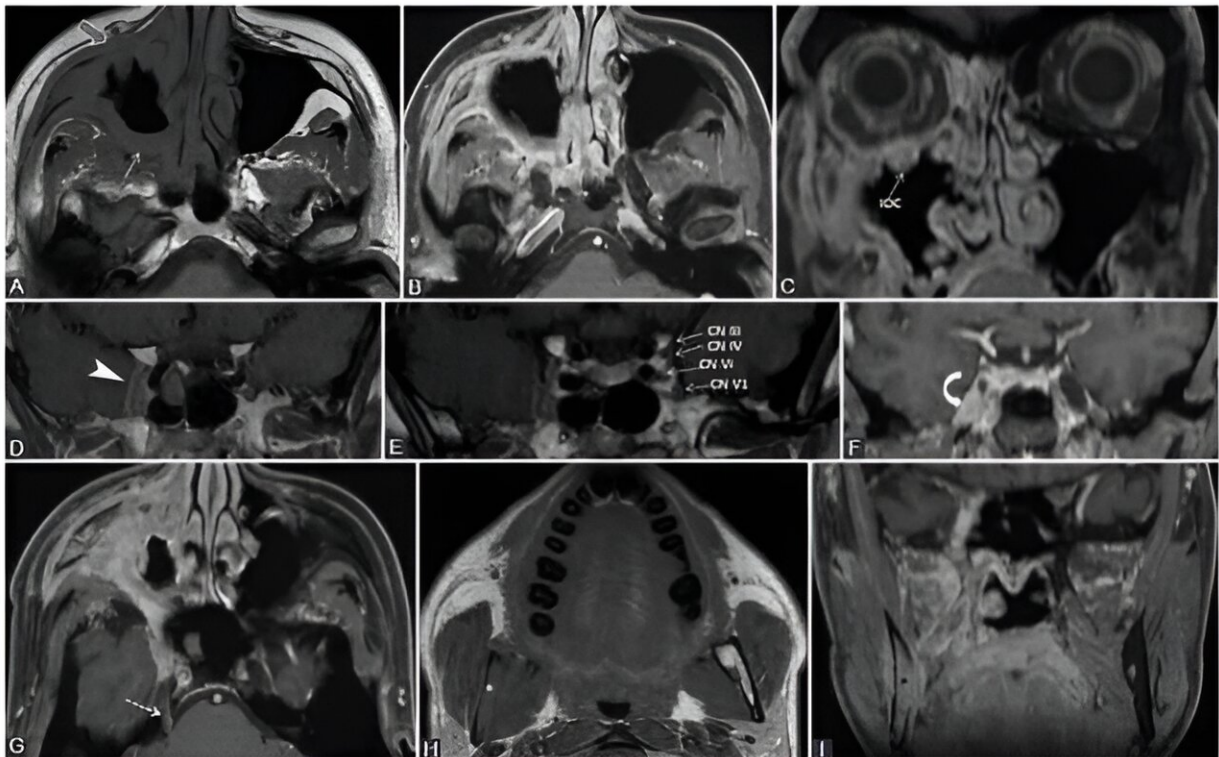


The hidden challenge: Imaging perineural invasion in head and neck tumors

September 6 2023



A. 39-year-old male diagnosed with adenoid cystic carcinoma of maxillary sinus, with multiple extensions. Clinically: Right abducens nerve palsy, diplopia, right infraorbital anesthesia. Axial T1-weighted (A, H), axial (B, G), and coronal (C, F, I) con-contrast-enhanced (CE) 3D T1 FSPGR; coronal contrast enhanced in Phase T1 FSE IDEAL (D, E) images. The probable first point of PNS is PPF with fat obliteration (white arrow) and CE (black arrow), where the V2 nerve is involved. In an anterograde direction, the tumor reaches the right infraorbital nerve, demonstrated by infraorbital canal enlargement with CE (IOC) and preantral fat obliteration (gray arrow). Following the main V2 trunk, the tumor

reaches the cavernous sinus which appears larger and shows CE (arrowhead). Note that in CN III, IV, V1, and V2 are situated in the lateral wall of the cavernous sinus, the cavernous segment of CN VI is located medially to the CN V1, implying the tumoral involvement of the mentioned nerves. There is Meckel's cave CE (curved arrow) and the tumor traveled back up to the main trigeminal trunk (cisternal segment, dashed arrow). Notice the right mandibular fat replacement (white), associated with mandibular CE (black), and cortical disruption, meaning an anterograde PNS from the Meckel's cave to the inferior alveolar nerve (branch of V3). Credit: Bosnian Journal of Basic Medical Sciences

Peripheral neural spread (PNS) is a specific mode of cancerous invasion where tumor cells utilize nerves as pathways for local extension. This phenomenon is particularly significant in the realm of head and neck malignancies but can occur elsewhere in the body. The ability to accurately diagnose and understand PNS could revolutionize how we treat patients with head and neck cancers.

