

## CLINICAL INVESTIGATION

# International Consensus Guideline on Delineation of the Clinical Target Volumes at Different Dose Levels for Nasopharyngeal Carcinoma (2024 Version)



Shao-Jun Lin, MD,<sup>a,b</sup> Qiao-Juan Guo, PhD,<sup>a,b</sup> Qin Liu, MBChB,<sup>c</sup> Wai-Tong Ng, FRCR,<sup>d</sup> Yong Chan Ahn, MD,<sup>e,f</sup> Hussain AlHussain, FRCPC,<sup>g</sup> Annie W. Chan, MD,<sup>h</sup> James Chow, FRCR,<sup>i</sup> Melvin L.K. Chua, FRCR,<sup>j</sup> June Corry, FRANZCR,<sup>k</sup> Fei Han, MD,<sup>l</sup> Vincent Grégoire, MD,<sup>m</sup> Kevin J. Harrington, FRCR,<sup>n</sup> Chao-Su Hu, MD,<sup>o</sup> Kenneth Jensen, PhD,<sup>p</sup> Johannes A. Langendijk, MD,<sup>q</sup> Quynh Thu Le, MD,<sup>r</sup> Nancy Y. Lee, MD,<sup>s</sup> Victor Lee, FRCR,<sup>c</sup> Jin-Ching Lin, MD,<sup>t</sup> Jun Ma, MD,<sup>u</sup> William M Mendenhall, MD,<sup>v</sup> Brian O'Sullivan, MD,<sup>w</sup> Enis Ozyar, MD,<sup>x</sup> David I. Rosenthal, MD,<sup>y</sup> Yun-Gan Tao, MD,<sup>z</sup> Ren-Sheng Wang, MD,<sup>aa</sup> Joseph Wee, FRCR,<sup>j</sup> Zhi-Yuan Xu, MD,<sup>d</sup> Jun-Lin Yi, MD,<sup>ab</sup> Sue S. Yom, MD,<sup>ac</sup> Dai-Ming Fan, MD,<sup>ad,ae</sup> Hai-Qiang Mai, MD,<sup>l</sup> Jian-Ji Pan, MD,<sup>a,af</sup> and Anne W.M. Lee, DSc<sup>d,ae</sup>

<sup>a</sup>Clinical Oncology School of Fujian Medical University, Fujian Cancer Hospital, Fujian Medical University, Fujian, China; <sup>b</sup>Fujian Key Laboratory of Translational Cancer Medicine, Fuzhou, Fujian, China; <sup>c</sup>Department of Clinical Oncology, The University of Hong Kong, Hong Kong SAR, China; <sup>d</sup>Clinical Oncology Center, The University of Hong Kong-Shenzhen Hospital, China; <sup>e</sup>Department of Radiation Oncology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Republic of Korea; <sup>f</sup>Ilsan Cha Medical Center, Republic of Korea; <sup>g</sup>Department of Radiation Oncology, Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia; <sup>h</sup>Department of Radiation Oncology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts; <sup>i</sup>Department of Clinical Oncology, Queen Elizabeth Hospital, Hong Kong SAR, China; <sup>j</sup>National Cancer Centre Singapore, Singapore; <sup>k</sup>Radiation Oncology, Genesis Care, St. Vincent's Hospital, Melbourne, Australia; <sup>l</sup>State Key Laboratory of Oncology in South China, Guangdong Key Laboratory of Nasopharyngeal Carcinoma Diagnosis and Therapy, Guangdong Provincial Clinical Research Center for Cancer, Sun Yat-sen University Cancer Center, Guangzhou, China; <sup>m</sup>Centre Léon Bérard, Lyon, France; <sup>n</sup>The Royal Marsden/The Institute of Cancer Research, London, United Kingdom; <sup>o</sup>Department of Radiation Oncology, Fudan University Shanghai Cancer Center, China; <sup>p</sup>Danish Centre for Particle Therapy, Aarhus University Hospital, Denmark; <sup>q</sup>Department of Radiotherapy, University Medical Center Groningen, University of Groningen, The Netherlands; <sup>r</sup>Department of Radiation Oncology, Stanford University, Stanford, California; <sup>s</sup>Department of Radiation Oncology, Memorial Sloan Kettering Cancer Center,

Corresponding author: Anne W.M. Lee; E-mail: [awmlee@hku.hk](mailto:awmlee@hku.hk)

Shao-Jun Lin, Qiao-Juan Guo, Qin Liu, and Wai-Tong Ng made equal contributions as co-first authors to this study.

Hai-Qiang Mai, Jian-Ji Pan, and Anne W.M. Lee contributed equally as corresponding authors.

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New York; <sup>1</sup>Department of Radiation Oncology, Taichung Veterans General Hospital, National Yang-Ming University, Taipei, Taiwan; <sup>2</sup>Department of Radiation Oncology, Sun Yat-sen University Cancer Center, Guangzhou, China; <sup>3</sup>Department of Radiation Oncology, University of Florida College of Medicine, Gainesville, Florida; <sup>4</sup>Department of Radiation Oncology, University of Toronto, Princess Margaret Cancer Centre, Toronto, Ontario, Canada; <sup>5</sup>Department of Radiation Oncology, Acibadem University School of Medicine, Istanbul, Turkey; <sup>6</sup>Department of Radiation Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas; <sup>7</sup>Department of Radiation Oncology, Institut Gustave Roussy, Paris-Saclay University, Villejuif, France; <sup>8a</sup>The First Affiliated Hospital of Guangxi Medical University, Guangxi, China; <sup>8b</sup>Cancer Hospital of the Chinese Academy of Medical Sciences, Beijing, China; <sup>9</sup>Department of Radiation Oncology, University of California, San Francisco, California; <sup>10</sup>China Anti-Cancer Association, China; <sup>11</sup>World Association for Integrative Oncology, Hong Kong SAR, China; and <sup>12</sup>Department of Radiation Oncology, Xiamen Humanity Hospital, Xiamen, Fujian, China

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**Purpose:** Radiation therapy planning for nasopharyngeal carcinoma is one of the most challenging tasks for radiation oncologists due to the notoriously narrow therapeutic margin. The first International Guideline (IG-2018 Version) has served as a practical guide for contouring clinical target volumes (CTVs). With increasing data on locoregional extension patterns and outcomes from studies on optimizing CTV and doses, an updated International Guideline is pressingly needed to provide a reference for enhancing precision.

**Methods and Materials:** A comprehensive literature review was conducted to assess existing guidelines and emerging data related to contouring. A preliminary questionnaire was distributed to 30 international experts (from 26 centers in 14 countries/regions) with extensive experience in nasopharyngeal carcinoma treatment, aiming to capture diverse practices and opinions. Following initial voting and iterations, a comprehensive survey was prepared for consensus building.

**Results:** The initial questionnaire revealed marked variations in clinical practices related to CTV contouring and prescribed doses among experts. The final Delphi survey consisted of 58 questions: 20 (34%) parameters attained consensus ( $\geq 75\%$  agreement) and 32 (55%) attained agreement (60%-74% agreement). In the current guideline (IG-2024), 36 parameters involved changes/clarifications compared with IG-2018. The major differences focus on the use of postinduction chemotherapy gross tumor volume (except in patients with advanced extranodal extension) for CTV(p/n) to 70 Gy equivalent, stepwise refinement of elective coverage to ipsilateral anatomical structures for eccentric primary tumor, selective coverage of nodal levels, and a lower elective dose of 50 Gy equivalent.

**Conclusions:** Amidst the challenges of diverging practices, a comprehensive consensus guideline has been devised based on updated evidence and collective agreement among international experts. This serves as a practical reference for optimal target coverage at different dose levels to maximize locoregional control while minimizing toxicities and guiding principles for generating automated contouring programs to enhance standardization. © 2025 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

## Introduction

Radiation therapy (RT) is the primary treatment modality for nasopharyngeal carcinoma (NPC), but the therapeutic margin is notoriously narrow due to the anatomic proximity to critical structures. The importance of accurately delineating the gross tumor volume (GTV) and organs at risk using state-of-the-art imaging techniques cannot be overemphasized. Given the highly infiltrative nature of NPC, optimal contouring of the clinical target volume (CTV) to encompass regions at risk of microscopic involvement is essential.

