr>
</tbody>
</table>


Answer 17
HPV + disease tends to occur in younger, Caucasian men with limited smoking histories. It has been associated with higher number of (oral) sexual partners and marijuana use. It more frequently also presents with smaller primaries (T1/2), more advanced nodal disease (N2/3) that are often cystic appearing. HPV – disease tends to occur in patients with heavier smoking and alcohol histories, and more commonly affects older, non-Caucasian men. It is more often presents as T3/4 disease.


Answer 18
Less than 5% overall. In one study of patients who underwent up-front bilateral neck dissections and had negative CT necks in levels IB and V, the rates of pathologically positivity were 3% and 1%, respectively. Based on this data, some are not routinely covering these nodal stations in patients who fit these criteria.


Answer 19
Early reports suggest excellent local control and functional outcomes. Results from the Univ. of Pennsylvania group suggest 98% local-regional control, with overall function returning to near baseline 1-year post treatment. About 80% of patients will require adjuvant RT with or without chemotherapy.

### Question 20
What are the subsites of the oral cavity?

### Question 21
What defines an oral cavity lesion as T4?

### Question 22
What factor is an independent prognostic factor predictive of local and regional recurrence in oral tongue cancer treated primarily with surgery?

### Question 23
For early stage tumors of oral tongue/floor of mouth being treated with definitive RT, what is the recommended treatment approach?
Answer 20
Mucosal lip, buccal mucosa, gingival (upper and lower), retromolar trigone, floor of mouth, mobile tongue (anterior to circumvallate papillae), hard palate.


Answer 21
T4 (Lip) – Invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face (i.e., chin or nose).
T4a (Oral cavity) – Invades through cortical bone, into deep (extrinsic) muscle of tongue, maxillary sinus, or skin of face.
T4b (all) – Involves masticator space, pterygoid plates, or skull base, or encases internal carotid artery.


Answer 22
Depth of invasion of the index lesion is prognostic. A depth of invasion of ≥ 5 mm has been shown to be prognostic for increased risk of regional failures.


Answer 23
A combination of EBRT and interstitial implant yields the best results. One large review demonstrated 33–60% failure with treatment with either EBRT or brachytherapy alone. EBRT dose of < 40 Gy with high proportion of brachytherapy (30–40 Gy IDR equivalent) yielded highest LC (92%). There was also a 44% neck recurrence rate when only the primary was treated.

### Question 24
**PARanasal SinUS**
What is the significance of Ohngren’s line and the Vidian canal in paranasal sinus tumors?

### Question 25
What is the rate of subclinical nodal involvement for patients with maxillary sinus and nasal cavity tumors?

### Question 26
How does orbital involvement affect the T stage of a maxillary sinus tumor?

### Question 27
What is the anticipated 5-yr LRC and OS for patients with paranasal sinus tumors treated with surgical resection and post-op RT?
Answer 24
Ohngren’s line is a theoretical diagonal plane extending from the medial canthus to the angle of the mandible. Tumors arising above this line (suprastructure) have a worse prognosis than those that arise from below this line (infrastructure). The pterygoid/vidian canal is a passage in the skull leading from just anterior to the foramen lacerum in the middle cranial fossa to the pterygopalatine fossa and is a potential route of spread from the maxillary sinus to the middle cranial fossa.


Answer 25
The overall rate for subclinical nodal involvement is about 15%, making elective nodal radiotherapy controversial. Some report significantly distinct rates of nodal involvement based on histology. While it approaches 30–40% for poorly differentiated squamous carcinomas, it is only 10% for mucoepidermoid and adenocarcinomas.


Answer 26
Involvement of the floor or medial wall of the orbit is a T3, of the anterior orbital contents is a T4a and of the orbital apex is a T4b.


Answer 27
5-yr LRC ranges from 70–90% for T1/2 tumors and 50–60% for T3/4 tumors. 5-yr DFS is 40–50% overall. Unresectable tumors portend significantly worse prognosis.

Question 28
What is the staging system for esthesioneuroblastoma, and how is it generally treated?
What are expected outcomes?

Question 29
What is the continuum of histologies of neuroendocrine differentiation that occur in the paranasal sinus/base of skull region, and their respective outcomes?

Question 30
What structures are encountered, and in what sequence, during endoscopic examination of the nasopharynx?
Answer 28
The Kadish system is most commonly used: Kadish A is limited to the nasal cavity, Kadish B extends to the paranasal sinuses, and Kadish C extends outside of the sinuses. Generally, these patients should be managed by aggressive surgical resection and postoperative radiotherapy, with expected 5-year DFS of 80–90%. Recent reports suggest a high rate of nodal failure (27%) when not electively treated.


