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Nasopharynx
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1 Introduction

Cancer of the nasopharynx is a relatively uncommon disease in Western countries (0.5-2/100 000/year), but more frequent in some parts of Asia (30-80/100 000/year) and North Africa (8-12/100 000/year). It has been correlated with genetic predisposition as well as with environmental factors such as Epstein Barr Virus (EBV) infection.

First symptoms are in most cases nasal obstruction and/or hypoacousia, while progression can be with paralysis of a cranial nerve or cervical node.

Because of their anatomic situation at the base of skull, most nasopharyngeal tumours are inoperable. Most tumours spread early to cervical nodes and distant metastasis is also frequent. Most nasopharyngeal tumours are however sensitive enough for local control to be achieved with exclusive external beam irradiation or chemoradiation, so that endocavitary brachytherapy is indicated in the treatment of relatively few cases, as a boost or for recurrent disease.

Main prognosis factors are the local extension of the tumours (invasion of the base of skull and paralysis of the cranial nerves) and lymph node metastasis.

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Fig 13.1: Anatomical topography: A sagittal; B transverse drawing of CT image
1 = Eustachian tube; 2 = Rosemuller fossa; 3 = Soft palate
2  **Anatomical Topography**

The nasopharyngeal cavity is a somewhat cuboid space, which communicates anteriorly with the nasal cavities through the choanae and inferiorly with the oropharynx (Fig 13.1). The sphenoid body limits it superiorly, the first two vertebrae posteriorly, and the soft palate inferiorly. The Eustachian tubes open into its lateral walls, in front of the fossa of Rosenmüller.

The oropharynx has a rich lymphatic plexus, whose branches terminate in lymph nodes at the mastoid tip and in the spinal and subdigastric areas.

The main critical organs are the brain, and more particularly the brain stem and temporal lobes, the cranial nerves and the optic chiasm, the salivary glands, the masseters, and the inner ears.

3  **Pathology**

About 80% of primary tumours are carcinomas. In the majority of cases, they are undifferentiated and related to EBV infection or poorly to well-differentiated squamous cell carcinomas unrelated to EBV infection. Other tumours, such as lymphomas, are not suitable for brachytherapy.

Lymph node metastasis is noted at presentation in up to more than 80% of patients and is often bilateral. Distant metastases are frequent.

4  **Work Up**

All patients undergoing irradiation for nasopharyngeal cancer require a detailed clinical examination (including endoscopy) of the head and neck region as well as a thorough general physical examination, biopsy of the primary tumour, CT-scanner and MRI of the base of skull, evaluation of the dental status, EBV serology, chest CT-scan, bone scan, liver ultrasonography, and the assessment of the clinical stage according to the UICC-TNM classification:

T1: tumour confined to the nasopharynx.
T2: Tumour extends to soft tissue of oropharynx and/or nasal fossa.
   T2a: without parapharyngeal extension.
   T2b: with parapharyngeal extension.
T3: Tumour invades bony structures and/or paranasal sinuses.
T4: Tumour with intracranial extension and/or involvement of cranial nerves, infratemporal fossa, hypopharynx, or orbit.

CT-scan, cervical ultrasonography, and needle aspiration are all useful for diagnosis of metastatic cervical nodes.

5  **Indications, Contra-indications**

Because the nasopharynx is deeply situated and surrounded by bone, vessels and nerves, only endocavitary techniques can be performed. The thickness of the clinical target volume should therefore not exceed 10 mm, and consequently only superficial tumours or those that have shrunk
enough after initial external beam radiotherapy and/or chemoradiation and not involving the underlying bone or deeply infiltrating the infratemporal space are suitable for a brachytherapy application. Brachytherapy indications are therefore restricted to boost minimal residual local disease after external irradiation or as salvage therapy for well-circumscribed and superficial local recurrences limited to the nasopharyngeal cavity. Tumours extending into the nasal cavities or the oropharynx should not be accepted for brachytherapy.