To standardize treatment practices and enhance the quality of RT, an International Guideline for CTV delineation in NPC was developed in 2018 (IG-2018) as a practical reference for global applications.<sup>1</sup> With advances in imaging technology and the accumulation of knowledge on locoregional extension patterns (see [Table E1](#) for details), new evidence has emerged advocating for more selective coverage. Thus, it is essential to devise an updated International Guideline (IG-2024) to further optimize target volumes and radiation doses.

## Methods and Materials

A comprehensive literature search was conducted to identify studies on locoregional extension patterns, and CTV contouring/dose prescription for NPC. Detailed descriptions of the search methodology and Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow for identifying relevant articles are provided in the supplementary information ([Figure E1](#)). A total of 70 publications, including prospective/retrospective studies and guidelines published between January 2008 and September 2023, were reviewed. Of these, 33 publications presented new data prompting the need to update IG-2018. Recent studies published after the search cutoff date were also considered in the “Discussion” section. Detailed recommendations from 6 major guidelines<sup>1-6</sup> were summarized in [Table E2](#).

An international panel was formed, comprising previous experts who devised IG-2018 and those with relevant publications or extensive experience in NPC treatment from leading academic institutions worldwide. A total of 30 international experts from 26 centers in 14 countries/regions

(demographic information is shown in Table E3) participated to ensure diverse perspectives and global representation.

A preliminary questionnaire was circulated to panel members to gather information on variations in practice and comments on contentious issues (Table E4). Following initial anonymized voting and iterations, a comprehensive Delphi survey with 58 questions was conducted for consensus building. In IG-2024, proposed recommendations are defined as attaining “consensus” if agreement  $\geq 75\%$ , “agreement” if 60%-74%, and “divided opinion” if  $< 60\%$ , in line with cutoff levels adopted in more recently published articles/guidelines.<sup>7-12</sup> The quality of evidence (QoE) and the strength of recommendation (SoR) are assessed according to the ASTRO Clinical Practice Guideline Methodology Guide<sup>13</sup>; details of the criteria are shown in the supplementary material. To reflect the different degrees of overall validity for practical use, we use the term “strongly recommend” for recommendations supported by consensus and/or high QoE, “recommend” for those with agreement and/or moderate QoE, and “suggest” for those with divided opinion, but definable acceptable range based on moderate QoE, or those with agreement, but low QoE.

## Results and Discussion

All 30 panel experts completed 2 rounds of the Delphi process. Among the 58 parameters surveyed, 34% attained consensus and 55% attained agreement, whereas 10% had a divided opinion. Table 1 summarizes the IG-2024 recommendations (with the corresponding percentage of agreement, QoE, and SoR) and comparisons with IG-2018. In addition, information on alternative suggestions was listed in Table E5 for a comprehensive understanding of the diverse opinions.

### GTV postinduction chemotherapy

#### Recommendations

- Primary tumor: GTVp based on postinduction volume (agreement: 73%), with a prescribed dose of 70 Gy (consensus: 97%).
- Nodal region without advanced extranodal extension (ENE): GTVn based on postinduction volume (consensus: 90%), with a prescribed dose of 70 Gy (consensus: 97%).
- Nodal region with advanced ENE: GTVn based on preinduction volume (agreement: 67%), with a prescribed dose of 70 Gy (consensus: 97%).

Induction chemotherapy followed by concomitant chemo-radiation therapy is commonly used in the treatment of locoregionally advanced NPC.<sup>14-16</sup> Given the high chemo-sensitivity, most patients achieve substantial tumor regression. This leads to the controversy of whether to

prescribe a full therapeutic dose to the pre- or postinduction GTV. IG-2018 recommended using the preinduction GTV regardless of subsequent shrinkage, aligning with recommendations from other head and neck cancers.<sup>17</sup> In contrast, most Chinese guidelines recommend covering only the postinduction volume (except for skull base diseases where regression is difficult to determine) to 70 Gy equivalent (CTVp\_70) while ensuring the preinduction GTV receives 60 Gy equivalent (CTVp\_60). This approach is supported by several retrospective and prospective trials.<sup>18-26</sup>

The first randomized study by Xiang et al<sup>25</sup> (n = 212) showed a non-inferior locoregional recurrence-free survival (LR-RFS) of 90% at 5 years comparing patients with delineation based on postinduction GTV versus preinduction GTV (25). This was the key evidence available during our Delphi survey, and the agreement was only 73%. However, a recent publication of another phase 3 randomized controlled trial by Tang et al<sup>26</sup> (n = 445) confirmed not only non-inferior LR-RFS (91.5% at 3 years) but also reduced toxicities and enhanced quality of life.

Given this robust high QoE, IG-2024 strongly recommends using the postinduction volume for delineating GTVp and GTVn without extranodal extension (ENE), but tumor infiltration at the skull bases should be based on preinduction volume due to difficulty in determining regression and the entire preinduction tumor volume should be fully encompassed within CTVp\_60. Furthermore, we call for special caution in patients with advanced ENE (unequivocal involvement of adjacent muscle, skin, and/or neurovascular structures), a newly added criterion for N3 disease by the AJCC/UICC TNM Version 9. This is associated with significantly adverse outcomes in all aspects (including nodal control),<sup>27</sup> and the panel recommends using the preinduction volume for delineating GTVn in this poor prognostic cohort.

### Delineation of CTV for the primary tumor

The delineation for the primary tumor (CTVp) involves two fundamental components: geometric expansion margins and anatomical editing to account for tumor spreading along neural pathways and foramina.<sup>28-30</sup> Growing evidence indicates that most local recurrences were in-field failures, and locoregional extension follows an orderly stepwise pattern (Table E1).<sup>28-30</sup> This raises the possibility of using narrower expansion margins and limiting elective coverage to ipsilateral adjacent structures for eccentric tumors.

### High-risk CTVp to 70 Gy equivalent (CTVp\_70)

#### Recommendation for geometric expansion

- GTVp plus margin ranging from 0 to 5 mm suggested (*divided opinion*: 53% suggesting 0 mm margin, 47% suggesting 3-5 mm margin) (Fig. 1).

**Table 1 Recommendations listed in the International Guideline 2024 Version and differences in comparison with the previous 2018 version**