Answer 29
There are at least four distinct histologies with variable outcomes as illustrated by one of the larger series in this disease from MD Anderson Cancer Center with median f/u of almost 7 years. The data is summarized in tabular form:

<table>
<thead>
<tr>
<th>Histology</th>
<th># of Pts</th>
<th>Treatment*</th>
<th>5-yr LC</th>
<th>5-yr RC</th>
<th>5-yr DMFS</th>
<th>5-yr OS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esthesioneuroblastoma</td>
<td>31</td>
<td>Local only – 81%</td>
<td>96%</td>
<td>92%</td>
<td>100%</td>
<td>93%</td>
</tr>
<tr>
<td>Sinonasal undifferentiated carcinoma</td>
<td>16</td>
<td>Local + CTX – 63%</td>
<td>79%</td>
<td>84%</td>
<td>75%</td>
<td>63%</td>
</tr>
<tr>
<td>Neuroendocrine carcinoma</td>
<td>18</td>
<td>Local + CTX – 67%</td>
<td>72%</td>
<td>87%</td>
<td>86%</td>
<td>64%</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
<td>7</td>
<td>Local + CTX – 71%</td>
<td>67%</td>
<td>56%</td>
<td>25%</td>
<td>29%</td>
</tr>
</tbody>
</table>

*Local treatment consisted of surgery, or RT, or both; CTX = chemotherapy; DMFS = distant metastasis free survival; LC = local control; RC = regional control


Answer 30
Upon entering the nasopharynx, the lateral walls first reveal the torus tubarius, a prominence in the cartilaginous portion of the eustachian tube, followed by the eustachian tube orifice, which the torus surrounds. Posterolateral to these structures is Rosenmuller’s fossa (i.e., pharyngeal recess), the most common site of origin for NPC.

Question 31
What is the TNM staging for NPC according to the AJCC 7th edition?

Question 32
What are the different histologic subtypes of NPC?
What risk factors are associated with each?
**Answer 31**

Several changes were made to the staging system for NPC in the revised 7th edition of the staging manual. Note than N staging for NPC is unique. An alternative staging system used in Asia is the Ho staging system.

<table>
<thead>
<tr>
<th>T1</th>
<th>Confined to the nasopharynx or extends to oropharynx and/or nasal cavity w/o parapharyngeal extension</th>
<th>N1</th>
<th>≤ 6 cm: unilateral cervical above the SCV fossa, or unilat/bilat RP nodes</th>
<th>I</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Tumor with parapharyngeal extension</td>
<td>N2</td>
<td>≤ 6 cm: bilateral cervical LNs, above SCV fossa</td>
<td>II</td>
<td>T2T1-2</td>
<td>N0N1</td>
<td>M0M0</td>
</tr>
<tr>
<td></td>
<td>Tumor involves bony structures of skull base and/or paranasal sinuses.</td>
<td>N3a</td>
<td>&gt; 6 cm in dimension</td>
<td>III</td>
<td>T3T1-3</td>
<td>N0-2N2</td>
<td>M0M0</td>
</tr>
<tr>
<td>T4</td>
<td>Intracranial extension and/or involvement of cranial nerves, infratemporal fossa, masticator space, hypopharynx, or orbit</td>
<td>N3b</td>
<td>Supraclavicular fossa</td>
<td>IVA</td>
<td>T4</td>
<td>N0-2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>M1</td>
<td>Distant metastases</td>
<td>IVB</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td></td>
</tr>
</tbody>
</table>


**Answer 32**

Type 1 (*sporadic form*): keratinizing squamous cell carcinoma—these are histologically similar to other head and neck SCC and accounts for 20% in North America and is associated with alcohol and tobacco use. Presence of keratin has been associated with reduced local control and survival.

Type 2: Non-keratinizing carcinoma (associated with Epstein Barr Virus)

- Type 2a: differentiated – formerly WHO Type II – 30–40% in North America
- Type 2b: undifferentiated – formerly WHO Type III (lymphoepithelial carcinoma—endemic form) – 40–50% in North America.
**Question 33**
What are common clinical presentations for NPC?

What percentage of patients have associated lymphadenopathy?

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**Question 34**
What is the general treatment paradigm for early stage nasopharyngeal lesions?

What are the approximate numbers for LRC and OS?
Answer 33

The most common presenting feature is a painless neck mass. 85–90% present with cervical lymphadenopathy with 50% having bilateral involvement. Other presentations can be refractory otitis media, decreased hearing, nasal obstruction (causing altered voice), epistaxis, referred ear pain, and cranial neuropathies. Multiple cranial nerves can be affected in NPC, and some are associated with the following clinical syndromes:

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Cranial Nerves</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jacod's (petrosphenoid)</td>
<td>Superior Orbital Fissure (III, IV, V1, VI) Foramen Rotundum (V2) Foramen Ovale (V3) Foramen Lacerum – pathway to these CN</td>
<td>Unilateral trigeminal neuralgia, ptosis, ophthalmoplegia, blindness</td>
</tr>
<tr>
<td>St. Villaret's (retroparotid)</td>
<td>Compression of CN IX–XII via retropharyngeal nodes</td>
<td>Dysphagia, abnl taste post 1/3 tongue, hoarseness, anesthesia of mucous membranes, hemiparesis of soft palate, Horner’s syndrome, and atrophy of SCM, trapezius &amp; tongue</td>
</tr>
<tr>
<td>Vernet’s (jugular foramen)</td>
<td>CN IX–XI via invasion of jugular foramen</td>
<td>Paralysis of soft palate, tonsils, pharynx, and hoarseness</td>
</tr>
</tbody>
</table>


Answer 34

Surgery is generally not part of the treatment strategy of NPC aside from diagnosis, biopsy, and neck dissection for residual disease. For T1N0 disease, RT alone results in excellent LC (75–90%) and OS (70–80%). The RT target includes bilateral elective nodes (levels IB-V, RP) with a nasopharyngeal boost, delivered with conformal EBRT or brachytherapy. More recently, IMRT has been used with superior ability to spare critical intracranial structures. The management of T2N0 patients is controversial as some advocate RT alone. NCCN guidelines recommend CRT.

