# Chapter 6
# Nasal Cavity and Paranasal Sinus Cancer

III

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## PEARLS

- Epidemiology
  - 4500 cases per year in the USA.
  - Maxillary cancers are most common (70%).
  - Incidence higher in Japan and South Africa.
  - More common in males (2:1).
- Anatomy
  - Nasal cavity borders: base of skull (superior); hard palate (inferior); skin (anterior); choanae (posterior).
  - Nasal cavity subsites: vestibule, lateral walls, floor, septum.
  - Paranasal sinus borders: orbital floor (superior); hard palate (inferior); facial bone/zygomatic arch (anterior/anterior lateral); infratemporal fossa/pterygopalatine fossa (posterior/posterior lateral).
  - Paranasal sinus subsites: ethmoid, maxilla, sphenoid, frontal (named according to bones at the tumor location).
  - Ohngren's line runs from the medial canthus of the eye to the angle of the mandible.
    - Tumors superior-posterior to Ohngren's line historically had a poorer prognosis.
  - Lymphatic drainage of maxillary antrum to submandibular, parotid, jugulodigastric, retropharyngeal, and jugular nodes.
- Histology: most common is SCC (70%). Adenocarcinoma, adenoid cystic, mucoepidermoid carcinoma, neuroendocrine



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(esthesioneuroblastoma/sinonasal undifferentiated carcinoma (SNUC)/sinonasal neuroendocrine carcinoma (SNEC)/small cell), plasmacytoma, lymphoma, melanoma, and sarcoma also seen.

- See Chap. 12 for more information on esthesioneuroblastoma.

# WORKUP

- H&P, nasal endoscopy, CT/MRI, biopsy, CXR. Consider PET/CT for stage III/IV.
- Consider pretreatment baseline serum blood tests including IGF-1, free thyroxin, cortisol, and prolactin.

# STAGING: NASAL CAVITY AND PARANASAL SINUS CANCER

*Editors' note*: All TNM stage and stage groups referred to elsewhere in this chapter reflect the 2010 AJCC staging nomenclature unless otherwise noted as the new system below was published after this chapter was written.

**Table 6.1 (AJCC 7TH ED., 2010)**

| **Primary tumor (T)** |
|---|
| TX: Primary tumor cannot be assessed |
| T0: No evidence of primary tumor |
| Tis: Carcinoma in situ |
| Maxillary sinus |
| T1: Tumor limited to maxillary sinus mucosa with no erosion or destruction of bone |
| T2: Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates |
| T3: Tumor invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses |
| T4a: Moderately advanced local disease. Tumor invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses |

**Table 6.1** (continued)

**Primary tumor (T)**

T4b: Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus

Nasal cavity and ethmoid sinus

T1: Tumor restricted to any one subsite, with or without bony invasion

T2: Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion

T3: Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate

T4a: Moderately advanced local disease. Tumor invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses

T4b: Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V2), nasopharynx, or clivus

**Regional lymph nodes (N)**

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension

N2: Metastasis in a single ipsilateral lymph node, more than 3 cm, but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, not more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, not more than 6 cm in greatest dimension

N2a: Metastasis in a single ipsilateral lymph node, more than 3 cm, but not more than 6 cm in greatest dimension

N2b: Metastasis in multiple ipsilateral lymph nodes, not more than 6 cm in greatest dimension

N2c: Metastasis in bilateral or contralateral lymph nodes, not more than 6 cm in greatest dimension

N3: Metastasis in a lymph node, more than 6 cm in greatest dimension

**Distant metastasis (M)**

M0: No distant metastasis

M1: Distant metastasis

**Anatomic stage/prognostic groups**

| | |
|---|---|
| Stage 0 | Tis N0 M0 |
| Stage I | T1 N0 M0 |
| Stage II | T2 N0 M0 |
| Stage III | T3 N0 M0 |
| | T1–T3 N1 M0 |
| Stage IVA | T4a N0 M0 |
| | T4a N1 M0 |
| | T1–T3 N2 M0 |
| | T4a N2 M0 |
| Stage IVB | T4b Any N M0 |
| | Any T N3 M0 |
| Stage IVC | Any T Any N M1 |

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## Table 6.2 (AJCC 8TH ED., 2017)