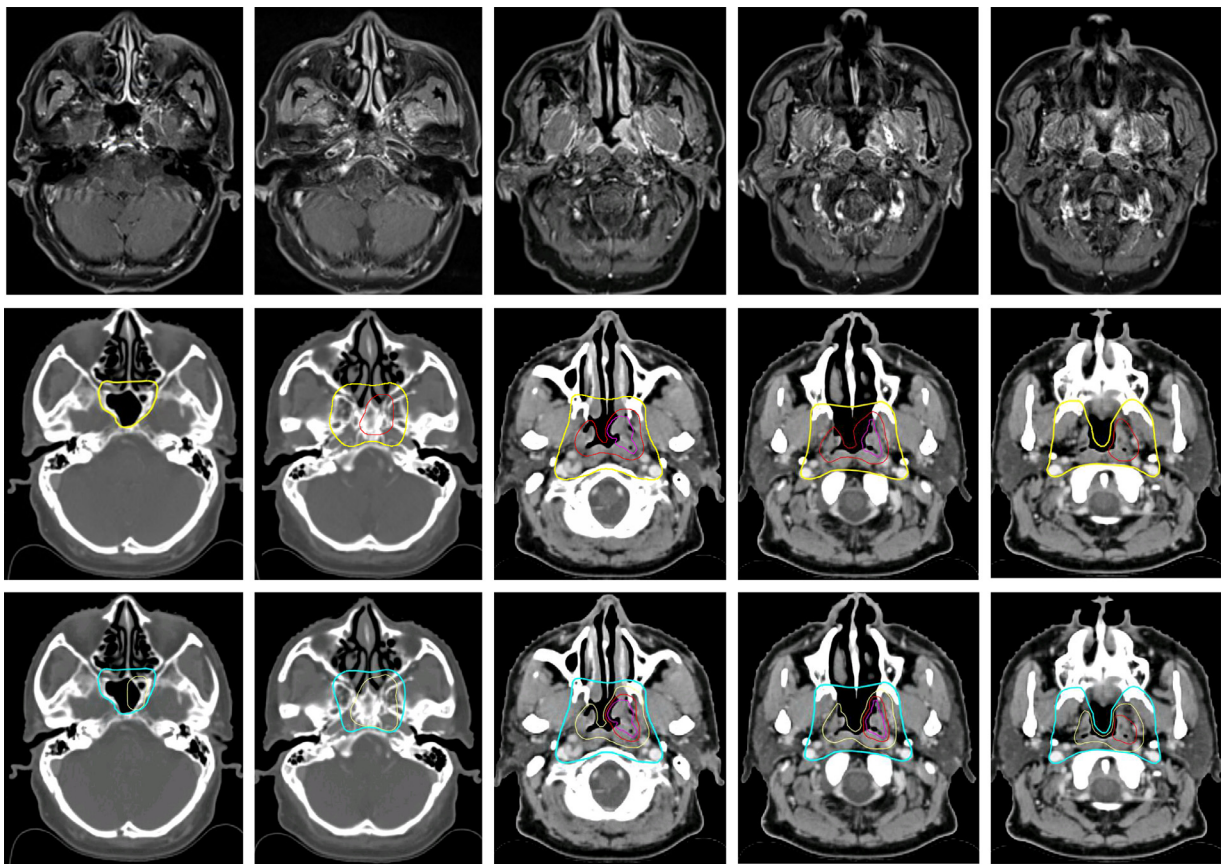
Parameter	IG-2018 Recommendation	IG-2024				
		Recommendation	Agreement (%)	QoE	SoR	
<b>Gross tumor volume (GTV) for patients treated with induction chemotherapy</b>						
GTVp	Delineation	Based on preinduction GTVp	Based on <b>postinduction GTVp</b>	22/30 (73%)	High <sup>25,26</sup>	Strong
	Dose	70 Gy	70 Gy	29/30 (97%)	High <sup>25,26</sup>	Strong
GTVn	Delineation	Without ENE: Based on preinduction GTVn	Without ENE: Based on <b>postinduction GTVn</b>	27/30 (90%)	High <sup>25,26</sup>	Strong
		With ENE: Based on preinduction GTVn	With ENE: Based on preinduction GTVn	20/30 (67%)	Moderate <sup>19,25,42</sup>	Conditional
	Dose	70 Gy	70 Gy	29/30 (97%)	High <sup>19,25,26,42</sup>	Strong
<b>Expansion margin for CTvp and coverage of the whole nasopharynx</b>						
CTvp_70	Margin	GTVp + 5 mm	GTVp + <b>0-5 mm</b>	0 mm 16/30 (53%) 3-5 mm 14/30 (47%)	Moderate <sup>26,40-42,52</sup>	Conditional
CTvp_60	Margin	GTVp + 10 mm	GTVp + <b>8-10 mm</b>	21/30 (70%)	Moderate <sup>26,39,41,42,55</sup>	Conditional
Whole Nasopharynx	Dose	60-70 Gy	<b>60 Gy</b>	23/30 (77%)	Moderate <sup>36,39,42,53,55</sup>	Strong
<b>Elective coverage of anatomical structures for CTvp</b>						
Posterior nasal cavity	Coverage	At least 5 mm from choana	At least 5mm from choana	22/30 (73%)	Moderate <sup>43,53</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b> (if cover*)	14/22 (64%)	Moderate <sup>43,53</sup>	Conditional
Posterior maxillary sinuses	Coverage	At least 5 mm from the posterior wall	At least 5 mm from the posterior wall	19/30 (63%)	Moderate <sup>52,53</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b> (if cover*)	12/19 (63%)	Moderate <sup>42,53</sup>	Conditional
Pterygoid process	Coverage	Include pterygoid plates and fossa	Include pterygoid plates and fossa	26/30 (87%)	Moderate <sup>36,53</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b>	18/30 (60%)	Moderate <sup>36,53</sup>	Conditional
Parapharyngeal space	Coverage	To include retro-styloid space	To include retro-styloid space	20/30 (67%)	Moderate <sup>43,58,90</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	21/30 (70%)	Moderate <sup>43,53</sup>	Conditional
Posterior ethmoid sinuses	Coverage	Include vomer	Include vomer	19/30 (63%)	Moderate <sup>41,42,53</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	12/19 (63%)	Moderate <sup>42,53</sup>	Conditional
Sphenoid sinuses	Coverage	Inferior half if T1-2; whole if T3-4	<b>Inferior 5-10 mm; whole if involved</b>	24/30 (80%)	Moderate <sup>36,43,53</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b>	21/30 (70%)	Moderate <sup>36,53</sup>	Conditional
Cavernous sinus	Coverage	Ipsilateral, if T3-4	Ipsilateral, if T3-4	24/30 (80%)	Moderate <sup>28,30,44,49</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b> (if cover*)	21/30 (70%)	Moderate <sup>42,49,53</sup>	Conditional
Foramen lacerum	Coverage	Bilateral for all	Bilateral for all	19/30 (63%)	Moderate <sup>36,43,53</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	18/30 (60%)	Moderate <sup>36,43,53</sup>	Conditional
Foramen ovale	Coverage	Bilateral for all	Bilateral, <b>but ipsilateral for eccentric tumor</b>	21/30 (70%)	Moderate <sup>44,50</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	20/30 (67%)	Moderate <sup>41,42,50</sup>	Conditional

(Continued)

Parameter		IG-2018 Recommendation	IG-2024			
			Recommendation	Agreement (%)	QoE	SoR
Foramen rotundum	Coverage	Bilateral for all	Bilateral for all or Ipsilateral for eccentric tumor	Bilateral for all (53%) Ipsilateral for eccentric tumor (47%)	Moderate <sup>28,44,50,51</sup>	-
	Dose	50-60 Gy	<b>50 Gy</b> (if cover*)	21/30 (70%)	Moderate <sup>41,53</sup>	Conditional
Petrous tip	Coverage	Bilateral for all	Bilateral for all or Ipsilateral for eccentric tumor	Bilateral for all (40%) Ipsilateral for eccentric tumor (30%) Not routinely cover (30%)	Moderate <sup>28,30,43</sup>	-
	Dose	50-60 Gy	<b>50 Gy</b> (if cover*)	13/21 (62%)	Moderate <sup>41,43,53</sup>	Conditional
Clivus	Coverage	Anterior one-third if uninvolved; whole if involved	Anterior one-third if uninvolved; whole if involved	28/30 (93%)	Moderate <sup>41,42,53</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b>	19/30 (63%)	Moderate <sup>41,42,53</sup>	Conditional
<b>Expansion margin for CTVn and equivocal LN</b>						
CTVn_70	Margin	Without ENE: GTVn + 5 mm	Without ENE: GTVn + <b>0-5 mm</b>	0 mm 15/30 (50%) 3-5 mm 15/30 (50%)	Moderate <sup>39,42,55</sup>	Conditional
		With ENE: GTVn + 10 mm	With ENE: GTVn + <b>5-10 mm</b>	23/30 (77%)	Expert opinion <sup>57</sup>	Strong
Equivocal LN	Margin	-	<b>0 mm</b>	21/30 (70%)	Expert opinion	Conditional
	Dose	60-70 Gy	<b>60 Gy</b>	25/30 (83%)	Expert opinion	Strong
Low-risk CTVn	Margin	Without ENE: GTVn + 10 mm	<b>encompassing CTVn_60-70 &amp; cover corresponding nodal level</b>	22/30 (73%)	Moderate <sup>41,42</sup>	Conditional
		With ENE: GTVn + 15 mm		20/30 (67%)	Moderate <sup>41,42</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	18/30 (60%)	Moderate <sup>41,42</sup>	Conditional
<b>Elective coverage of levels for CTVn</b>						
Lateral Retropharyngeal LN	Coverage	Bilateral for all	Bilateral for all	27/30 (90%)	Moderate <sup>43,55</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b>	20/30 (67%)	Moderate <sup>43,55</sup>	Conditional
Level II	Coverage	Bilateral for all	Bilateral for all	28/30 (93%)	High <sup>39,42,64</sup>	Strong
	Dose	50-60 Gy	<b>50 Gy</b>	20/30 (67%)	Moderate <sup>39,64</sup>	Conditional
Level III & Va	Coverage	Bilateral for all	Bilateral for all	22/30 (73%)	High <sup>39,42,64</sup>	Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	26/30 (87%)	Moderate <sup>39,64</sup>	Strong
Level IV & Vb-c	Coverage	Omit if N0 or N1 based solely on retropharyngeal LN involvement	<b>Cover only if ipsilateral Level III/Va involved</b>	20/30 (67%)	Moderate <sup>39,63,64</sup>	Conditional
	Dose	50 Gy	50 Gy	29/30 (97%)	Moderate <sup>39,64</sup>	Strong