| Question 35 | What is the recommended treatment strategy for locally-advanced NPC?  
What evidence supports this approach? |
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 36</td>
<td>What is the role of induction or adjuvant chemotherapy following definitive chemoradiotherapy or radiotherapy for advanced stage NPC?</td>
</tr>
<tr>
<td>Question 37</td>
<td>What are the recommended dose constraints for the optic nerves/chiasm and brainstem when treating a NPC with IMRT?</td>
</tr>
</tbody>
</table>
Answer 35
Chemoradiotherapy is the mainstay of treatment for locally advanced disease. Several Phase III studies confirmed a LC and OS advantage with the addition of chemotherapy. The Intergroup 00-99 Al-Sarraf study randomized patients with Stage III or IV NPC to RT (70 Gy in 2 Gy/fx) vs chemoRT (70 Gy + concurrent cisplatin (100 mg/m² on days 1, 22, 43) × 3 + adjuvant cisplatin/5-FU × 3 cycles). The trial closed prematurely due to the highly significant advantage to chemotherapy for both 5-yr PFS (58% vs 29%) and OS (67% vs 37%). A duplicative study from Singapore confirmed this finding, as did phase III studies from Hong Kong, and Taiwan, although these latter 2 trials did not use adjuvant chemotherapy.


Answer 36
The use of induction chemotherapy prior to definitive RT has been tested in several trials in advanced stage NPC and has failed to demonstrate a survival benefit. There are no trials that have compared standard concurrent chemoradiotherapy +/- adjuvant chemotherapy. Although adjuvant chemotherapy was given on the experimental arm of the INT-0099 trial, only 55% of patients were able to complete this portion of their therapy. Other studies that did not use adjuvant chemotherapy appear to produce similar results achieved in the INT-0099 trial as well. This question is currently being studied by the Hong Kong Nasopharyngeal Cancer Study group, in which high risk patients (residual EBV DNA following the completion of CRT) are being randomized to adjuvant chemotherapy vs observation.


Answer 37
RTOG 0615 recommends restricting the dose to the actual optic nerve/chiasm to a maximum dose of 50 Gy, and the planning risk volume (PRV) to a maximum dose of 54 Gy. The actual brainstem should be restricted to a maximum dose of 54 Gy, while 1% for the PRV brainstem can receive 60 Gy. PRVcord = cord + 5 mm in each direction. PRVoptic nerves/chiasm = optic nerves/chiasm + at least 1 mm in each direction. Of note, CTV expansions can be as little as 1 mm when disease abuts but does not invade the brainstem.

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**Question 38**
What radiation related factor other than total dose significantly influences the risk of optic neuropathy?

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**Question 39**
What is the incidence of LN metastases in glottic cancer, stratified by T stage?

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**Question 40**
Is there any randomized evidence supporting altered fractionation in T1 SCC of the glottis?

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**Question 41**
What is the anticipated local control for a T2N0 glottic tumor?

Is there any role for altered fractionation in this disease?
Answer 38
A study from the University of Florida found that dose per fraction has been shown to significantly correlate with rates of optic neuropathy. The rate of symptomatic optic neuropathy (20/100 visual acuity or worse) was 0% for doses of < 59 Gy. For doses of ≥ 60 Gy, the rate of optic neuropathy was 11% when the dose per fraction was kept below 1.9 Gy vs 47% with dose per fraction of ≥ 1.9 Gy.


Answer 39
T1: 1%; T2: 3%; T3: 15–20%; T4: 20–30%


Answer 40
Yes. A single institution Japanese randomized trial examined 180 patients with T1N0 glottic cancer and found that 2.25 Gy/fx (to total dose of 56.25–63 Gy) improved 5-year LRC from 77% to 92%, compared to conventional fractionation of 2 Gy/fx (to total dose of 60 or 66 Gy). Other outcomes were similar.


Answer 41
In general T2N0 tumors that exhibit impaired mobility and/or subglottic extension have inferior outcomes that those with only supraglottic extension. A large retrospective study by Le, et al found 5-yr local control of 79% vs 45% for patients without and with impaired mobility, respectively, and 77% vs 58% for those without and with subglottic extension, respectively. That same study also found patient treated with ≥ 65 Gy, ≥ 2.25 Gy/day and in ≤ 43 days had improved local control. As such, RTOG 95–12 was a randomized phase III trial in T2N0 glottic tumors comparing 70 Gy/35 fx to 79.2 Gy at 1.2 Gy BID as a means of dose escalating RT to improve LC. The study was slightly underpowered, but the results demonstrated trends towards benefit in 5-yr LC (79% vs 70%, p = .11) and 5-yr DFS (51% vs 37%, p = .07). As such, many advocate either an accelerated schedule, or the addition of chemotherapy for poor risk T2N0 tumors.


Question 42
What are the classic field borders for T1N0 glottic tumors?
T2N0?

Question 43
What was the schema of the phase III VA larynx trial and what was its clinical significance?

Question 44
In RTOG 91–11, a three arm randomized trial between different larynx preservation regimens, what were the treatment arms?
What regimen achieved the best results?

