# Head & Neck Site Group – Nasal Cavity and Paranasal Sinus

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1. Introduction

- Carcinomas of the nasal cavity and paranasal sinuses account for ~0.5% of all malignant neoplasms, and 3% of those occurring in the head and neck
  - Higher rates of sinonasal carcinoma are reported in Japan, China, and some parts of India
- By anatomical subsite, approximately 60% occur in the maxillary sinus, 25% in the nasal cavity, 10-15% in the ethmoids, and ~1% in the sphenoid and frontal sinuses
- Histological tumor types occurring in the sinonasal region include:
  - Malignant epithelial:
    - squamous cell carcinoma and variants
    - sinonasal undifferentiated carcinoma (SNUC)
    - salivary-gland-type carcinomas arising from minor salivary gland tumors
      - adenoid cystic carcinoma
      - adenocarcinomas
    - olfactory neuroblastoma (esthesioneuroblastoma)
- Very rare malignant tumors include carcinoids and small-cell carcinoma, mesenchymal tumors of bone / soft tissue, lymphomas, plasmacytoma, mucosal melanomas
- benign epithelial tumors including inverting papillomas and salivary-type adenomas

2. Etiology & Prevention

- Etiology
  - Occupational exposures
    - The main known risk factor is exposure to hardwood dusts, with the strongest association being with increased risk of adenocarcinomas
    - Other suspected occupational risks are nickel refining, chromate pigment manufacture, and formaldehyde
  - An association between tobacco-smoking and sinonasal squamous cell carcinoma (SCC) has been demonstrated
- Strategies for prevention of sinonasal cancers should focus on smoking cessation, as well as reduction in exposure to known occupational hazards

3. Screening and Early Detection

- There is currently no role for screening for cancers of the nasal cavity / paranasal sinuses

4. Diagnosis / Initial Assessment

All patients should be assessed prior to treatment intervention, by the multidisciplinary Head & Neck Team
History and Physical evaluation:

- Record height, weight and ECOG performance status
- History and Physical examination including mucosal survey for synchronous primaries
  - Record smoking and alcohol history
    - Smoking
      - Non-smoker / Current / ex-smoker
      - pack years
      - For current smokers smoking cessation is to be advised and a referral to cessation services made
    - alcohol history in standard drinks/week;
      - None / Light <10 drink/wk/ Mod 10-20 / Heavy >20
  - Record smoking history of exposures to other carcinogens
  - Record stage (current edition TNM)
  - Specify location of primary including dimensions and involvement of anatomic subsites:
    - Nasal cavity
    - Maxillary antrum
    - Ethmoid sinus
    - Sphenoid sinus
  - Regions of tumor extension beyond the primary anatomic subsite should be documented
  - Documentation of specific nodal level(s) involved
    - Size and extent of nodal involvement (e.g. fixed/mobile)

Investigations (Baseline):

- Panendoscopy or examination under anaesthesia if deemed necessary
- Biopsy
  - pathology review, molecular diagnostic testing if indicated
- CT scan Head and Neck
- Positron Emission Tomography (PET) in node positive presentations
- MRI Head and Neck (T1+gadolinium and T2 sequences) if indicated
- CT thorax if indicated (e.g. node-positive disease, smoking history), or otherwise CXR
- Bloodwork: CBC, creatinine, electrolytes, liver function, glucose, coagulation studies (APTT, INR)
- Pregnancy test where indicated
- Other staging investigations as clinically indicated (bone scan etc)
5. Pathology

- Histological types occurring in the sinonasal region are summarized in the introduction to this guideline, however several bear mention with regard to pathology:
  - Squamous cell carcinoma (SCC)
    - Keratinizing type is identical to SCC of other head and neck subsites
    - Non-keratinizing subtype characterized by a ribbon-like growth pattern; unequivocal evidence of invasion can be difficult to demonstrate
    - Variants of SCC occur as for other head and neck subsites (e.g. verrucous, basaloid), although these are rare
    - Precursor lesions include the Schneiderian (inverting) papilloma, with the frequency of association estimated at ~10%
  - Sinonasal undifferentiated carcinoma (SNUC): a rare, aggressive neoplasm with a high propensity for distant metastasis
  - Adenoid cystic carcinoma: often presents with perineural spread to skull base (cavernous sinus) with a propensity for late distant metastasis and infrequent nodal involvement
  - Adenocarcinoma (low grade intestinal subtype): more frequently observed in ethmoid region with less aggressive patterns of nodal and distant involvement and relatively high rates of locoregional control
  - Olfactory neuroblastoma (esthesioneuroblastoma): a rare tumor arising from olfactory epithelium in upper nasal cavity, ethmoid and cribriform plate