(Continued)

Parameter		IG-2018 Recommendation	IG-2024			
			Recommendation	Agreement (%)	QoE	SoR
Level IB	Indications	Ipsilateral coverage if involved <ul style="list-style-type: none"> <li>• Ib LN</li> <li>• Submandibular gland</li> <li>• 1<sup>st</sup> echelon site: oral cavity or anterior half of nasal cavity</li> <li>• Level II LN with ENE</li> <li>• Level II LN with axial diameter &gt;2 cm</li> </ul>	Ipsilateral coverage if involved <ul style="list-style-type: none"> <li>• Ib LN</li> <li>• Submandibular gland</li> </ul>	26/30 (87%) 24/30 (80%)	Moderate <sup>78,81,83,84</sup>	Strong Strong
			<ul style="list-style-type: none"> <li>• 1<sup>st</sup> echelon site: oral cavity or anterior half of nasal cavity</li> </ul>	19/30 (63%)		Conditional
	Dose	50-60 Gy	<b>50 Gy</b>	15/30 (50%) 14/30 (47%)	Moderate <sup>81,84,85</sup>	-
Submandibular gland	Coverage	-	<b>Cover only if involved</b>	25/30 (83%)	Moderate <sup>78,81,83,84</sup>	Strong
<b>Clarification on anatomical borders</b>						
Anatomical border for CTVn	Cranial border of Level II & retro-styloid LN	Skull base	Skull base	23/30 (77%)	Moderate <sup>58,90</sup>	Strong
	Caudal border	At least ipsilateral one level below the involved level	Levels I, II, III, Va involved: one level below the involved level <b>Levels IV/Vb-c involved: to clavicular head and 2 cm below involved LN</b>	23/30 (77%) 18/30 (60%)	Expert opinion <sup>58</sup> Expert opinion <sup>58</sup>	Strong Conditional
	Anterior border of Level IVa	Anterior edge of sternocleidomastoid muscle-	<b>Posterior edge of infrahyoid ribbon muscle</b>	25/30 (83%)	Moderate <sup>89,91</sup>	Strong
<p><i>Abbreviations:</i> ENE = extranodal extension; CTVp/n_70, CTVp/n_60, CTVp/n_50 = clinical tumor volume to 70 Gy, 60 Gy, 50 Gy equivalent, respectively; QoE = quality of evidence; SoR = strength of recommendation.</p> <p>* The agreement on the prescribed dose was based on those experts who recommended elective coverage of the corresponding structure.</p> <p>Recommendations marked in bold: change/clarification as compared with IG-2018.</p>						



**Fig. 1.** Delineation of the primary clinical target volume (CTVp) for T1 lateralized tumor. Upper row: magnetic resonance imaging (MRI) of a well-lateralized primary tumor at the left lateral wall of the nasopharynx. Middle row: CTV delineation in accordance with International Guideline-2018 (IG-2018). Lower row: CTV delineation in accordance with IG-2024. In the lower row, the CTVp<sub>70</sub> (red line) is based on primary gross tumor volume (GTVp) (purple line) with a 3-mm margin (acceptable range 0-5 mm); the CTVp<sub>60</sub> (yellow line) is GTVp with an 8-mm margin, encompassing the whole nasopharynx. The CTVp<sub>50</sub> (blue line) covers the vomer, the inferior 5 mm of the sphenoid sinus, bilateral foramen lacerum, ipsilateral foramen ovale, the anterior third of the clivus, the posterior 5 mm of the nasal cavity and maxillary sinus, bilateral pterygoid processes and fossae, as well as the bilateral parapharyngeal and retro-styloid spaces.

Data on microscopic extension from the primary tumor in NPC are limited, as surgery is not a primary treatment modality. The recommendation of a 5-mm margin in IG-2018 was extrapolated from a surgical series on recurrent NPC by Chan et al<sup>31</sup>, showing that the recurrent tumors were typically 3-4 mm larger histologically when compared with radiological images. This aligned with the recommendations for other head and neck cancers.<sup>32-34</sup>

Recent studies suggested omitting expansion, based on the radiobiological principle that tumor control probability is associated with clonogenic cell burden, subclinical involvement with lower tumor density may be effectively managed with a lower irradiation dose compared with gross tumor. This approach is supported by several studies from China<sup>25,26,35-43</sup> and one study from the United States,<sup>44</sup> reporting excellent local failure-free survival (L-FFS) exceeding 90% with a 0-mm margin.

Opinion is divided regarding the expansion margin: 53% of the panel opted for a 0-mm margin, whereas 47% maintained a 3-5-mm margin as a reference for global

application to minimize the risk of inadequate coverage. This reflects emerging data supporting tighter margins in experienced centers, but there were no rigid prerequisites specified in the studies advocating a 0-mm margin. Ideally, high-quality magnetic resonance imaging, optimal fusion for RT planning, and precision setup with image guidance are needed. Furthermore, target delineation should be performed by radiation oncologists with subspecialty expertise in NPC and imaging interpretation. Therefore, IG-2024 does not specify a dogmatic recommendation but suggests a more inclusive range of 0 to 5 mm, taking into consideration the practical realities of varying institutional capabilities.

### **Intermediate-risk CTVp to 60 Gy Equivalent (CTVp<sub>60</sub>)**

#### **Recommendation for geometric expansion margin**

- GTVp plus 8-10 mm (*agreement:70%*)

In IG-2018, a margin of GTVp plus 10 mm was recommended. This was based on extrapolation from the study by

Chan et al<sup>31</sup>, which demonstrated that the maximum invasion distance was within 10 mm from the gross recurrent tumor. It also aligned with the 10-mm recommendation for other head and neck cancers.<sup>45</sup>

IG-2024 recommends a flexible range of 8-10-mm margin from GTVp. This recommendation is supported by retrospective studies showing that an 8-mm margin provides adequate coverage.<sup>41,42</sup> A recent study by Guo et al<sup>41</sup> (n=471), using an 8-mm margin from GTVp to CTVp<sub>50</sub>, reported an excellent 4-year L-FFS of 96.6% with no out-of-field recurrence.<sup>41</sup> Similarly, the NRG-HN001 protocol also used an 8-mm margin from GTVp to CTVp<sub>56-59.4</sub>.<sup>4</sup> It is worth noting that 30% of panel members supported an even tighter margin of 5 mm.

### Recommendation on anatomical editing

- Include the whole nasopharynx in CTVp<sub>60</sub> (*consensus: 77%*).

In IG-2018, opinion was divided on whether the entire nasopharynx should be irradiated to a full therapeutic dose. Specifically, 53% of experts advocated its inclusion in CTVp<sub>70</sub>. This recommendation was based on a CT-based study by Sham et al<sup>46</sup>, which showed that 13.8% of NPC patients had a submucosal growth pattern and 51.4% had an occult microscopic extension. However, studies using modern imaging reported excellent accuracy by MRI with sensitivity and negative predictive value reaching 100%.<sup>47</sup>

In IG-2024, consensus was reached among experts against routine irradiation of uninvolved nasopharyngeal regions to 70 Gy, as subclinical mucosal involvement does not necessitate a full therapeutic dose, whereas 23% of the panel even advocated a reduced dose of 50 Gy. IG-2024 strongly recommends an intermediate dose of 60 Gy for the entire nasopharynx (Fig. 1).

### Low-risk CTVp to 50 Gy equivalent (CTVp<sub>50</sub>)

In IG-2024, there is a major trend toward stepwise consideration based on actual tumor extent and the corresponding risk of adjacent structures (Table E1). Given the current understanding of the orderly infiltration pattern, sparing contralateral structures is considered reasonably safe for eccentric tumors that do not extend to the midline. In IG-2018, no recommendations were made regarding prescribed doses; most centers adopted 50-60 Gy based on local practice. With growing clinical evidence supporting the safety of 50 Gy, IG-2024 now recommends a prescribed dose of 50 Gy.