Question 45
For patients who fail organ preservation, what is the rate of successful salvage laryngectomy?
What is the most common postoperative complication?
Answer 42
For T1 tumors, use opposed laterals with 5 × 5 – 6 × 6 cm field. Upper border 0.5–1 cm above thyroid notch, posterior border 1 cm behind thyroid cartilage, inferior border at the bottom of the cricoid cartilage, and 1 cm fall off anteriorly. For T2 tumors, elective nodal irradiation is controversial but generally not used unless there is significant supra/subglottic extension or bulky T2b disease. Per RTOG 95–12, no elective nodal irradiation for T2 tumors; may cone down posteriorly off the arytenoids if the posterior 1/3 of the vocal cord is not involved by tumor. Bolus (2–5 mm) may be used over the anterior neck skin to ensure complete coverage of lesions involving the anterior 1/3 of the vocal cords or the commissure.


Answer 43
It was a phase III trial that randomized patients with operable stage III/IV larynx cancer to total laryngectomy + postop RT vs induction cisplatin and 5-FU with evaluation after 2 cycles. Patients with a partial response (54%) or a complete response (31%) went on to receive one more cycle of chemotherapy followed by RT alone (66–76 Gy). Patients who failed to respond were treated with TL + postop RT. Of note, 57% of pts had vocal cord fixation. OS were equivalent (68%); LRC (92% vs 80%) was better in the surgical arm; DM was lower in the conservation arm (11% vs 17%). Laryngectomy free survival was 64% in the conservation arm.


Answer 44
The three arms were RT alone (70 Gy) vs induction cisplatin 100 mg/m² + 5-FU C.I. 1000 mg/m² q3 weeks × 3 cycles. Followed by RT (if CR or PR) or laryngectomy if poor response vs concurrent cisplatin 100 mg/m² q3 weeks + RT. Results shown in the table. Concurrent CRT achieved the best results.

<table>
<thead>
<tr>
<th>Arm</th>
<th>5-yr LFS</th>
<th>5-yr LP</th>
<th>5-yr LRC</th>
<th>DM</th>
<th>5-yr DFS</th>
<th>5-yr OS</th>
<th>5-yr CSD</th>
</tr>
</thead>
<tbody>
<tr>
<td>1: I + RT</td>
<td>44.6%</td>
<td>70.5%</td>
<td>54.9%</td>
<td>14.3%</td>
<td>38.6%</td>
<td>59.2%</td>
<td>43.8%</td>
</tr>
<tr>
<td>2: CRT</td>
<td>46.6%</td>
<td>83.6%</td>
<td>68.8%</td>
<td>13.2%</td>
<td>39%</td>
<td>54.6%</td>
<td>34%</td>
</tr>
<tr>
<td>3: RT</td>
<td>33.9%</td>
<td>65.7%</td>
<td>51%</td>
<td>22.3%</td>
<td>27.3%</td>
<td>53.5%</td>
<td>58.3%</td>
</tr>
</tbody>
</table>

*p*-value 0.011
0.0029 (2 vs 1), 0.0018 (2 vs 1), 0.06, 0.016 (1 vs 3), NS 0.0007 (2 vs 3)
0.0017 (2 vs 3) 0.0005 (2 vs 3) 0.0005 (2 vs 3)


Answer 45
A subset analysis of RTOG 91–11 revealed that while more patients in the RT alone arm required salvage laryngectomy as compared to the induction + RT and the CRT arms, their survival after salvage laryngectomy were similar. LRC was achieved in 75–90% of patients with 2-yr OS about 70%. Most common complication was pharyngocutaneous fistula (15–30%).

Question 46
What are classic contraindications to larynx preservation with definitive chemoradiotherapy?

Question 47
What are indications to boost the tracheal stoma after a total laryngectomy?

Question 48
Have organ preservation strategies been studied in hypopharyngeal cancer?

Question 49
Is there evidence that supports the use of 60 Gy as the routine postoperative dose in head and neck cancer?
Answer 46
Patients with bulky T4 tumors had poor response rates to induction chemotherapy on the VA larynx cancer study, and over half of them required salvage laryngectomy. Based on this finding, patients with bulky T4 tumors (i.e., invaded cartilage and/or > 1 cm of the tongue) were excluded from RTOG 91–11 trials and are traditionally treated with TL + postop (CRT). There are some published experiences with reasonably good outcomes for these patients with conservation approaches, but NCCN guidelines and ASCO consenus statement still recommend surgery as the primary mode of therapy.


Answer 47
The tracheal stoma should be boosted to 60 Gy if there is evidence of subglottic extension, tumor invasion into the soft tissues of the neck, positive tracheal margin, or an emergency tracheostomy through tumor.


Answer 48
Yes. A prospective randomized trial following the same schema as the VA larynx trial was tested by the EORTC for stage II–IVB cancers of the pyriform sinus or AE fold. LRC and OS were similar between the two groups of patients. The organ preservation arm demonstrated significantly lower rates of distant failure (25% vs 36%). The rate of functional larynx preservation at 5 yrs was 35%.


Answer 49
Yes. A phase III PRT (RTOG 73–03) compared 50 Gy preop RT to 60 Gy postop RT. This demonstrated a LRC advantage to the postop arm (58% vs 70%) without impacting survival. There is also prospective data that confirmed that a dose of > 57.6 Gy correlated to improved local control compared to lower doses.

Question 50
What minimum postoperative dose is recommended for dissected LN with + ECE?
Based on what evidence?

Question 51
Is there a benefit to altered fractionation in the postoperative setting?

Question 52
What are the indications and evidence for the addition of concurrent chemotherapy to postoperative radiotherapy in head and neck cancer?
Answer 50

A randomized trial was conducted in the 1980s that randomized low risk patients (1 risk factor) to 57.6 Gy (1.7 Gy/fx) vs 63 Gy and high risk patients (> 1 risk factor and/or ECE) to 63 Gy vs 68 Gy. There was no statistically significant improvement to dose escalation in general. However, patients with ECE that were treated with ≤ 57.6 Gy had inferior LC than those treated with ≥ 63 Gy (2-yr LRC 52% vs 74%, respectively).