**Definitions of AJCC TNM**

**Definition of Primary Tumor (T)**

**Maxillary sinus**

| T category | T criteria |
|---|---|
| TX | Primary tumor cannot be assessed |
| Tis | Carcinoma in situ |
| Tl | Tumor limited to the maxillary sinus mucosa with no erosion or destruction of the bone |
| T2 | Tumor causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to the posterior wall of the maxillary sinus and pterygoid plates |
| T3 | Tumor invades any of the following: the bone of the posterior wall of the maxillary sinus, subcutaneous tissues, floor or medial wall of the orbit, pterygoid fossa, and ethmoid sinuses |
| T4 | Moderately advanced or very advanced local disease |
| T4a | Moderately advanced local disease. Tumor invades anterior orbital contents, skin of the cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid, or frontal sinuses |
| T4b | Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than maxillary division of trigeminal nerve (V2), nasopharynx, or clivus |

## NASAL CAVITY AND ETHMOID SINUS

| T category | T criteria |
|---|---|
| TX | Primary tumor cannot be assessed |
| Tis | Carcinoma in situ |
| T1 | Tumor restricted to any one subsite, with or without bony invasion |
| T2 | Tumor invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion |
| T3 | Tumor extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate |
| T4 | Moderately advanced or very advanced local disease |
| T4a | Moderately advanced local disease. Tumor invades any of the following: anterior orbital contents, skin of the nose or cheek, minimal extension to the anterior cranial fossa, pterygoid plates, sphenoid, or frontal sinuses |
| T4b | Very advanced local disease. Tumor invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V2), nasopharynx, or clivus |

## DEFINITION OF REGIONAL LYMPH NODE (N)
## Clinical N (CN)

| N category | N criteria |
|---|---|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in a single ipsilateral lymph node, 3 cm or smaller in the greatest dimension and ENE(-) |
| N2 | Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in the greatest dimension and ENE(-) *or* metastases in multiple ipsilateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-), *or* in bilateral or contralateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-) |
| N2a | Metastasis in a single ipsilateral node larger than 3 cm but not larger than 6 cm in the greatest dimension and ENE(-) |
| N2b | Metastasis in multiple ipsilateral nodes, not larger than 6 cm in the greatest dimension and ENE(-) |
| N2c | Metastasis in bilateral or contralateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-) |
| N3 | Metastasis in a lymph node larger than 6 cm in the greatest dimension and ENE(-) *or* metastasis in any node(s) with clinically overt ENE(+) |
| N3a | Metastasis in a lymph node larger than 6 cm in the greatest dimension and ENE(-) |
| N3b | Metastasis in any node(s) with clinically overt ENE ($ENE_C$) |

*Note:* A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L) Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+)

## PATHOLOGICAL N (PN)

| N category | N criteria |
|---|---|
| NX | Regional lymph nodes cannot be assessed |
| N0 | No regional lymph node metastasis |
| N1 | Metastasis in a single ipsilateral lymph node, 3 cm or smaller in the greatest dimension and ENE(-) |
| N2 | Metastasis in a single ipsilateral lymph node, 3 cm or smaller in the greatest dimension and ENE(+) *or* larger than 3 cm but not larger than 6 cm in the greatest dimension and ENE(-), *or* metastases in multiple ipsilateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-), *or* in bilateral or contralateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-) |

*continued*

| N category | N criteria |
|---|---|
| N2a | Metastasis in single ipsilateral or contralateral node 3 cm or less in the greatest dimension and ENE(+) *or* a single ipsilateral node larger than 3 cm but not larger than 6 cm in the greatest dimension and ENE(-) |
| N2b | Metastasis in multiple ipsilateral nodes, not larger than 6 cm in the greatest dimension and ENE(-) |
| N2c | Metastasis in bilateral or contralateral lymph nodes, not larger than 6 cm in the greatest dimension and ENE(-) |
| N3 | Metastasis in a lymph node larger than 6 cm in the greatest dimension and ENE(-) *or* in a single ipsilateral node larger than 3 cm in the greatest dimension and ENE(+) *or* multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+) |
| N3a | Metastasis in a lymph node larger than 6 cm in the greatest dimension and ENE(-) |
| N3b | Metastasis in a single ipsilateral node larger than 3 cm in the greatest dimension and ENE(+) *or* multiple ipsilateral, contralateral, or bilateral nodes, any with ENE(+) |

*Note:* A designation of "U" or "L" may be used for any N category to indicate metastasis above the lower border of the cricoid (U) or below the lower border of the cricoid (L) Similarly, clinical and pathological ENE should be recorded as ENE(-) or ENE(+)