### Recommendations regarding anatomical editing of adjacent structures

- Posterior nasal cavity: 5 mm from the nasal choanae for all cases (*agreement: 73%*), with a prescribed dose of 50 Gy (*agreement: 64%*).
- Posterior maxillary sinus: posterior 5 mm for all cases (*agreement: 63%*), with a prescribed dose of 50 Gy (*agreement: 63%*).

All current guidelines advocate routine coverage of the posterior nasal cavity (Table E2). However, there are variations in the recommended extent, ranging from the posterior one-fourth to one-third, or 5 mm from the choanae.<sup>1,2,6</sup> IG-2024 recommends adopting the specification of 5 mm from the choanae.

The maxillary sinus is considered a low-risk structure in NPC, with an involvement rate of less than 5%.<sup>28-30</sup> IG-2018 recommended covering the posterior maxillary sinus to ensure adequate inclusion of the pterygo-maxillary fissure and pterygo-palatine fossae, aligning with most guidelines.<sup>4-6</sup> Similar to the recommendations for the nasal cavity, there are varying recommendations for the extent of coverage. IG-2024 recommends adopting the specification of posterior 5 mm. It is worth noting that 37% of experts did not recommend routine coverage of the posterior maxillary sinus. This approach was supported by Sanford et al<sup>44</sup> and Billan et al,<sup>48</sup> who advocated for sparing the clivus, nasal cavity, maxillary sinus, ethmoid sinus, or sphenoid sinus unless they are involved.

- Pterygoid process and fossa: bilateral coverage for all cases (*consensus: 87%*), with a prescribed dose of 50 Gy (*agreement: 60%*).
- Parapharyngeal space: includes retro-styloid space (*agreement: 67%*), with a prescribed dose of 50 Gy (*agreement: 70%*).

All established guidelines consistently recommend routine coverage of bilateral pterygoid processes and parapharyngeal spaces. This recommendation remains unchanged in IG-2024. Regarding the delineation of parapharyngeal spaces, 67% of experts support the coverage of the retro-styloid space. However, recent studies suggest that sparing these structures may be feasible in selected cases. Sanford et al<sup>44</sup> covered only the ipsilateral pterygoid fossa and parapharyngeal spaces. Similarly, Miao et al<sup>49</sup> proposed ipsilateral coverage of both structures for T2 eccentric tumors and even suggested omitting bilateral pterygoid fossa for T1 tumors. Wu et al<sup>30</sup> further showed that for eccentric tumors, the incidence of contralateral involvement of the pterygoid fossa and parapharyngeal spaces was below 5%, suggesting that contralateral sparing might be feasible. Xie et al<sup>50</sup>, using a wide margin of 15-20 mm, also showed that sparing contralateral parapharyngeal space did not lead to recurrence in contralateral structures for eccentric tumors.

- Ethmoid sinus: include the posterior part for all patients to ensure coverage of the vomer (*agreement: 63%*), with a prescribed dose of 50 Gy (*agreement: 63%*).

IG-2018 recommended the inclusion of the posterior-inferior part of the ethmoid sinus to ensure coverage of the vomer, which is the superior anatomical border of the nasopharynx. However, the involvement rate of the ethmoid

sinus is relatively low, at approximately 5%.<sup>28-30</sup> Recent studies have raised questions about the necessity of routine coverage of the posterior ethmoid sinus.<sup>44,49</sup> Sanford et al<sup>44</sup> reported a 5-year L-FFS of 94% for their series (n=73, majority with T3-4 disease) treated with selective coverage (including sparing the ethmoid sinus unless involved). Similarly, a prospective study by Miao et al<sup>49</sup> involving 103 T1-2N0-1 patients demonstrated a 10-year L-FFS of 90.3%, with only one in-field failure reported.

IG-2024 recommends coverage of the vomer to 50 Gy. However, it is worth noting that 37% of experts supported omitting this as routine inclusion or considered covering this only in cases where the nasal cavity is invaded, particularly for T3-4 tumors.

- Sphenoid sinus: include the inferior 5-10 mm for all patients and cover the whole sinus if involved (*consensus: 80%*), with a prescribed dose of 50 Gy (*agreement: 70%*).

IG-2018 recommended including the inferior half of the sphenoid sinus for T1-2 tumors and the entire sinus for T3-4 tumors. However, recent studies have demonstrated successful sparing of the sphenoid sinus when not involved.<sup>44,48</sup>

IG-2024 strongly recommends maintaining routine coverage of the inferior part of the sphenoid sinus, but the extent specification is changed to the “inferior 5-10 mm” for clarity, and the coverage of the entire sphenoid sinus is now recommended only for patients with overt involvement, rather than for all T3-4 diseases.

- Cavernous sinus: spare if T1-2 and cover if T3-4 (ipsilateral for eccentric tumors) (*consensus: 80%*), with a prescribed dose of 50 Gy (*agreement: 70%*).

IG-2024 maintains the recommendation from IG-2018 to spare the cavernous sinuses in T1-2 tumors and to cover them in T3-4 tumors on the involved side. This approach aligns with the NRG-HN001 protocol<sup>4</sup> and the 2021 CMDA/CMA guidelines.<sup>2</sup> This approach is supported by Miao et al<sup>49</sup> for T1-2 disease and by Wu et al<sup>30</sup> who showed that contralateral invasion occurred in only 0.5% of eccentric tumors (Table E1).

Other guidelines have introduced more specific indications for cavernous sinus inclusion. The 2023-2024 CSCO guidelines<sup>3</sup> confined the indication to patients with clivus, petrous tip, or foramen lacerum involvement. In contrast, the 2020 DAHANCA guideline<sup>6</sup> recommended inclusion only for those with suspicious cavernous sinus involvement. Sparing the cavernous sinus may be considered in rare cases where the T4 category is solely due to inferior extension (e.g., hypopharynx). However, long-term outcome data supporting these specific suggestions are currently lacking, and further validation is needed.

- Skull base foramina

- Foramen lacerum: bilateral coverage for all patients (*agreement: 63%*), with a prescribed dose of 50 Gy (*agreement: 60%*).
- Foramen ovale: bilateral coverage, but ipsilateral for eccentric tumors (*agreement: 70%*), with a prescribed dose of 50 Gy (*agreement: 67%*).
- Foramen rotundum: routine coverage is recommended with a prescribed dose of 50 Gy (*agreement: 70%*) but divided opinion as to whether to choose bilateral coverage for all cases similar to foramen lacerum (53%) or ipsilateral coverage for eccentric tumors (47%).
- Petrous tip: routine coverage is recommended (*agreement: 70%*) with a prescribed dose of 50 Gy (*agreement: 62%*) but divided opinion as to whether to choose bilateral coverage for all cases similar to foramen lacerum (40%) or ipsilateral coverage for eccentric tumors (30%).

IG-2018 recommended covering bilateral skull base foramina, including foramen lacerum, foramen ovale, foramen rotundum, and petrous tip, aligning with most published guidelines. The recommendation to cover the foramen lacerum bilaterally for all cases remains unchanged in IG-2024, as it is a high-risk structure with an involvement rate of 35% to 50%.<sup>28-30</sup>

Nevertheless, emerging evidence suggests that selective sparing of certain foramina may be appropriate in selected cases.<sup>30,44,49-51</sup> Miao et al<sup>49</sup> proposed omitting coverage of the foramen ovale for T1 NPC, whereas Sanford et al<sup>30</sup> and Wu et al<sup>44</sup> proposed omitting contralateral coverage of the foramen ovale for eccentric tumors. Xie et al<sup>50</sup>, using a wide margin of 15-20 mm from GTVp, reported a 5-year L-FFS of 97% with sparing contralateral skull base foramina.

The coverage of foramen rotundum is controversial. Liang et al<sup>28</sup> reported an involvement rate of 9.2%. One practical challenge is accurately depicting the foramen rotundum, particularly in individuals with dysplasia of the sphenoid bone or excessive pneumatization of the sphenoid sinus. All panel members agreed to routinely cover the foramen rotundum to a recommended dose of 50 Gy, but opinion is divided on the extent (bilateral coverage for all cases or ipsilateral coverage for eccentric tumors).