Answer 51

A multi-institutional randomized trial that compared 63 Gy in 7 weeks vs 63 Gy in 5 weeks using a concomitant boost RT technique did not show a significant LRC or DFS benefit to altered fractionation in the postoperative setting for patient with high risk disease.


Answer 52

Two phase III trials were conducted comparing postop RT vs postop CRT. Chemotherapy was cisplatin 100mg/m² q3wk × 3. The EORTC 22931 trial demonstrated significantly improved LC (82% vs 69%), PFS (47% vs 36%) and OS (53% vs 40%) at 5 yrs with CRT. RTOG 95–01 demonstrated a LC (82% vs 72%) and DFS advantage with no OS advantage at 2 yrs. Eligibility criteria differed between studies. While the RTOG study included only those patients with + ECE, + margins, or ≥ 2 LN+, the EORTC trial also included patients with other factors including T3/4, +PNI, +LVSI or level IV/V nodes for oral cavity/oropharynx tumors. A pooled analysis of these two trials that compared RT alone to RT + cisplatin demonstrated that ECE and positive margins were the only two scenarios in which the addition of concurrent chemotherapy improved LC and OS.


<table>
<thead>
<tr>
<th>Question 53</th>
<th>SALIVARY GLAND TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the most common type of benign salivary gland tumor?</td>
<td></td>
</tr>
<tr>
<td>Where is it usually found?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 54</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>What are the common malignant salivary gland tumor histologies?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 55</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the most common histologic subtype of cancer in the submandibular or minor salivary glands?</td>
<td></td>
</tr>
<tr>
<td>What is unique about its pattern of spread and natural history?</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 56</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the proportion of benign and malignant lesions found in parotid glands?</td>
<td></td>
</tr>
<tr>
<td>Submandibular glands?</td>
<td></td>
</tr>
<tr>
<td>Minor salivary glands?</td>
<td></td>
</tr>
</tbody>
</table>
### Answer 53

Pleomorphic adenoma is the most common benign salivary gland tumor and comprises 75% of parotid tumors. Other benign tumors include Warthin’s tumor (papillary cystadenoma lymphomatosum), Godwin’s tumor (benign lymphoepithelial lesions associated with Sjogren’s syndrome) and oncocytomas.


### Answer 54

Mucoepidermoid carcinoma is the most common malignant histology. It most commonly presents in the parotid gland. Other common malignant histologies include adenoid cystic carcinoma and adenocarcinoma. Acinic cell carcinoma is a common low grade malignant histology. Salivary gland tumors can be either low or high grade, which is a factor that significantly influences treatment approaches. While squamous cell carcinomas of the parotid is a recognized entity, these are more commonly found to be metastases from cutaneous SCC of the skin.


### Answer 55

Adenoid cystic carcinoma. It tends to infiltrate and spread along nerves. Perineural invasion is common, especially for higher grade tumors, and is an indication to electively target the facial nerve up to the base of skull, including its origin from the stylomastoid foramen. These tumors tend not to spread to lymph nodes, and do not require elective nodal irradiation. They are also notorious for late relapses (> 10–20 yrs), most often in the form of lung metastases (40% lifetime risk).


### Answer 56

In general, the smaller the gland, the more likely a tumor it is to be malignant. While only 25% of parotid lesions are malignant, about 50% of submandibular gland lesions, 75% of minor salivary gland lesions, and nearly all sublingual gland lesions are malignant.

<table>
<thead>
<tr>
<th>Question 57</th>
</tr>
</thead>
<tbody>
<tr>
<td>When is sacrifice of the facial nerve indicated in resection of a malignant parotid gland cancer?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 58</th>
</tr>
</thead>
<tbody>
<tr>
<td>What are the indications for post operative radiotherapy in resected salivary gland tumors?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 59</th>
</tr>
</thead>
<tbody>
<tr>
<td>What is the evidence for benefit to adjuvant radiotherapy in salivary gland cancer?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Question 60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is there any advantage to the use of fast neutron therapy in locally advanced/unresectable salivary gland tumors?</td>
</tr>
</tbody>
</table>
Answer 57
Preoperative weakness or paralysis of the facial nerve usually indicates tumor involvement, and in these instances, the main trunk or the involved nerve branches may have to be sacrificed. The nerve or its involved branches should also be sacrificed if there is intra-operative evidence of gross invasion or microscopic infiltration of the nerve by tumor, even in the presence of normal preoperative facial nerve function. If the nerve appears both clinically and intraoperatively uninvolved, it should be preserved even for tumors involving the deep lobe of the gland requiring a total parotidectomy.


Answer 58
In general, postoperative RT is indicated for close or positive margins, lymph node metastases, locally advanced disease, bone or nerve involvement, recurrent disease, or a combination of other adverse features, such as high nuclear grade, perineural invasion, and lymphovascular space invasion.


Answer 59
While there are no randomized data, several large institutional series have demonstrated 20–40% improvements in local control and DFS with the addition of RT to surgery alone. A match-pair analysis from MSKCC, for example, found that patients with stage III/IV disease, positive lymph nodes, or high grade tumors had improved local control and, in some instances, improved survival with the addition of adjuvant radiotherapy, while those with low grade, or early stage (I/II) disease did not appear to benefit.