- Pathology reporting (for surgical specimens) should follow a standard format for carcinomas of the nasal cavity and paranasal sinuses, and include the following SYNOPSIS DATA, as per College of American Pathologists 2011 cancer protocols, (see www.cap.org for full detail):
  - Specimen:
  - Procedure:
  - Specimen Size:
    - Greatest dimension:
    - Additional dimension(s):
  - Specimen Laterality:
  - Tumor Site:
  - Tumor Focality:
  - Tumor Size:
    - Greatest dimension:
    - Additional dimension(s):
  - Histologic Type
    - Histologic Grade:
  - Margin status for invasive carcinoma
    - Margin(s):
  - Margin status for carcinoma in situ
6. Management

**OVERALL MANAGEMENT APPROACH**

- The management of malignancies of the nasal cavity and paranasal sinuses has evolved empirically, largely based on experience and retrospective analysis of single institution series. Given the rarity of these tumors, there are no randomized phase III studies examining different treatment strategies. Many retrospective series combine tumors of widely varying histologies (and clinical behavior) and do not take into account the inherent selection bias when comparing outcomes achieved with varying treatment strategies. As a consequence (and not surprisingly), the majority of retrospective studies report superior outcomes for patients selected to undergo primary surgical resection and postoperative radiation treatment, which is considered a standard approach in many centers.

- Treatment for any given patient should be individualized based on location and extent of disease, patient performance status and histopathologic subtype of tumor and availability of local expertise; because of the rarity of these tumors, consideration should be given to referring patients to centers with experience in their management.

- Treatment decisions should involve the patient and take into account their preference once informed of their options

- Treatment options include
  - Pre-operative moderate dose radiation therapy followed by definitive surgical resection (for esthesioneuroblastoma presentations)
  - Definitive high dose radiation therapy +/- concurrent chemotherapy with surgery reserved for salvage
  - Primary definitive surgical resection followed by post-operative radiation therapy +/- concurrent chemotherapy

- All patients should be assessed for inclusion on available current trial protocols and, if eligible and appropriate, offered inclusion on trial

**PRE-TREATMENT ASSESSMENT:**
• Written consent to be obtained prior to treatment
• Dental assessment
• Nutritional assessment and consultation
  o Feeding G-J tube
    ▪ Should be considered for patients receiving chemo-radiotherapy if significant volumes of pharyngeal mucosa are to be treated
    ▪ Patients with existing nutritional impairment (due to swallowing dysfunction etc), for radical treatment
• Pharyngeal function assessment (speech/swallow)
• Audiology
  o Pts receiving platinum-type chemotherapy
  o Pts receiving high-dose adjacent to auditory apparatus
• Ophthalmology assessment

TREATMENT: NASAL CAVITY AND PARANASAL SINUS SITES

The treatment guidelines below apply to squamous cell carcinomas presenting in nasal cavity or paranasal sinus. A summary of variations in these guidelines for alternate histologies is provided at the end of the section.

Early Stage Disease  T1-T2

• Anteriorly-located tumors of nasal cavity or vestibule for which surgical resection would result in significant cosmetic defect should be treated with definitive radiation therapy, with surgery for salvage
• Tumors in maxillary antrum or mid-to-posterior nasal cavity that can be resected with acceptable cosmetic defect can be treated with either primary surgery and postoperative radiotherapy (RT) or definitive RT +/- concurrent chemotherapy

Advanced Stage  T3-T4

• Primary surgical resection if resectable with orbital preservation and postoperative RT
• Definitive RT +/- concurrent chemotherapy is an option for cases not undergoing primary surgical resection
• T4b disease with intracranial extension and brain invasion and/or extension into cavernous sinus is deemed unresectable and should be treated with definitive RT +/- concurrent chemotherapy
• Patients for whom curative treatment is not appropriate due to extent of the primary cancer, poor performance status or the presence of distant metastasis may be offered palliative RT (SECTION 12)
Neck Management