6 Target Volume

The PTV is defined upon the information given by endoscopy, CT-Scan and MRI. However, because of the difficulty in delineating the tumour extension and defining the depth of the GTV precisely, it is advised to take a large safety margin around the gross disease. Most tumours are situated at the roof (i.e. the soft tissue situated between the mucosa and the base of skull) and / or the lateral walls of the nasopharynx. In central tumours, the clinical target volume may include both roof and lateral walls. In well-lateralised tumours, the irradiation may be limited to the roof and one lateral wall. In most cases, the depth of PTV does not exceed 10 mm.

7 Technique

7.1 Mould Technique

In the customised mould technique, two to four sagittally oriented plastic tubes are fixed on the surface of a rigid acrylic applicator, made from an individual impression of the nasopharyngeal cavity (Fig 13.2) (2). General anaesthesia is prohibited during the procedure by the relative obstruction of the oropharynx produced by an endotracheal tube. The procedure is therefore performed under neuroleptic analgesia, during which the pharyngeal reflexes and moderate muscular tonicity are maintained. Nasal secretions are suctioned and the mucous membranes anaesthetised with 5% xylocaine spray until it is possible to manipulate the oropharynx without provoking pain or triggering the gag reflex.

*Fig 13.2 : Insertion of the moulded applicator by traction to the Nelaton tubes introduced through the nose earlier.*
First, rubber Nelaton catheters are passed through both nostrils and brought out the mouth. The oral end of the catheters is than tied to cords attached to a dummy applicator. This dummy is much smaller than a normal nasopharyngeal cavity and is thickly coated with a quick-setting silicone paste. By pulling the nasal catheters, it enters the oral cavity, passes behind the soft palate and comes into contact with the walls of the nasopharynx. The paste, which should overflow slightly into the posterior choanae, will set up within minutes but remains elastic and is easily extracted from the nasopharynx. An exact impression of the nasopharynx is obtained, demonstrating surface details of the tumour lesion. If the impression appears incomplete, the procedure is repeated after adding more paste in the defective areas. The patient is then kept under light anaesthesia, while the rigid applicator is fabricated from the impression.

A bivalve plaster of Paris negative mould is first prepared from the impression. The rigid applicator with walls about 2 - 5 mm thick is then made in this mould using a acrylic compound. The applicator surface is carefully smoothed with a grinder and a double nylon cord is attached to its lower posterior aspect to be used later for removing it from the nasopharynx. Two rubber strips are attached at its upper anterior aspect at the level of the small projections, which extends into the posterior choanae, where the paste overflowed. These strips hold the applicator in position when brought out through the nostrils and tied together in the front of the nasal septum.

The radiation oncologist determines the position of the sources with respect to the topography of the tumour, as it appears imprinted on the applicator. Boundaries of the tumour are highlighted in ink and source position that will provide optimal coverage of the lesion are indicated with sagittal lines. Spacing between sources varies from 10 to 15 mm. In an averaged sized nasopharynx, two sources can be placed on one lateral wall, three sources on two walls, for example the roof and one lateral wall or four sources on three walls.

Shallow groves are ground into the surface of the applicator as designed to cradle plastic tubes, which are glued into the grooves with acryl. These tubes should be blind-ended and if not have to be sealed at the end of the applicator. Prior to inserting the applicator into the nasopharynx, the endoluminal trajectory is checked with dummy sources. Appropriate source lengths are precisely determined and recorded.

Nasal secretions are again suctioned and the rubber Nelaton catheters are reinserted, and brought out of the mouth, carefully avoiding crossover in the nasopharynx.

The applicator is placed upside down on the patient's chest. Then the rubber bands and the plastic guide tubes attached to the applicator are introduced several centimetres up inside the distal end of the corresponding nasal catheter and a ligature is tied lightly around them. While elevating the soft palate with a retractor, traction placed on the nasal catheters causes the applicator to enter the oral cavity and slide behind the soft palate to fit exactly in the nasopharynx.