Answer 60
A randomized trial by the RTOG/MRC that compared photon/electron therapy vs fast neutron therapy demonstrated significantly improved local control (56% vs. 17%) in the fast neutron therapy arm, but distant metastases and overall survival in this arm had inferior outcomes. Severe late side effects were noted in long-term survivors. As such, it has fallen out of favor. However, dose escalation with proton and carbon ion therapies are still being investigated.

Question 61
Are there discrete molecular phenotypes that are histology specific in salivary gland tumors? Does this impact treatment options?

Question 62
MELANOMA
Is there an advantage to hypofractionation in treating melanoma with radiotherapy?

Question 63
Is there randomized evidence supporting the use of adjuvant RT after resection of melanoma? What is the benefit of RT in this setting?
Answer 61
Yes. The following table summarizes the molecular profiles of several common malignant histologies:

<table>
<thead>
<tr>
<th>Histology</th>
<th>EGFR</th>
<th>HER2</th>
<th>c-kit</th>
<th>VEGF</th>
<th>Androgen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucoepidermoid</td>
<td>40%</td>
<td>25–35%</td>
<td>Rare</td>
<td>50%</td>
<td>rare</td>
</tr>
<tr>
<td>Adeno/Adenocarcinoma</td>
<td>30–40%</td>
<td>20–30%</td>
<td>Rare</td>
<td>65%</td>
<td>15–40%</td>
</tr>
<tr>
<td>Duct Carcinoma</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adenoid Cystic</td>
<td>20%</td>
<td>rare</td>
<td>80–90%</td>
<td>85%</td>
<td>rare</td>
</tr>
</tbody>
</table>

Inhibitors of these various targets are currently being investigated in the metastatic setting, and some early reports suggest efficacy in a significant proportion of patients.


Answer 62
It is unclear. In the definitive setting, large older retrospective series suggested doses of > 4 Gy per fraction significantly improved complete response rates (59% vs 33%). RTOG 8305 randomized patients with measurable melanoma to 50 Gy in 20 fx daily, vs 32 Gy in 4 weekly fractions of 8 Gy. Overall, there was no difference in response rates between the two regimens. In the postoperative setting, MDACC pioneered a regimen of 30 Gy in 5 fractions given twice weekly, which yielded 5-yr LRC of 88%. However, other retrospective series report equivalent efficacy with hypofractionated and conventionally fractionated regimens.


Answer 63
Based on a previous phase II study, the Trans-Tasman Radiation Oncology Group (TROG) performed a phase III randomized study comparing adjuvant nodal RT (48 Gy in 20 fx) vs observation in patients who had recurrent melanoma with ≥ 1 parotid, ≥ 2 cervical or axillary or ≥ 3 groin positive nodes; or extra nodal spread of tumour; or minimum metastatic node diameter of 3 cm (neck or axilla) or 4 cm (groin). There was a significant reduction in regional failure from 31% to 18%. OS were similar between arms.

Question 64
What is the rate of grade 3 lymphedema when radiating the axilla postoperatively for melanoma?
What is the risk for the groin?

Question 65
What is the role of sentinel lymph node biopsy (SLNB) in intermediate thickness melanoma?

Question 66
What margin of resection is recommended for Merkel cell carcinoma (MCC)?
What is the role of sentinel LN biopsy (SLNB)?

Question 67
What are the indications for adjuvant radiotherapy in Merkel cell carcinoma (MCC)?
What benefit does RT offer?
**Answer 64**
In the phase II TROG series, the risk of grade 3 lymphedema was 9% for the axilla and 19% for the groin.


**Answer 65**
A phase III randomized controlled study compared SLNB + completion LND if SLN+ for intermediate thickness melanoma vs observation + complete LND at nodal relapse. 5-yr DFS was significantly better with SLNB (78% vs 73%), but no difference in OS. SLN+ was a powerful predictor of outcome and its removal slowed progression of disease, but did not affect overall survival.


**Answer 66**
Wide margins of 2 cm is generally recommended as these tumors have a high rate of recurrence. A recent study found that SLNB was feasible and the rate of sentinel lymph node positivity was at least 15–20% in all groups of patients. SLN positivity was significantly associated with the clinical size of the lesion, greatest horizontal histologic dimension, tumor thickness, mitotic rate, and histologic growth pattern. SLNB is considered standard in MCC.


**Answer 67**
Indications for adjuvant RT include size > 2 cm, close/positive margins, LVSI, LN+ disease, LN not stages by SLNB or LND. A large review found that nodal recurrence rates range between 40–50% in the unsampled primary echelon nodal basin. A recent SEER analysis demonstrated an overall survival advantage for adjuvant RT. For unresectable tumors, definitive RT is appropriate, as MCC is a radiosensitive tumor.

**Question 68**
What dose of RT is used for adjuvant radiotherapy to the tumor bed?
To lymphatic region?
For unresectable disease?

**Question 69**
Has adjuvant chemotherapy been investigated for Merkel cell carcinoma (MCC)?

**Question 70**
What is the workup for a patient that presents with a squamous cell carcinoma metastatic to a cervical lymph node, without evidence of an obvious primary?
Answer 68
For the primary tumor bed, NCCN guidelines recommend a dose of 50–56 Gy for negative margins, 56–60 Gy for close/microscopically positive margins, and 60–66 Gy for grossly positive margins or unresectable disease. For uninvolved nodal basin, a dose of 46–50 Gy is recommended with higher doses used for gross nodal disease, or ECE.