- If the initial approach is surgical, patients presenting with clinical evidence of gross nodal involvement should have neck dissection performed at the time of primary surgical resection, followed by post-operative RT to the neck according to post-op guidelines
- Patients treated with pre-operative radiotherapy require subsequent resection of grossly involved nodes as well as primary site, unless treated to definitive (radical) dose and complete radiological and clinical response is demonstrated
- Patients undergoing definitive RT with or without concurrent chemotherapy should have all gross nodes treated to high dose, and the remainder of bilateral (elective) necks treated to microscopic dose
- Patients undergoing definitive RT without clinical evidence of gross nodal involvement (N0), should have regions of the neck deemed at risk of harbouring occult metastasis treated to microscopic dose
  - In the N0 patient the first echelon nodes (depending on location of primary, these may include zones I, II and/or retropharyngeal), should be treated
  - Bilateral neck treatment should be undertaken when the primary site reaches midline
  - for anteriorly located nasal cavity tumors, facial nodal regions should be treated

Post-Operative Radiotherapy

- Most patients should undergo a course of postoperative radiotherapy to the primary site (surgical bed) and necks as described above
  - Indications for post operative radiation include
    - T3-T4 primary disease
    - Microscopic margins <5mm (irrespective of intra-operative revision or additional post-resection sampling of the surgical site)
    - >1 additional features at primary:
      - High-grade disease
      - Peri-neural invasion (PNI)
      - Lymph-vascular invasion (LVSI)
  - Neck
    - Lymph node involvement at pathology:
      - ≥2 lymph nodes
      - Any lymph node >3 cm (N2+)
      - Level IV-V LN positive
      - Extracapsular extension (ECE)

- concurrent chemotherapy should be considered for patients with
  - Positive (inked) margin
Extracapsular extension

Management of Non SCC Histologies

- Adenoid cystic carcinoma
  - When resectable, primary surgery followed by post-operative radiation is the preferred approach
  - When defining radiation treatment volumes, careful assessment and inclusion of potential routes of perineural spread is required
  - Patients presenting with no clinical evidence of gross nodal involvement do not require neck dissection or irradiation
  - High-dose radiation to the primary site may be considered even in the presence of distant metastasis, given the potential for slow growth and prolonged survival, in this histology

- Olfactory Neuroblastoma (esthesioneuroblastoma)
  - Managed with pre-operative radiation 50Gy in 25 fractions followed by surgical resection
  - Radiation volumes to include nodal zones at risk of harbouring microscopic disease

Patients not suitable for radical treatment

- Refer to separate guideline: Palliative Management of Patients with H&N malignancy (SECTION 12)

6.1 Surgical Management

- Primary site
  o Endoscopic examination under anesthesia with mapping biopsies (if indicated) is considered helpful in surgical planning
  o Specific surgical approach to the primary site is dictated by the location and extent of the primary tumour with the goal of obtaining a margins clear resection with acceptable morbidity and functional outcome
  o Surgical defects may be reconstructed with free vascularized tissue transfer
  o Endoscopic resection can be considered in localized malignancies with no brain, orbital or skin invasion, and the surgery removes the same structures that would have been removed with an open approach
    - Contraindications to endoscopic treatment:
      o extensive dural, parenchymal brain, or intraorbital involvement, or tumor sites not accessible by endoscopic approaches
endoscopic resection should only be undertaken where there is available surgical expertise and experience with this technique

- **Neck**
  - N0: no neck treatment
  - If clinical or radiographic neck disease at presentation, perform neck dissection dictated by location of neck disease and tumor histology

### 6.2 Chemotherapy

- Concurrent high dose cisplatin is delivered when concurrent chemotherapy is appropriate in combination with definitive radiation for squamous cell and undifferentiated histologies
- Patients being treated for adenoid cystic histology are not given chemotherapy
- For patients being treated with postoperative radiation with extra capsular nodal involvement and positive margins concurrent chemotherapy should be considered

**CONCURRENT CHEMO-RADIOTHERAPY:**
- **DEFINITIVE:**
  - Cisplatin 100mg/m², concurrent with weeks 1, 4, 7 of radiotherapy
- **POST-OPERATIVE:**
  - Cisplatin 100mg/m², concurrent with weeks 1, 4 of radiotherapy

- **SETTING:**
  - Overnight admission in inpatient chemotherapy suite
- **Pre-treatment Assessment:**
  - Bloodwork: CBC, lytes, creatinine, liver function hepatitis B and C profile, weight, height and BSA.
- **Pre-Medication / Hydration**
  - Anti-emetics:
    - ondansetron 16 mg IV q24hrs day 1,2 over 15 minutes
    - dexamethasone 10 mg IV day 1 (dose reduction or omission based on Hep B profile may occur), then 2 mg IV day 2 (AM)
    - aprepitant 125 mg PO day 1, 80 mg PO day 2
    - prochlorperazine 10 mg IV/PO q6hrs prn
  - Hydration with
    - 1000 mL Normal Saline (0.9%) + Potassium Chloride 20mEq + magnesium sulfate 2g IV over 2 hr, pre-cisplatin