Another area of controversy is the coverage of the petrous tip, which is a high-risk structure with reported involvement rates ranging from 34.6% to 46.7%.<sup>28-30</sup> Contralateral invasion rates were reported as 6.3% for eccentric tumors and 28.7% for central lesions.<sup>30</sup> Anatomically, the petrous tip abuts the foramen lacerum. IG-2018 recommended routine bilateral coverage of the petrous tip, aligning with the 2023-2024 CSCO guidelines.<sup>3</sup> Other published guidelines did not specify coverage of the petrous tip.<sup>2,5,6</sup> IG-2024 recommends routine coverage to 50 Gy to ensure adequate coverage of the foramen lacerum, but opinions are divided regarding the extent (bilateral coverage for all cases or ipsilateral coverage for eccentric tumors).

- Clivus: cover the anterior one-third if uninvolved and the whole clivus if involved (*consensus: 93%*), with a prescribed dose of 50 Gy (*agreement: 63%*).

The clivus is a high-risk structure, with involvement rates ranging from 38.3% to 50.8%.<sup>28-30</sup> The 2023-2024 CSCO guidelines and the RTOG 0225 protocol advocate for routine inclusion of the entire clivus, regardless of involvement.<sup>3,52</sup> However, most other published guidelines cover only the anterior portion of the clivus in the absence of overt invasion. Full coverage is limited to cases with overt invasion (Table E2). This approach is supported by a prospective study that encompassed only anterior one-third of the clivus, with no observed recurrences in the posterior clivus.<sup>53</sup> IG-2024 strongly recommends maintaining the current clivus coverage and specifies 50 Gy as the recommended dose.

## Delineation for nodal CTV

### High-risk nodal CTV to 70 Gy equivalent

#### Recommendation for geometric expansion

- Patients without ENE: GTVn plus margin ranging from 0 to 5 mm suggested (*divided opinion with 50% suggesting a 0-mm margin, 50% suggesting a 3-5-mm margin*).
- Patients with advanced ENE: GTVn plus 5-10 mm margin (*consensus: 77%*).

In IG-2018, it was recommended to encompass GTVn plus a 5-mm margin for patients without ENE and 10 mm for those with ENE to a full therapeutic dose of 70 Gy. This recommendation aligns with the 2020 DAHANCA guidelines.<sup>6</sup> However, there is limited surgical and pathological data on the microscopic extension of nodal metastasis in NPC. The only relevant clinicopathological study by Wei et al.<sup>54</sup>, which analyzed resected neck specimens from 27 recurrent NPC patients, showed that ENE was common (84%), but detailed data on the tumor infiltration range beyond the capsule were not reported (Figs. 2 and 3).

Emerging data support reducing the expansion margin to 0 mm,<sup>35-39,42,55</sup> with a 5-year regional failure-free survival (R-FFS) of approximately 95%. This approach is adopted in most guidelines from China (Table E2).

Similar to the discussion on expansion margin for GTVp to CTVp\_70, opinion is divided for patients without ENE: 50% of the panel opted for a 0-mm margin, whereas 50% maintained a 3-5-mm margin as a reference for global application. Hence, IG-2024 would not specify a dogmatic recommendation but suggests a more inclusive range of 0 to 5 mm taking into consideration practical realities of varying institutional capabilities.

For patients with ENE, the IG-2018 recommendation of a 10-mm margin was based on the guideline by Grégoire et al.<sup>56</sup>, which states that for patients with infiltration of the adjacent muscle, the muscle (at least for the entire invaded

level) should be included. Data from non-NPC head and neck cancers suggested that 96% of nodes with extranodal infiltration were situated within <5 mm from the capsule.<sup>57</sup> In IG-2024, consensus was attained among panel members for patients with advanced ENE, an expansion margin of 5-10 mm is strongly recommended for delineating nodal (CTVn)\_70.

### Equivocal LN

#### Recommendation

- No additional expansion margin (*agreement: 70%*), with a prescribed intermediate dose of 60 Gy (*consensus: 83%*).

Detailed information about the criteria for defining positive LN is shown in the Supplementary material. For equivocal LNs that fall short of these defining criteria, both IG-2018 and the 2021 CMDA/CMA guidelines recommended a therapeutic dose of approximately 70 Gy, but geometric margins were not specified.<sup>1,2</sup> Other protocols suggested a lower dose for equivocal LNs, with variations in geometric expansion: the NRG-HN001 protocol recommended 61.45 Gy with a 3-mm margin,<sup>4</sup> whereas the 2014 AIRO guideline recommended 60 Gy without specifying a margin.<sup>5</sup> IG-2024 suggests a 0-mm margin for equivocal LN and strongly recommends a prescribed dose of 60 Gy.

### Low-risk nodal CTV to 50 Gy equivalent

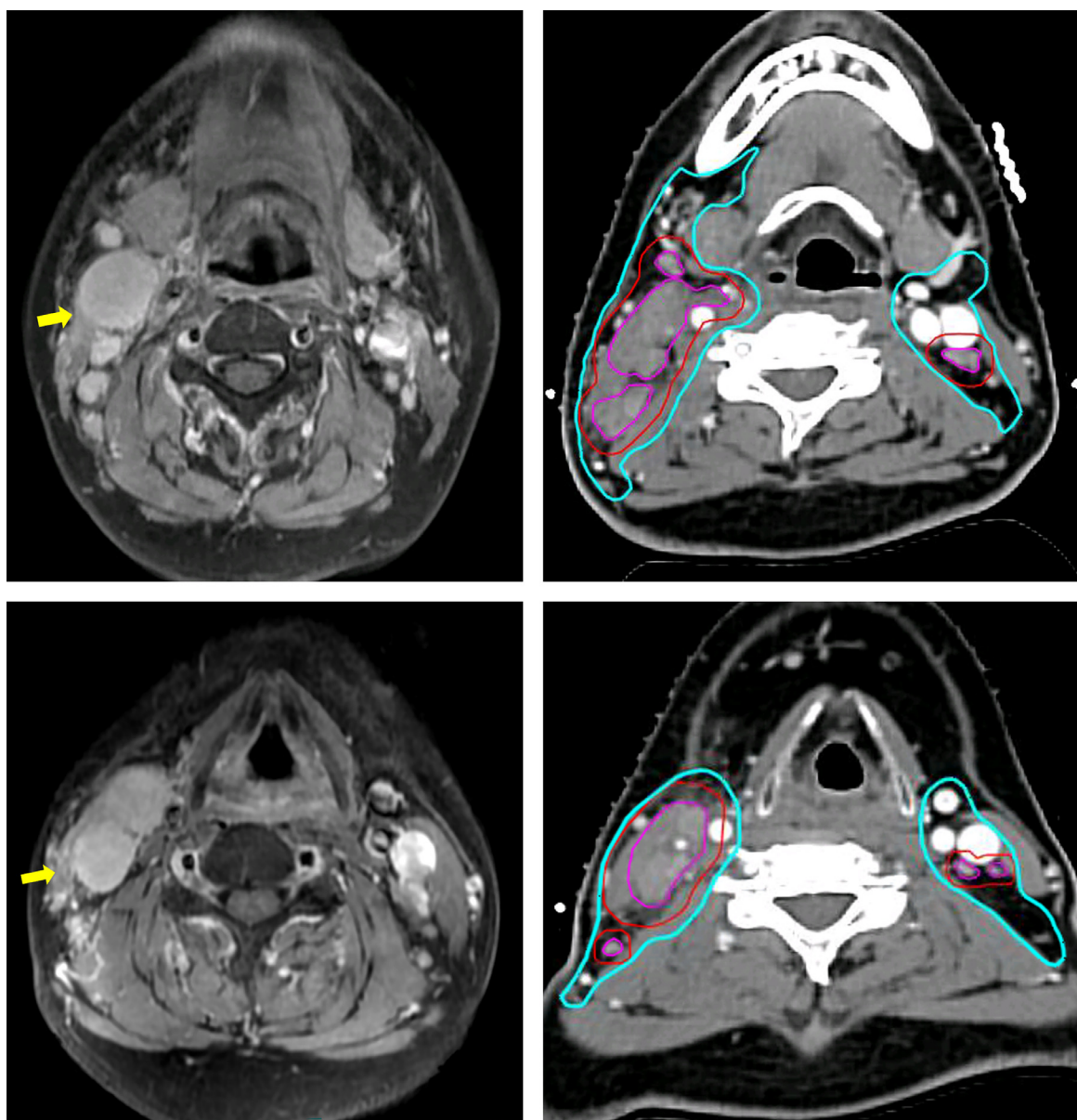
#### Recommendation

- Encompass CTVn\_60-70 and cover the corresponding nodal levels (*agreement: 73%*), with a prescribed dose of 50 Gy (*agreement: 60%*).

