Practical Tips for MR Imaging of Perineural Tumor Spread

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KEYWORDS

• Perineural tumor spread • Perineural invasion • Perineural involvement • Adenoid cystic carcinoma • Trigeminal nerve • Facial nerve • Auriculotemporal nerve • Greater superficial petrosal nerve • MR imaging

KEY POINTS

- Any cranial nerve can be affected by perineural tumor spread even in asymptomatic patients.
- Perineural tumor spread may not be continuous on imaging and can occur in antegrade or retrograde direction, requiring the radiologist to map the entire nerve from its origin to all distal branches.
- Radiologists need to be aware of preexisting connections between different nerves to appropriately map the extent of perineural tumor spread.

INTRODUCTION

More than 500,000 new head and neck cancers are diagnosed worldwide annually, accounting for approximately 300,000 deaths annually.[1] Major prognostic factors of head and neck cancer include locoregional metastases, lymphatic or vascular invasion, positive surgical margins, extracapsular metastatic lymphadenopathy, and perineural invasion (PNI) or perineural tumor spread (PNS).[2–8]

Perineural involvement by head and neck cancer was first noted in the literature in the 1800s.[9,10] However, it was not until 1963 that clinicians began to realize that this occurred more often than previously thought. They noted that there was a relation between clinical symptoms and tumor recurrence.[11] Currently, PNI is defined as tumor cells within any of the 3 layers of the nerve sheath (epineurium, perineurium, and endoneurium) or tumor cells surrounding at least 33% of the nerve.[5,6,8,12,13] PNI is inconsistently visualized radiographically. In contrast, PNS, defined as dissemination of the main tumor along the cranial nerve (CN), is often radiographically detectable, even before patients become symptomatic.[4] Although it is mandated by the United Kingdom's Royal College of Pathologists[14] and the American College of Pathologists to report the histopathological presence or absence of PNI or PNS for head and neck malignancies,[15] there is no universally accepted definition.[16] Lack of a universal standard means that the reported histopathologic detection rates of PNI and PNS may vary depending on the specimen, immunohistochemistry staining, relation to resection margins, and pathologist's expertise.[17]

The importance of determining PNI and PNS cannot be understated because the extent of PNS and its relation to the tumor margin correlates with decreased disease-free survival, regardless of the type or size of the involved nerve.[6] The mechanism allowing cancer to spread along nerves remains unknown. Recent research of

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cutaneous squamous cell cancers, revealed differentially expressed genes between tumors with PNI versus tumors without PNI.[12,13] However, why certain tumors, such as adenoid cystic carcinoma (ACC), have a propensity for PNI or PNS remains unknown. Because PNI and PNS cannot be differentiated on imaging, the term PNS will be used for both types of neural involvement in the subsequent sections of this article.

ACC of the minor or major salivary glands is the tumor most likely to develop PNS, with a prevalence of up to 56%. However, because ACC is a rare tumor, representing 1% to 3% of all head and neck cancers, it accounts only for a small number of patients reported with PNS.[18,19] The highest number of PNS is diagnosed in patients with squamous cell carcinoma because it is the most common head and neck cancer even though it has lower propensity for neural involvement than ACC with reported incidence of 2% to 34%.[19–22] Additional tumors that may develop PNS include mucoepidermoid and basal cell carcinomas, as well as desmoplastic melanomas, sarcomas, and lymphomas.[23,24]

Because PNS is associated with increased risk of tumor recurrence and higher morbidity and mortality, accurate radiographic determination of PNS is imperative for early initiation of appropriate treatment.[24,25] Delineation of PNS requires detailed knowledge of the neural anatomic pathways that the primary tumor may take and of pertinent juxtaforaminal fat planes that may be effaced. The trigeminal nerve (CN V) and facial nerve (CN VII) are most commonly involved by PNS with the highest prevalence seen along the maxillary division of CN V.[25–27] Although CN V and CN VII are frequently affected by PNS, the radiologist must be aware that any CN and/or preexisting connections between different nerves may be involved by PNS, leading to variable pathways of neuronal involvement.[26,27]

This article provides practical tips for perineural spread using MR imaging and, for the sake of ease of understanding, focuses on 6 major Ps: CN Pathways, fat Pads, CN V and CN VII Points of connection, and MR imaging Protocols with radiographic Pathologic assessment and Pearls for diagnosing PNS.

NORMAL ANATOMY AND IMAGING TECHNIQUES

As previously mentioned, CN V and CN VII are the 2 nerves most commonly affected by PNS. To adequately map PNS, the radiologist must be familiar with the course of each nerve from the brainstem to its distal innervation, juxtaforaminal fat pads and connecting points between CN V and CN VII that may allow tumor to spread between these 2 nerves (**Figs.** 1 and **2**).[25,28]

Trigeminal Nerve

The trigeminal nerve, CN V, provides sensory innervation for touch, pain and temperature of the skin and/or mucous membranes of the face, scalp, intracranial dura, orbit, sinonasal region, oral cavity, teeth, and palate via the paired ophthalmic (V1), maxillary (V2) and mandibular

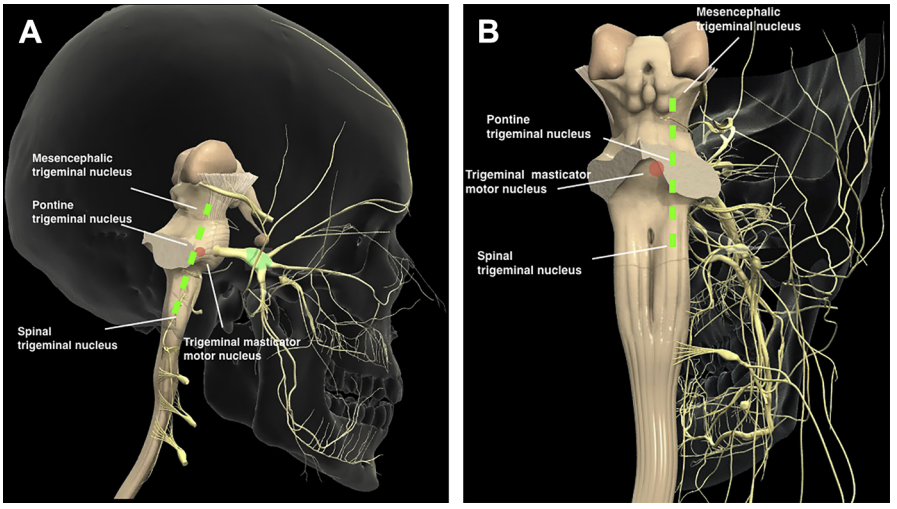

Fig. 1. CN V (*A, B*): Sensory nuclei (*dashed green line*). The mesencephalic nucleus for proprioceptive fibers from muscles of mastication is in the midbrain. The dominant pontine trigeminal nucleus for facial pressure and touch is anterolateral to the fourth ventricle in the pons, the spinal trigeminal nucleus is located inferiorly in medulla to and extends inferiorly to approximately the C2 cervical vertebral level for deep touch, pain, and pain temperature.