- **CHEMO: CISPLATIN** 100mg/m² IV in 1000mL normal saline, with mannitol 20g over 2 hrs
- Post-chemo supportive care:
1000mL Normal Saline (0.9%) over 4 hours post-cisplatin, then decrease to 30 mL/hr until discharge

dexamethasone 2 mg IV-int over 15 minutes q12hrs for 3 doses while in hospital, starting with the second dose of ondansetron (dose reduction of omission depending on Hep B profile may occur)

Anti-emetics on discharge on day 2:
- ondansetron 24 mg po q24hrs day 3,4
- dexamethasone 2 mg PO bid starting day 2 (PM) x 5 doses (i.e day 2-4)
- aprepitant 80 mg PO day 3
- prochlorperazine 10 mg IV/PO q6hrs prn

o dose reduction / delay of chemotherapy dose should be considered for toxicities including (but not limited to):
  - Cytopenia
    - Absolute neutrophil count (ANC)
      - 1-1.4 x 10e9/L: consider delay for 1 week, or 75% dose reduction
      - <1.0 x 10e9/L: delay cycle, and recheck bloodwork 1 week
  - Renal impairment
    - >60 ml/min: 100% dose; 45-59 ml/min: consider 50-75% dose; <45 ml/min omit cisplatin
  - Weight loss: less than 10% from baseline: 100% dose; > 10% loss: consider 75% dose, or discontinuation at physician’s discretion
  - Neurotoxicity and Ototoxicity: dose modification or discontinuation may be required

o Other precautions:
  - Potential mutagen: Women of childbearing age must practice an appropriate form of contraception while being treated.
  - Neutropenia: fever of other evidence of infection should be investigated promptly and treated aggressively
  - Hepatitis B: For patients who are Hepatitis B surface antigen positive, consider anti-viral prophylaxis and lower dose of dexamethasone to lower the risk of viral reactivation
  - Appropriate management of constipation with stool softeners and laxatives if required

- OTHER CHEMOTHERAPY TREATMENT OPTIONS: CONCURRENT RADIOTHERAPY and WEEKLY CISPLATIN
  - Consider for patients not suitable for high-dose cisplatin
  - SETTING:
    - Out-patient chemotherapy suite
  - Pre-treatment Assessment:
    - Bloodwork: CBC, lytes, creatinine, liver function hepatitis B and C profile, weight, height and BSA.

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o Pre-Medication / Hydration
  ▪ Anti-emetics:
    • dexamethasone 8mg PO or IV at least 1 hour prior to chemotherapy
    • ondansetron 16 mg po or IV starting at least 1 hour prior to chemotherapy
  ▪ Others:
    • Magnesium sulfate 2g IV in normal saline 250 ml over 1 hour only if magnesium level = 0.5-0.6 mmol/L (call physician for magnesium level less than 0.5 mmol/L).

o CHEMO:
  ▪ CISPLATIN 40 mg/m² IV in 500 cc normal saline, over 1 hrs

o Post-chemo supportive care:
  ▪ Hydration 500 cc normal saline over 30-60 minutes
  ▪ Ondansetron 16 mg PO day 2
  ▪ Dexamethasone 4mg BID PO days 2-3
  ▪ Prochlorperazine 10mg Q6H PRN

o dose reduction / delay of chemotherapy dose should be considered for:
  ▪ Cytopenia
    • Absolute neutrophil count (ANC)
      o 1-1.4 x 10e9/L: consider delay for 1 week, or 75% dose reduction
      o <1.0 x 10e9/L: delay cycle and recheck bloodwork 1 week
  ▪ Renal impairment
    • Creatinine clearance >60 ml/min: 100% dose; 45-59 ml/min: consider 50-75% dose; <45 ml/min omit cisplatin
  ▪ Weight loss: less than 10% from baseline: 100% dose; > 10% loss: consider 75% dose or discontinuation at physician’s discretion
  ▪ Neurotoxicity and Ototoxicity: Dose modification or discontinuation may be required

o Other precautions:
  ▪ Potential mutagen: Women of childbearing age must practice an appropriate form of contraception while being treated.
  ▪ Neutropenia: fever of other evidence of infection should be investigated promptly and treated aggressively
  ▪ Appropriate management of constipation with stool softeners and laxatives if required

6.3 Radiotherapy
  • For definitive RT, patients are treated with
    o Gross disease: once daily radiation with 2 Gy fractions to total dose of 70 Gy in 35 fractions, over 7 weeks

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When delivered without chemotherapy in the curative setting radiotherapy will be accelerated to deliver 70 Gy in 35 fractions over 6 weeks by the addition of a bid treatment once a week for 5 of the 6 weeks.