## DEFINITION OF DISTANT METASTASIS (M)

| M category | M criteria |
|---|---|
| M0 | No distant metastasis (no pathologic MO, use clinical M to complete stage group) |
| M1 | Distant metastasis |

## AJCC PROGNOSTIC STAGE GROUPS

| When T is... | And N is... | And M is... | Then the stage group is... |
|---|---|---|---|
| Tis | N0 | M0 | 0 |
| T1 | N0 | M0 | I |
| T2 | N0 | M0 | II |
| T3 | N0 | M0 | III |
| T1, T2, T3 | N1 | M0 | III |
| T4a | N0, N1 | M0 | IVA |
| T1, T2, T3, T4a | N2 | M0 | IVA |
| Any T | N3 | M0 | IVB |
| T4b | Any N | M0 | IVB |
| Any T | Any N | M1 | IVC |

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# TREATMENT RECOMMENDATIONS

**Table 6.3 TREATMENT RECOMMENDATIONS**

| Stage | Recommended treatment |
|---|---|
| Nasal cavity and ethmoid sinus | T1-2N0: Resection → post-op RT for close/+ margins or PNI Alternatively, definitive RT. Choice depends on size, location, and expected cosmetic outcome<br>T3-4N0: Resectable: resection → post-op RT<br>Unresectable or inoperable: Definitive RT or chemo-RT<br>N+: Resection + neck dissection → post-op RT or chemo-RT Alternatively, definitive chemo-RT |
| Maxillary sinus | T1-2N0: Resection → post-op RT for close margin, PNI, adenoid cystic. For + margin, re-resect (if possible) → post-op RT<br>T3-4N0 resectable: Resection → post-op RT or chemo-RT<br>Unresectable or inoperable: Definitive RT or chemo-RT<br>N+: Resection + neck dissection → post-op RT or chemo-RT Alternatively, definitive chemo-RT |
| SNUC/SNEC/small cell | Include chemotherapy with treatment as above |

# STUDIES

## NASAL CAVITY

- Allen (IJROBP 2008): 68 patients with nasal cavity or nasal septum cancer. Forty-seven percent received definitive RT. Nineteen percent received neck RT. 5/10-yr LC 86/76%, DFS 86/78%, OS 82/62%.

## PARANASAL SINUS

- Le (IJROBP 2000): 97 patients with maxillary sinus tumors. Fifty-six had surgery first and 41 had pre-op or definitive RT. 12% LN relapse at 5 years. T3–4 SCC were associated with a high incidence of initial nodal involvement and nodal relapse. None of the patients presenting with SCC histology and N0 necks had nodal recurrence after elective neck radiation. Recommended elective ipsilateral neck RT for T3–4 SCC.

- Bristol (IJROBP 2007): 146 patients with maxillary sinus tumors treated with post-op radiotherapy. Group 1 included 90 patients treated before 1991. Group 2 included 56 patients treated after 1991, when radiotherapy technique incorporated coverage of the base of skull for patients with perineural invasion, elective neck RT in SCC or undifferentiated histology, and techniques to improve dose homogeneity to target. No difference in 5-yr OS (51% vs. 62%), RFS, LRC, DM between the two groups, but base of skull and nodal failures reduced in at-risk patients. Advanced age, need for enucleation, and positive margins were independent predictors of worse OS. Need for enucleation predicted worse LRC.

## NASAL CAVITY AND PARANASAL SINUS

- Dulguerov (Cancer 2001): 220 patients with nasal cavity and paranasal sinus cancer. 5-yr OS 40%, LC 59%. Prognostic factors: histology, T stage, primary site, and treatment type. Local extension factors associated with worse survival: extension to pterygomaxillary fossa, extension to frontal and sphenoid sinuses, erosion of cribriform plate, and invasion of the dura. In the presence of an intraorbital invasion, enucleation was associated with better survival.
- Chen (IJROBP 2007): 127 patients with sinonasal carcinoma. 5-yr OS, LRC, and DFS were 52%, 62%, and 54%, respectively. No significant difference in 5-year OS rates for patients treated in the 1960s, 1970s, 1980s, 1990s, and 2000s. Significantly reduced incidence of severe (Grade 3 and 4) toxicity over the decades.
- Madani (IJROBP 2009): 73 primary and 11 locally recurrent sinonasal tumors definitively treated by IMRT. No chemo. 64% patients had adenocarcinoma histology. Median follow-up 40 mo with 5-year LRC, OS, and DFS were 71%, 58%, and 59%, respectively.
- Snyers (IJROBP 2009): 178 patients with sinonasal cancer. 62% of long-term survivors had hormonal disturbances and 24% had multiple hormonal deficiencies.
- Wiegner (IJROBP 2012): 52 patients with tumors of the nasal cavity and paranasal sinuses treated post-op or