The rubber bands and plastic tubes now protruding through the nostrils are released from the catheters and the bands tied lightly together in front of the nasal septum. Immobilisation buttons are threaded over the plastic tubes up to the level of the nares. The applicator is afterloaded, following a final check film of its position and after dosimetric calculations are completed (fig 13.3A and 13.3B).
7.2 Rotterdam Nasopharyngeal Applicator

The Rotterdam nasopharyngeal applicator is a standard applicator, made out of soft silicone, which is well tolerated by the patient (Fig 13.4) (3). It is suitable for applications with stepping source afterloaders for PDR or HDR-brachytherapy, as well as for classical LDR. The applicator can remain in situ for the duration of the treatment, which varies from 2 to 6 days, and can be performed on an outpatient basis in case of HDR brachytherapy. The two silicone tubes, with an outer diameter of 15 French and an inner diameter of 9 French, can accommodate standard 6 French afterloading catheters. The shape of the silicone applicator closely conforms to the nasopharyngeal vault. The radioactive sources are consequently positioned closer to the base of the skull than to the soft palate.

Application is rather easy. After local anaesthesia of the nasal cavities and the oropharynx with a 2% xylocaine spray, a flexible guide wire is introduced into one nasal cavity. The end is recuperated with a forceps in the oropharynx and brought outside the mouth. The procedure is repeated at the other side. The applicator is then advanced over the guide wires, fixed to them by clamps, and pulled gently through the mouth and the oropharynx into the nasopharynx. The legs of the applicator sort through the nostrils and are fixed with a silicone bridge, pushed against the nasal septum. The applicator tubes are then brought into the applicator and fixed.
7.3 Massachusetts General Hospital Technique

The procedure uses two paediatric endotracheal tubes with inner and outer diameter of 5 and 6.8 mm, respectively. They can be afterloaded each with 20-mg radium-equivalent caesium 137 slugs or stepping source PDR or HDR afterloaders.

After topical anaesthesia of the nasal and the nasopharyngeal mucosa, endotracheal tubes are introduced into the nasopharynx through the nostrils. Under fluoroscopic control, the distal tip of the dummy slugs are placed at the free edge of the soft palate posteriorly and at the posterior wall of the maxillary sinus anteriorly.

The inflated balloon, which is attached to the distal end of the endotracheal tube, is used to anchor the tubes and to create a distance between the radiation sources and the nasopharyngeal vault to obtain a better depth dose. The entire implant treatment can be performed as an outpatient procedure.

7.4 Transnasal Permanent Interstitial Implants

The procedure is performed under general anaesthesia (6). The soft palate is retracted forward with a retractor, and the nasopharynx is visualised, by means of a fiber optic nasopharyngoscope. After satisfactory visualisation of the tumour site has been obtained, hollow afterloading needles are introduced into the nasal passages and are advanced through the posterior choanae, and inserted into the mucosal surface. Radioactive $^{125}$I seeds are then introduced submucosally through these needles, and the needles are withdrawn.

8 Dosimetry

Related to the PTV, dummy sources are loaded into the plastic tubes and their correct position verified with fluoroscopy. Orthogonal radiographs are taken to document the source position. CT-scan cuts are carried out through the central plane of the sources. The dose is usually prescribed to an isodose covering the surface of the underlying bone, which is situated at 5 - 10 mm from the mucosal surface. Dose distribution is optimised when possible so that the reference isodose follows the bone surface.
Dosimetry can also be carried out on the basis of two orthogonal films. Levendag et al. have published a comprehensive method based on distribution of dose at several anatomical points related to target and critical organs; dose is prescribed at a reference point (Na) situated on the midline at the bony surface of the nasopharyngeal roof. (3)

Whatever the dose prescription point, it is always advisable, for the purpose of comparison, to record and report the dose delivered at 10 mm from the mucosal surface in the central plane.

9 Dose, Dose Rate, Fractionation

Some literature data are strongly suggestive for the existence of a dose-response relationship above 65 Gy in nasopharyngeal carcinoma (3). However, escalation of dose is limited by the tolerance of neighbouring critical structures. Brachytherapy can be used to deliver an additional dose to a small volume after a full course of external beam radiation therapy. Wang delivers with low-dose-rate afterloading intracavitary implant 7 - 12 Gy at 5 mm below the mucosa (7). Levendag et al. (3) deliver after a rest period of 1 - 2 weeks, a booster dose to the primary site with high-dose-rate brachytherapy, with two 3 Gy fractions per day at 6 hour interval (3). Total of fractions is 6 (after 60 Gy external beam irradiation) for T1 - 3 tumours, and 4 (after 70 Gy external beam irradiation) for T4 tumours.