Answer 69
Yes. A phase II study (TROG 96–07) investigated adjuvant RT (50 Gy/25 fx) with concurrent carboplatin/etoposide for patients with 1 high risk feature (recurrence after initial therapy, involved nodes, size > 1 cm, gross residual disease, or occult primary with nodes). 3-yr LF, DM, OS were 25%, 24%, and 76%, respectively, and compared favorably to historical controls.


Answer 70
First, an FNA of the cervical LN should be performed to confirm the diagnosis of SCC. Then either a CT neck with contrast, or a PET/CT should be done. While not universally accepted, PET/CT is commonly used in this situation. One study found that it detected a primary site in 25% of patients in whom a primary had not been identified. If imaging studies are unrevealing, an EUA with direct nasopharyngolaryngoscopy and directed biopsies are then performed. In the absence of any putative primary site, biopsies are taken of the nasopharynx, BOT, and pyriform sinuses. Generally, bilateral tonsillectomies are also performed. Importantly, an isolated SCV node most likely points to a primary originating below the clavicles (e.g., esophagus, lung) rather than a true head and neck primary and should be worked up as such including bronchoscopy, esophagoscopy and CT chest, abdomen and pelvis.

### Question 71
In what percentage of unknown primary H&N SCC is a primary site found? What is the most common site?

### Question 72
What pathologic stains can be done to help identify a primary tumor site?

### Question 73
What is the recommended adjuvant therapy for a patient with an unknown primary with a single 2.5-cm level II node, found to have no additional LNs on comprehensive neck dissection and no ECE?

### Question 74
What areas are targeted in definitive radiation for an unknown primary with multiple left-sided level II and III lymph nodes, the largest measuring 4.5 cm?
**Answer 71**
In about 50–60% of cases, a primary site will be identified after full work-up. The base of tongue and tonsils account for ~80% of primary sites of unknown primary origin.

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**Answer 72**
For squamous histology, a positive EBV stain is highly suggestive of a NPC, while a positive HPV or p16 stain is highly suggestive of an oropharyngeal primary. With this information, fields can be modified to exclude the larynx/hypopharynx from the potential primary mucosal site targets, allowing for greater normal tissue sparing. For adenocarcinoma histology, calcitonin and thyroglobulin stains can be used to help identify a thyroid primary site.

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**Answer 73**
Observation is generally recommended in such a situation. This situation accounts for about 25% of unknown primary cases. The rate of expected failure in the neck is < 10%, with a 5% rate of a primary tumor manifestation in the future. For “all comers” with unknown primary SCC-HN, the mucosal emergence rate is closer to 15%.

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**Answer 74**
Management options include ipsilateral neck dissection, followed by comprehensive radiation vs definitive chemoRT. Typically, comprehensive radiation is used which includes bilateral cervical nodes, as well as putative primary sites (nasopharynx, oropharynx, hypopharynx, larynx). However, with a patient presenting with level II LN, there is mature data from the University of Florida in which the larynx/hypopharynx are not targeted, and spared with a traditional larynx block in an AP SCV field. With this approach, there are virtually no failures in either of those potential primary sites. Importantly, this data applies to a cohort of patients where HPV/p16 status was unknown. For patients presenting primarily with level III and/or IV LN, then the larynx and hypopharynx would be targeted as a putative mucosal site.

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Answer 75
While somewhat controversial, several studies have shown that unilateral RT results in inferior outcomes. One study showed that rates of contralateral neck failure (44% vs 14%) and mucosal primary site failure (44% vs 8%) were significantly higher for patients treated with unilateral RT.


Answer 76
Histology. Metastatic adenocarcinoma to cervical LN without a clear primary site is managed differently than a squamous cell carcinoma. Firstly, up-front neck dissection is favored over definitive (chemo) radiotherapy. Also, parotidectomy is advised as part of a comprehensive neck dissection for these patients. There are also additional putative primary sites to consider (e.g., salivary gland, paranasal sinuses) which can alter the radiation plan and argue against comprehensive radiation including potential mucosal sites.


Answer 77
Choice of dose/fractionation regimen depends on size and location of tumor as well and desired cosmetic outcome. Typically, the more protracted regimens yield improved long term cosmesis. NCCN recommended regimens include 64 Gy/32 fx, 55 Gy/20 fx, 50 Gy/15 fx and 35 Gy/5 fx. Other hypofractionated regimens include 40 Gy/10 fx and 20 Gy/2 fx.


Answer 78
Often superficial/orthovoltage therapy or electron beam therapy is used. Superficial (50–150 kv) and orthovoltage (150–500 kv) have D90 at 5 mm and 2 cm, respectively. Advantages over electrons include maximum dose at skin surface, ability to use smaller fields as there is less beam constriction at depth, and less penetration through eye shield. Electrons are typically prescribed to ensure the 90% IDL covers the deepest extent of the tumor. Wider margins (1–2 cm) are typically needed as high isodose lines constrict at depth. Advantages of electrons are widespread availability and sharper dose fall off. To minimize scatter into adjacent structures, a lead shield can be placed on patient’s skin.
Question 79
Is there any evidence that higher dose/fraction is associated with improved control rates?

Question 80
When is adjuvant RT indicated after MOHS resection of a BCC/SCC?

Question 81
What factors predict for LN involvement in cutaneous SCC of the H&N?