definitively with IMRT. 2-year LRC, in-field LRC, FFDM, and OS were 64%, 74%, 71%, and 66%. Grade ≥ 3 mucositis 37%, dermatitis 15%, one late optic toxicity.

- Multiple other published series report that IMRT is safe and effective for sinonasal carcinomas (e.g., Askoxylakis, Radiat Oncol 2016) and that it is often the preferred radiotherapy technique in particular for normal tissue sparing (Chi, J Hematol Oncol 2013).
- Some physicians extrapolate from the Bernier and Cooper head and neck cancer studies (*NEJM* 2004, *Head and Neck* 2005) to support using post-op concurrent chemo and RT in patients with SCC of the paranasal sinuses having positive margins or extranodal extension.

### INDUCTION CHEMOTHERAPY

- Hanna (Arch Otolaryngol Head Neck Surg 2011): 46 patients with T3–T4 squamous cell carcinoma of the paranasal sinuses or nasal cavity (maxillary sinus 67%). 26% had clinical evidence of nodal metastasis; 80% had stage IV. Induction chemotherapy was taxane-platinum in 80% or combined with ifosfamide or 5-fluorouracil, or taxane-5-fluorouracil. 67% of patients achieved at least partial response, 24% had progression, and 9% had stable disease. Surgery could be performed in 52% after induction. 2-year survival for stable or responding disease was 77% but was 36% for patients with progression on induction. The authors suggest that a lack of response to induction may indicate an inherently poor prognosis.

## RADIATION TECHNIQUES

### SIMULATION AND FIELD DESIGN

- Simulate supine with thermoplastic mask immobilization.
- Eyes open, straight ahead to keep posterior pole away from high dose region inferiorly.
- Consider tongue blade/cork to depress tongue out of fields.
- Consider filling surgical defects with tissue equivalent material.

- Recommend IMRT or 3DCRT planning to increase sparing of normal structures.
- GTV = clinical and/or radiographic gross disease.
- CTV1 = 1 cm margin on primary and/or nodal GTV.
- CTV2 = high-risk regions (depending on the presence or absence of anatomic boundaries to microscopic spread).
- CTV3 = elective neck.
- Individualized planning target volumes are used for the GTV, CTV1, CTV2, and CTV3 tailored to subsite and stage.
- Replanning may be considered during treatment if there is a potential for change in aeration of the sinuses in response to treatment, given the proximity to optic and central nervous system structures.

## DOSE PRESCRIPTIONS

- EBRT 1.8–2 Gy/fx.
- Definitive RT or chemo-RT: CTV1 to 66–70 Gy, CTV2 to 60–63 Gy, CTV3 to 54–57 Gy.
- Post-op RT: CTV1 to 60 Gy with optional boost to 66 Gy to high-risk areas (close/+ margins, ECE, PNI). CTV2 to 50–54 Gy.
- For selected nasal septum tumors, brachytherapy may be appropriate.

## DOSE LIMITATIONS

- Lens <10 Gy (cataracts).
- Retina <45 Gy (vision). May go higher if treating bid or partial volume.
- Optic chiasm and nerves <54 Gy at standard fractionation.
- Brain <60 Gy (necrosis).
- Mandible <60 Gy (osteoradionecrosis).
- Parotid mean dose <26 Gy (xerostomia).
- Lacrimal gland <30–40 Gy.
- Pituitary and hypothalamus mean dose <40 Gy.

## COMPLICATIONS

- Acute = mucositis, skin erythema, nasal dryness, xerostomia
- Late = xerostomia, chronic keratitis and iritis, optic pathway injury, soft tissue or osteoradionecrosis, cataracts, radiation-induced hypopituitarism

# FOLLOW-UP

- H&P, labs, and CXR every 3 months for the first year, every 4 months for second year, every 6 months for third year, and then annually. Imaging of the H&N at 3 months posttreatment and then as indicated.



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