In IG-2018, a 5-mm expansion margin from CTVn\_70 was recommended for delineating the CTVn\_50-60, aligning with the NRG-HN001 protocol and the 2020 DAHANCA Guidelines.<sup>4, 6</sup> However, other guidelines recommended including only CTVn\_70 and the corresponding nodal level (Table E2). This approach is based on the understanding that LN spread follows an orderly pattern along lymphatic vessels without peripheral drainage, except in cases with ENE. IG-2024 recommends encompassing CTVn\_70 and covering the corresponding nodal level.

- Retropharyngeal LN (RPLN): bilateral coverage of lateral RPLN for all cases (*consensus: 90%*), with a prescribed dose of 50 Gy (*agreement: 67%*).
- Level II LN: bilateral coverage for all cases (*consensus: 93%*), with a prescribed dose of 50 Gy (*agreement: 67%*).

For the delineation of RPLN, coverage can be confined to the lateral nodes, as the involvement of the medial nodes is rare.<sup>58-60</sup> In a prospective multicenter study conducted by

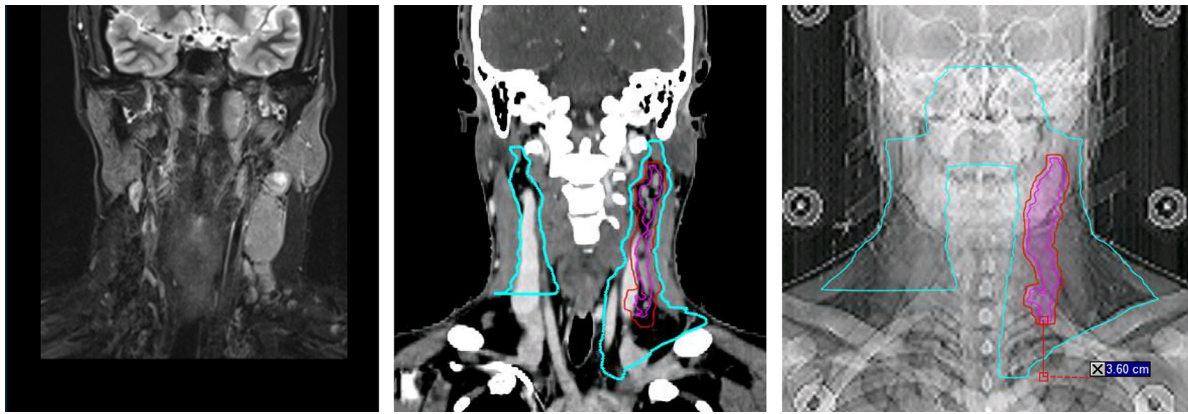


**Fig. 2.** Delineation of nodal clinical target volume (CTVn). Left column: The preinduction magnetic resonance imaging (MRI) depicts positive lymph nodes (LN) with advanced extranodal extension (ENE) infiltrating the sternocleidomastoid muscle of the right neck (yellow arrows) and contralateral LN without ENE in the left neck. Right column: The postinduction computed tomography (CT) planning images show delineation in accordance with International Guideline-2024 (IG-2024). For LN with advanced ENE in the right neck: nodal gross tumor volume (GTVn) (purple line) is based on the preinduction extent, including the infiltrated muscle, and CTVn<sub>70</sub> (red line) equals GTVn plus an 8-mm margin. For LN without ENE in the left neck: GTVn is based on the postinduction extent, and CTVn<sub>70</sub> equals GTVn plus a 3-mm (acceptable range 0-5 mm). The delineation of CTVn<sub>50</sub> (blue line) is based on the anatomical boundary of the corresponding nodal levels, encompassing CTVn<sub>70</sub>.

Mao et al<sup>55</sup>, patients receiving elective coverage of the lateral RPLN had a 3-year R-FFS comparable with those with coverage of both the medial and lateral RPLN (95.3% vs. 95.5%), with no recurrences observed in the medial RPLN region. Moreover, this approach led to a significant reduction in acute dysphagia and weight loss. IG-2024 strongly recommends bilateral coverage of lateral RPLN and level II for all cases; a prescribed dose of 50 Gy is recommended, aligning with other published guidelines.

- Level III and Va LN: bilateral coverage for all cases (agreement: 73%), with a prescribed dose of 50 Gy (consensus: 87%).

Coverage of bilateral level III and Va was recommended by all published guidelines (Table E2). Increasing data support a predominantly orderly pattern of LN extension from the upper to lower neck, with rare instances of skip metastases and minimal cross-drainage between bilateral LNs.<sup>29</sup>



**Fig. 3.** Caudal border for neck irradiation based on the extent of nodal involvement. Left: preinduction MRI depicts no positive lymph nodes (LN) in the right neck and LN (without advanced ENE) just reaching the upper border of level IV in the left neck. Middle and right: nodal gross tumor volume (GTVn) (purple line) is based on the postinduction extent, and nodal clinical target volume (CTVn)<sub>70</sub> (red line) equals GTVn plus a 3-mm (acceptable range 0-5 mm). CTVn<sub>50</sub> (blue line) covers level II (extending cranially to the skull base) to levels III and Va at the node-negative right neck and extends to the clavicle with at least a 2-cm margin below the lowest GTVn in the left neck.

Wang et al<sup>61</sup> showed that in patients without LN metastasis in level II and RPLN, skip involvement in level III/Va is uncommon (0.4%). Hence, they suggested covering only RPLN and level II for N0. For patients with unilateral RPLN/level II involvement, the incidence of ipsilateral drainage to level III/Va was 42.4% and level IV/Vb-c was 18.2%. In contrast, contralateral LN involvement at corresponding levels was only 1.5% and 0.5%, respectively.<sup>61</sup> Sun et al<sup>62</sup> reported an 8% occurrence of contralateral LN metastasis in patients with unilateral LN involvement. Among patients with unilateral RPLN/level II involvement, less than 1% had contralateral level III/Va metastases. IG-2024 recommends maintaining this coverage and strongly recommends a prescribed dose of 50 Gy. However, it is worth noting that 10% of the experts proposed omitting these nodal levels bilaterally in N0 disease, whereas another 17% proposed covering these levels ipsilaterally only if the corresponding level II is involved.

- Level IV and Vb-c: cover only if level III/Va on the corresponding side is involved (*agreement: 67%*), with a prescribed dose of 50 Gy (*consensus: 97%*) (Fig. 3).

IG-2018 recommended covering the ipsilateral lower neck only for patients with involved cervical LNs on the same side of the neck. This recommendation was supported by both retrospective and prospective studies.<sup>39,63-76</sup> The phase III randomized trial by Tang et al<sup>39</sup> on 446 patients with N0-1 disease showed that upper neck irradiation (UNI) achieved noninferior 3-year R-FFS (97.7% vs 96.3%) compared with whole neck irradiation (WNI). The study by Huang et al<sup>63</sup> on 291 patients with unilateral N3 disease showed comparable 5-year R-FFS between UNI at the contralateral uninvolved neck and WNI. Considering the orderly pattern of LN extension from the upper to lower neck and rare instances of skip metastasis, 67% of the experts in IG-2024 even

took a bolder step of recommending omission of the lower neck if level III/Va on the corresponding side is uninvolved, in line with the principle of extending the caudal border to one level below the involved level. A relevant prospective randomized phase III trial is currently ongoing to validate this approach (NCT05780372).

### Level Ib coverage

*Recommendation on indications for inclusion of ipsilateral level Ib.*

- Involvement of positive LNs in level Ib (*consensus: 87%*)
- Involvement of the submandibular gland (*consensus: 80%*)
- Involvement of structures that drain to level Ib as the first echelon site (i.e., the oral cavity, anterior half of nasal cavity) (*agreement: 63%*) with a prescribed dose of 50 Gy (*consensus: 83%*)
- Submandibular gland can be spared from routine coverage within level Ib unless involved (*agreement: 70%*).