Question 82
What are the primary thyroid cancer histologies and their respective incidence?
Answer 79

Yes. Some retrospective series indicate that doses of > 2 Gy per fraction are associated with improved outcomes for definitive RT, even with doses above 60 Gy. This does not apply to adjuvant RT.


Answer 80

NCCN guidelines recommend adjuvant EBRT in cases with positive margins, extensive perineural or large nerve involvement, or recurrent disease. One large retrospective study showed that failure rates were significantly higher for patients treated with surgery and postop RT when there was clinical nerve involvement (symptomatic/radiographic) as opposed to only pathologic perineural involvement (5-yr LC 57% vs 90%). For the latter category, BCC seemed to do better than SCC (5-yr OC 97% vs 84%). As such, some advocate for adjuvant RT for pathologic PNI of SCC, while BCC with pathologic PNI only can be observed. Similarly, some argue that microscopic positive margins can be observed for BCC as the recurrence rate is only ~30% and usually highly salvageable with repeat surgery.


Answer 81

Higher grade lesions, those with LVSI, those with invasion beyond the subcutaneous fat, larger lesions and recurrent lesions are associated with significant risks of nodal metastases. In one study, 37% of lesions > 4 cm and 31% of lesions invading more than 8 mm were LN+. Consider superficial parotidectomy +/- LN dissection in patients with these high risk features undergoing surgical management.


Answer 82

The most common histology is papillary (60%), followed by follicular (25%), medullary (5%), anaplastic (2%). Hurthle cell carcinoma (2%) is a rare form morphologically similar to follicular but with marked (> 75%) hypercellularity.

Question 83
What is the incidence of LN + disease in the various histologies?
What is their respective expected 10-yr OS?

Question 84
What stage is a 42 yo woman with a 3-cm thyroid tumor with metastasis to a level VI (Delphian) LN?

Question 85
What are the indications for post-thyroidectomy I-131 ablation?
Answer 83
Papillary cancer has a 30% risk of LN + and a 10-yr OS of 90–95%. Follicular cancer has a 10% risk of LN + disease and a slightly lower 10-yr OS of 85–90%. Medullary thyroid cancer has a worse survival of 80%, while anaplastic cancer is almost uniformly fatal.


Answer 84
It depends on histology. For a papillary or follicular tumor, this would be T3N1M0, stage I disease. For a medullary thyroid cancer, it would be T3N1M0, stage III, and for anaplastic thyroid cancer, it would be T4aN0M0, stage IVa. The staging scheme is as follows.

- Papillary or follicular (< 45 years)
  - Stage I – Any T, Any N, M0
  - Stage II – Any T, Any N, M1
- Papillary or follicular (≥ 45 yo) or medullary (any age)
  - Stage I – T1 N0 M0
  - Stage II – T2 N0 M0
  - Stage III – T3 or N1a
  - Stage IVA – T4a or N1b
  - Stage IVB – T4b, Any N, M0
  - Stage IVC – M1

*Anaplastic carcinomas* are considered stage IV
- Stage IVA – T4a, Any N, M0
- Stage IVB – T4b, Any N, M0
- Stage IVC – M1


Answer 85
In addition to TSH suppression, I-131 ablation is indicated for the following: a tumor > 1 cm, + margin, multifocal disease, LN + disease, aggressive histology (tall cell, columnar cell, poorly differentiated), gross soft tissue involvement.

Question 86
What is the procedure for postop I-131 imaging and ablation?

Question 87
What are some acute and long-term side effects of I-131 ablation?

Question 88
What are the indications for adjuvant external beam radiation therapy (EBRT) for resected thyroid cancer?
Answer 86

The procedure is as follows:

- Only applicable for patients with papillary and follicular histology.
- Withhold Synthroid (T4; levothyroxine) for 4–6 weeks. Cytomel (T3; liothyronine) can be substituted for 3–4 weeks, but discontinued at least 2 weeks before radioiodine studies. Iodine restrict diet for 2 wks prior to scan. Alternatively, rhTSH (Thyrogen) can be used to stimulate TSH without taking patients off of their synthroid.
- TSH should be 25–30 mU/L at the time of the radioiodine study
- Pregnancy test for females on day of test
- Administer 2–5 mCi I-131 tracer dose
- If high post-op uptake (> 10%), should have completion surgery.
- All others with uptake can have treatment dose of I-131.
- Dose is 30–100 mCi for patients with residual normal thyroid tissue
- Dose is 150–200 mCi for residual malignant thyroid tissue
- Perform total body scan 4–7 days after treatment dose to confirm ablation. Dose can be repeated if indicated.
- Administer levothyroxine suppressive therapy
- Repeat total body scan in 6 months, and then at q2–3 yr intervals.


Answer 87

Acute side effects include sialadenitis, cystitis and GI irritation. Patients are also instructed to use their own toilet, flush twice, wash hands well after urination, avoid close contacts for several days after ablation, especially with children, to avoid unnecessary exposure to others. Long term toxicities may rarely include pulmonary fibrosis, oligospermia, and leukemias.


Answer 88

For papillary and follicular histologies, indications for adjuvant EBRT include age > 45 and pT4 tumor; gross disease in neck despite I-131 therapy, gross residual disease with inadequate iodine uptake. EBRT is indicated in medullary cancers for patients with T4 disease and positive margins, or bulky nodal disease, or with gross ECE. All patients with anaplastic cancer should be treated with adjuvant (chemo)radiotherapy.