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RESEARCH HIGHLIGHT

Knowing nodal Rouviére: the power of human intelligence in toxicity reduction

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Patients with nasopharyngeal carcinoma (NPC) represent a distinct group of head and neck cancer patients. They are often non-smokers, non-drinkers, and on average 10 to 20 years younger than those with cancers of other head and neck sites. Given good baseline health status and the effectiveness of contemporary treatment [1], patients with NPC typically have long projected life expectancies and commonly develop late treatment adverse effects, such as dysphagia and swallowing dysfunction.

Delineation and coverage of microscopic disease within the clinical target volume (CTV) are crucial in head and neck radiation treatment planning. The retropharyngeal lymph node (RPLN) is the first echelon nodal drainage for NPC. RPLN represents a special entity as they are usually not clinically detectable. Their diagnosis is based on computed tomography (CT) and magnetic resonance imaging (MRI). RPLN was identified almost one hundred years ago. French anatomist Henri Rouviére (1875-1952), through his extensive work in the delineation and classification of human lymph nodes using fresh cadavers, identified a set of lymph nodes in the lateral retropharyngeal space (RPS) [2]. These lateral RPLNs were later named nodes of Rouviére. The nodes of Rouvière, along with the medial RPLN, form the retropharyngeal nodal group, which is located within the RPS. Above the level of the hyoid, RPS contains RPLN and adipose tissues. At the infrahyoid level, the RPS contains only adipose tissues. It is a common practice to delineate the entire RPS up to the level of the hyoid as a CTV target.

In this era when technology dominates the field of oncology, tremendous resources have been invested in the development of high-tech radiation delivery machines and pharmaceuticals. Much less effort has been put into the artistry of oncology, such as refining the delineation of target volumes in radiation planning, albeit a significantly less cost-effective and labor-intensive approach [3–6]. Recently, Mao *et al.* [7], in a multicenter randomized phase III trial, demonstrated how sparing of the medial retropharyngeal nodal group alone in radiation planning – a process that solely relies on human intelligence without any additional human effort or technological resources – results in 39% reduction in ≥ grade one clinician-rated acute dysphagia and 24% reduction in ≥ grade one weight loss. In addition, there was a significant improvement in patient-reported quality-of-life outcomes at 3 years, such as global health status, role-social function and swallowing function. No recurrence was observed in the medial RPLN sparing group. After adjusting for covariates, the regional relapse-free survival rates were similar in medial RPLN sparing and the medial RPLN non-sparing groups [7].

In the study by Mao *et al.* [7], utilizing the medial RPLN sparing approach, the mean dose to the middle pharyngeal constrictors decreased from 54 Gy to 49 Gy. Why would such a mild decrease in dose result in such modest improvement in clinician- and patient-rated swallowing function? It is a common misunderstanding that swallowing dysfunction from radiation is a direct result of muscle damage. The neural contribution of

List of abbreviations: NPC, nasopharyngeal carcinoma; CTV, clinical target volume; RPLN, retropharyngeal lymph node; MRI, magnetic resonance imaging; RPS, retropharyngeal space.

swallowing dysfunction is commonly overlooked. By sparing pharyngeal constrictor muscles, one also inevitably spares the pharyngeal nerve plexus, which lies on the posterior surface of the middle pharyngeal constrictor muscle. The pharyngeal nerve plexus contains fibers of cranial nerves IX, X, and superior sympathetic ganglion - the main sensory and motor nervous supply of the pharynx. Objective assessment of swallowing function using video fluoroscopic swallow study or high-resolution manometry of pharyngeal swallow pressure would help us to define the objective outcome of this medial RPLN and pharyngeal plexus sparing approach.

Developmentally, medial RPLN undergoes atrophy before puberty, and it usually disappears by the age of 5. Lateral RPLN, however, persists in adulthood. Tumor involvement of the medial RPLN is very rare [8]. In a study of 3,100 newly diagnosed NPC, using contemporary MRI techniques, medial PRLN involvement was only identified in 0.2% of the patients, and they were all located at the level of the second or third cervical vertebra [8]. The group by Mao *et al.* [7], by leveraging and transferring the knowledge of lymphatic development and pattern of tumor spread – human intelligence – into clinical treatment planning and toxicity reduction.

Much of the practice in medicine is based on myth and tradition. In the field of radiation oncology, it is common for clinicians to follow the one-size-fits-all rule by following national or protocol guidelines without understanding patterns of tumor spread or employing the-bigger-the-better approach while believing that a larger CTV would result in improved local control. It is not until we combine human intelligence with technological advancements will we see improved tumor control and quality of life in our patients.

DECLARATIONS

AUTHOR CONTRIBUTIONS

Annie W. Chan contributed substantially to the conception and drafted the article.

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