IG-2024 strongly recommends continuing to include involvement of LN within level Ib and/or the submandibular gland as indications for Ib irradiation. Another indication recommended is the involvement of first echelon structures.<sup>77-83</sup> However, opinions are divided regarding whether level II LNs with ENE (only 50% agreement) or a maximum axial diameter greater than 2 cm (47% agreement) should be included as indications for Ib coverage because recurrence rates in level Ib was low for patients with these 2 nodal characteristics.<sup>81,84,85</sup>

Recent studies showed that level Ib LNs are located in the anterolateral space, there is no evidence of metastatic LNs inside the submandibular gland.<sup>86-89</sup> IG-2024 recommends that the submandibular gland might be spared in level Ib coverage unless involved.

### Clarification on the anatomical border for CTVn

- Cranial border of level II: extend cranially to skull base (*consensus: 77%*)

Studies on nodal distribution patterns showed that 25%-30% of patients with level II LN involvement had nodes located more cranially than the caudal edge of the lateral process of C1.<sup>58,90</sup> IG-2024 strongly recommends extending the cranial border of CTVn\_50 to the skull base to ensure adequate coverage of level II, retropharyngeal, and retro-styloid LN. This aligns with level VII as recommended in the guideline by Grégoire et al.<sup>56</sup>

- Caudal border of CTVn\_50 for patients with level I, II, III, and Va involvement: one level below the involved level (*consensus: 77%*)
- Caudal border of CTVn\_50 for patients with level IV/Vb-c involvement: extend caudally to the clavicular head and ensure a 2-cm margin below the involved LN (*agreement: 60%*) (Fig. 3)

In alignment with the principle of encompassing one level beyond the involved level, IG-2018 recommended extending the coverage to include upper mediastinal nodes in CTVn\_50 for patients with level IV/Vb-c involvement. However, the benefit is questionable because most of these patients eventually develop distant metastases. In our Delphi survey, only 13% of experts supported the inclusion of the upper mediastinum for patients with level IV/Vb-c involvement. IG-2024 recommends extending the CTVn\_50 down to the clavicular head and ensuring a 2-cm margin below the GTVn, in alignment with the recommendation of the 2020 DAHANCA guidelines.<sup>6</sup>

- Anterior border of level IVa: specify at the posterior edge of infrahyoid ribbon muscles (*consensus: 83%*) (Fig. 4)

As per the 2013 consensus guideline by Grégoire et al<sup>56</sup>, the anterior edge of level IVa was originally defined as the anterior edge of the sternocleidomastoid muscle (cranially) or the body of the sternocleidomastoid muscle (caudally). However, the study by Lin et al (n=959) showed no LNs in

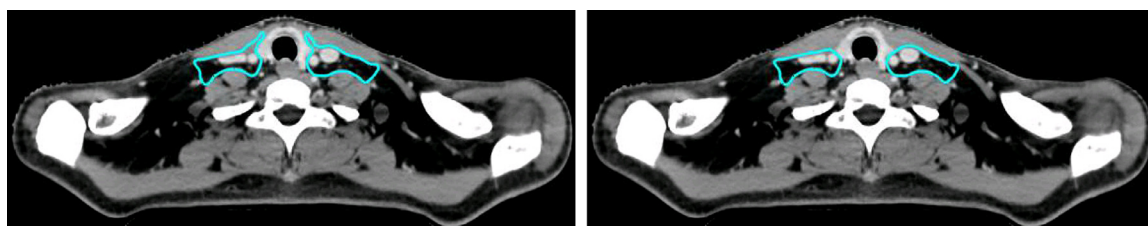
the gap between the sternocleidomastoid and infrahyoid ribbon muscles at level IVa.<sup>89</sup> A subsequent study by Zhong et al<sup>91</sup> concurred with these findings. IG-2024 strongly recommends modifying the anterior border of level IVa to the posterior edge of the infrahyoid ribbon muscles. This refinement will help reduce unnecessary doses to the thyroid gland.

### Concluding remarks

The formulation of an International Guideline for contouring CTV at different dose levels for NPC is a significant challenge, involving an in-depth review of emerging data and extensive consideration of diverse opinions and practices by international experts worldwide. IG-2024 is devised with extensive global representation; updated changes/clarification in 36 parameters were introduced (Table 2), compared with our previous IG-2018. The major changes focus on the use of postinduction chemotherapy GTV (except in patients with advanced ENE) for delineating CTV(p/n) to 70 Gy equivalent, stepwise refinement of elective coverage to ipsilateral anatomical structures for eccentric primary tumor, selective coverage of nodal levels, and a lower elective dose of 50 Gy equivalent.

However, there are several limitations to consider. First, the recommendations are based on expert-opinion consensus, although they are well supported by a systematic review of clinical data. Second, the supporting data largely originated from Asian countries with non-keratinizing carcinoma, further validation is needed for extrapolation to non-endemic regions or other histology subtypes. Validation studies are needed particularly on recommendations rated as “conditional” in strength. Furthermore, we must caution that although there are emerging data supporting tighter margins in experienced centers, wider coverage may have to be considered for centers with less optimal imaging support.

IG-2024 provides a practical reference for working towards safe de-escalation and enhanced precision in radiation therapy. The detailed recommendations on delineation and dose prescription will provide valuable guiding principles for developing automated contouring programs to facilitate the standardization of radiation therapy planning.



**Fig. 4.** Anterior border of level IVa. Left: The 2013 consensus guideline by Grégoire et al. specifies the anterior edge of the sternocleidomastoid muscle as the landmark. Right: The current recommendation by International Guideline-2024 (IG-2024) reduces the nodal clinical target volume (CTVn)\_50 (blue line) to the posterior edge of the infrahyoid muscles.

**Table 2** Concluding summary of changes in recommendations from IG-2018 to IG-2024

<b>Strong recommendations (based on consensus and/or high QoE)</b>	
Change in delineation	<ul style="list-style-type: none"> <li>• GTV for patients treated with induction chemotherapy: from preinduction to postinduction GTVp and GTVn (except those with advanced ENE);</li> <li>• Coverage to sphenoid sinus: from Inferior half to inferior 5-10 mm, and coverage of the whole sinus only in patients with gross involvement, rather than all T3-4 patients;</li> <li>• CTVn_70 for patients with ENE: from a specified expansion margin of 10 mm to a flexible range of 5-10 mm;</li> <li>• Anterior border of Level IVa: from the anterior edge of the sternocleidomastoid muscle to the posterior edge of the infrahyoid ribbon muscle.</li> </ul>
Clarification of dose	<ul style="list-style-type: none"> <li>• Elective coverage of the whole nasopharynx: from 60-70 Gy to 60 Gy;</li> <li>• Equivocal LN: from 60-70 Gy to 60 Gy;</li> <li>• Elective coverage of levels Ib, III, and Va: from 50-60 Gy to 50 Gy.</li> </ul>
<b>Conditional recommendations (based on agreement and moderate QoE)</b>	
Change in delineation	<ul style="list-style-type: none"> <li>• CTVp_60: from specified 10 mm margin to a flexible range of 8-10 mm;</li> <li>• CTVn_60 for equivocal LN: no expansion margin;</li> <li>• Elective coverage of foramen ovale: from bilateral for all to selective ipsilateral coverage for eccentric tumors;</li> <li>• Low-risk CTVn_50: encompass CTVn_60-70 and cover corresponding nodal level;</li> <li>• Elective coverage of levels IV and Vb-c: from “Omit if N0 or N1 based solely on retropharyngeal LN involvement” to confining coverage to those with ipsilateral level III/Va involvement;</li> <li>• Level Ib coverage: submandibular gland can be spared if uninvolved;</li> <li>• Caudal border of CTVn for patients with level IV/Vb-c involvement: from one level below the involved level to the clavicular head and 2 cm below the involved LN</li> </ul>
Clarification of dose	<ul style="list-style-type: none"> <li>• Elective coverage of anatomical structures from 50-60 Gy to 50 Gy</li> <li>• Elective coverage of lateral retropharyngeal LN, levels Ib, II, III, and Va from 50-60 Gy to 50 Gy.</li> </ul>
<b>Conditional recommendations (divided opinion, acceptable range based on moderate QoE)</b>	
Change in delineation	<ul style="list-style-type: none"> <li>• CTVp_70 and CTVn_70 (without ENE): from a specified expansion margin of 5 mm to a flexible range of 0-5 mm.</li> </ul>
<i>Abbreviations:</i> CTV = clinical target volume; ENE = extranodal extension; GTV = gross tumor volume; LN = lymph node; QoE = quality of evidence	

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