When brachytherapy is carried out for a nasopharyngeal tumour recurring in a previously irradiated area, 60 Gy are delivered in roughly 6 days with a low-dose-rate technique.

10 Monitoring

During the few days of the application, the patients receive sedatives and a liquid or pureed diet. Headache may occur, but a correctly made applicator remains well positioned and does not interfere with sleep. It is very important to check the applicator position, clinically or radiologically, and to suction the secretions, which accumulate at the nares, several times daily.

11 Results

Since 1974, at Massachusetts General Hospital, afterloading intracavitary implant has been carried out as a routine procedure to deliver a dose of 7-12 Gy as a boost to the nasopharynx for most T1 and T2 and occasionally T3 lesions (7). Table 1 shows the 5-year actuarial local control and disease-free-specific survival rates with the boost technique versus exclusive external beam radiation therapy alone. For T1 - 2 tumours, both actuarial local control and disease-free-specific survival rates were higher with brachytherapy boost; For T3 tumours, there was a trend to a higher local control rate with brachytherapy boost.

At Rotterdam Daniel Den Hoed Cancer Centre, in a prospective study of a consecutive series of 41 patients treated with 60-70 Gy external beam radiation therapy and 12 - 18 Gy high-dose rate brachytherapy boost, the 5-year local relapse free survival rate of T1 - 2 cancer patients (n = 29) was 96% versus 57% for T4 cancer patients (n = 12) (p = 0.002) (3). Chang et al. reported similar findings (1). Apparently, it seems that brachytherapy plays an apparently important role as boost modality in T1 - 3 tumours.

Brachytherapy may also be useful for retreatment of recurrent disease. Wang et al (7) reported on 38 patients who were re-irradiated (Table 2). Results were much better for T1-2 tumours and if a dose
of > 60 Gy was delivered. Overall, 52% of tumours were controlled when a dose of 60 Gy or more was delivered.

Table 1: five-year actuarial rates after radiation therapy for nasopharyngeal carcinoma related to boost techniques at Massachusetts General Hospital (7). Comparison of local control and disease-specific survival rates with and without brachytherapy: 1970-1994.

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<tr>
<th>N</th>
<th>Local control rate (%)</th>
<th>Disease-specific survival rate (%)</th>
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<tr>
<td>T1 - 2</td>
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<td></td>
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<tr>
<td>Brachytherapy</td>
<td>92</td>
<td>82</td>
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<td>No brachytherapy</td>
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<td>p = 0.0001</td>
<td>p = 0.0001</td>
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<tr>
<td>T3</td>
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<tr>
<td>T1 - 3</td>
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<td>81</td>
</tr>
<tr>
<td>No brachytherapy</td>
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<td>56</td>
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<td>p = 0.0001</td>
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Table 2: five-year actuarial rates after reirradiation (external beam irradiation and brachytherapy) for recurrent nasopharyngeal carcinoma (7).

<table>
<thead>
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<th>Local control rate (%)</th>
<th>Disease-specific survival rate (%)</th>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>1950-1994</td>
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<tr>
<td>Dose</td>
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<tr>
<td>&gt; 60 Gy</td>
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<td>&lt; 60 Gy</td>
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<td>p = 0.31</td>
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Fourteen patients were treated at the Gustave Roussy Institute for locally recurrent nasopharyngeal carcinoma, including seven with associated cervical lymph node recurrence, five months to seven years after initial radiation therapy (4). Patients received either brachytherapy alone or additional external irradiation. Total radiation doses administered to the recurrent disease varied widely between 40 and 90.5 Gy. Local control was achieved in seven patients, and two of the twelve patients who were continuously followed were disease free for at least five years.

Pryzant et al. treated 43 patients with locally recurrent or persistent nasopharyngeal carcinoma with megavoltage irradiation and 10 with a combination with brachytherapy (5). Patients who received a boost with intracavitary caesium had an improved 5-year disease-free survival rate (44% versus 14%, p = 0.19), and 5-year survival rate (60% versus 16%, p = 0.029). No severe complications were observed in patients treated with a combination of external beam irradiation and intracavitary caesium.
12 References