- Regions at risk of microscopic spread (anatomy adjacent to primary GTV and uninvolved at risk nodal zones) will receive 56 Gy in 35 fractions.

- Post operative RT will be delivered according to standard guidelines (according to evaluation of surgical pathology findings).

**TARGET VOLUMES** (see also APPENDIX 6)

- Definition of GTV for definitive treatment based on clinical exam and radiology with contrast enhanced CT, PET and/or MRI to define perineural and skull base invasion.
- High dose CTV
  - Primary: defined as 0.3 cm expansion on GTV limited by anatomic barriers to spread and expanded along potential anatomic routes of spread, or where there is uncertainty as to GTV extent.
  - Nodal: High dose CTV expansion of 0.5 cm will be applied to grossly involved nodes to be treated to 70 Gy.
- An intermediate dose nodal CTV expansion of 0.5 cm can be defined to treat nodes <1 cm in diameter to 63 Gy.
- Microscopic (low dose) CTV to be treated to 56 Gy
  - Primary: includes a further 0.5 cm expansion on the primary site high dose CTV and includes potential routes of anatomic spread (e.g. gross involvement of orbit or adjacent sinus requires expansion of the microscopic low dose CTV to include these structures).
  - Nodal: Microscopic low dose CTV defined to cover all nodal zones at risk of microscopic spread of tumor according to the location of the primary site and nodal anatomy.
- Volumes used to treat patients post-operatively are defined as expansions on high risk regions (anatomy adjacent to the resected primary site and gross nodes) to which a high dose CTV will be generated at a 0.5 cm expansion.

**TREATMENT**

- CLINICAL CARE DURING RADIOTHERAPY:
  - Pts shall be reviewed by the RO at least weekly during RT.
- ASSESSMENT:
  - acute toxicities (RTOG criteria) documented in MOSAIQ.
• Weight and nutritional review (weekly nutritional rv for pts with G-tube, or as clinically indicated)
• Bloodwork prior to each cycle of chemoRx, or as clinically indicated
  o Management of acute toxicities: refer to Nursing / Supportive Care guideline

6.4 Oncology Nursing Practice

Refer to Head and Neck Nursing Care

7 Supportive Care

7.1 Patient Education

Refer to general patient education practices

7.2 Dental Care

Refer to dental care for Head and Neck Cancers

7.3 Symptom Management

Refer to general symptom management care guidelines

7.4 Clinical Nutrition

Refer to general clinical nutrition care guidelines

7.5 Palliative Care

Refer to palliative management of Head and Neck Cancers

7.6 Speech Pathology

Refer to speech language pathology for Head and Neck Cancers

8. Follow-up Care

• Setting: Assessment in multidisciplinary clinic
• Schedule:
  o 2-6 weeks post radiotherapy
  o Q 3 months or more frequent for two years
  o Q 4 months or more frequent for third year
• Investigations and assessment (follow-up):
  o Fibre-optic nasendoscopy
  o Imaging
    ➢ repeat CT/MRI at 2-3 months post treatment with subsequent follow-up EUA/biopsy of any suspicious residual abnormalities
    ➢ patients with resolving abnormalities should have repeat imaging with 2-3 months to ensure these are either stable or continuing to regress
  o Pharyngeal function (speech/swallow) as indicated
  o Dental assessment where applicable
  o Audiometry where applicable
  o Ophthalmology review as applicable

**ASSESSMENT and MANAGEMENT of PERSISTENT / RECURRENT DISEASE (SALVAGE)**

• Biopsy / histological confirmation
• Record site of failure (local, regional, distant)
• Date of failure/recurrence
• Determine site of recurrence relative to the initial target volume
• RE-STAGE
  • CT Head, neck, thorax
  • PET
  • MRI H&N
  • Other imaging as clinically indicated
• salvage options:
  • refer to NECK DISSECTION policy above (*Surgery 6.1*) for management of suspected / confirmed persistent regional disease
  • RE-IRRADIATION: refer to guideline for re-treatment of pts with H&N malignancy for re-irradiation

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