Researchers from Cluj-Napoca, Romania, have now provided an in-depth understanding of peripheral neural spread (PNS) in head and neck cancers, opening the door to better diagnostic and treatment approaches.

Head and neck cancers, affecting vital areas like the mouth, throat, and nose, are challenging due to their location and the intricate neural pathways in this region. When these cancers proliferate along nerves, they exhibit what's known as [peripheral neural spread](#) or more commonly, perineural spread (PNS). It's essentially the travel of [cancer](#) cells along the nerve pathways.

Cancer cells can spread either retrogradely (from the [primary tumor](#) towards the [brain stem](#)) or anterogradely (spreading to the periphery once the primary tumor reaches key connection points). Radiologists are

cautioned to inspect the entire nerve as the spread might not be continuous.

Patients with PNS can present with a myriad symptoms, often misleading in their initial stages. These can range from numbness, tingling, or even pain in the regions served by the affected nerves. Some might experience facial weakness, difficulty swallowing, or altered sensations. Due to the subtle and varied presentation, a high index of suspicion is vital for early detection. Management may involve surgery to remove the tumor, radiation therapy to target the tumor cells, or a combination of both. The specific course of treatment depends on the extent of spread, the type of tumor, and its location.

Perineural invasion (PNI) describes the phenomenon where cancer cells invade the perineural space (the space surrounding the nerve). It's a pattern of invasion where [tumor cells](#) are actively infiltrating the nerve's protective layer. While PNI can be seen in various types of cancers, it's particularly prevalent in certain malignancies, including those of the head and neck, prostate, and skin (like cutaneous squamous cell carcinoma). Common manifestations include pain, often described as burning or shooting, numbness, and [muscle weakness](#), with symptoms becoming more pronounced due to the invasion into the nerve itself. Histopathological examination, which involves looking at tissue samples under a microscope, is the gold standard for diagnosing PNI as it allows for visualization of the cancer cells within the nerve space.

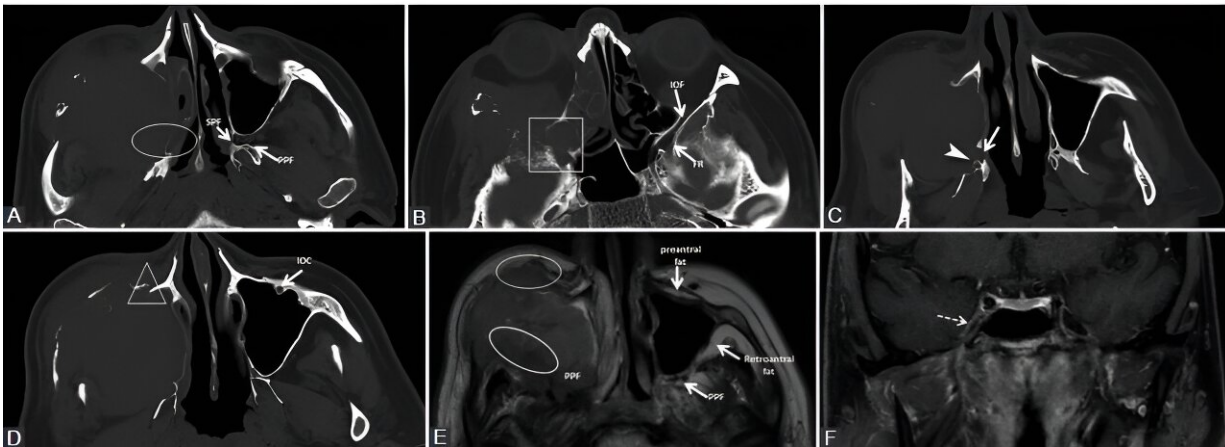
PNI and PNS have a strong association with poor prognosis in head and neck cancers across almost all sites. This association extends to reduced local and regional disease control, increased risk of metastasis (both local and distant), recurrence, and reduced survival rates. The presence of PNI often indicates a more aggressive tumor behavior. This suggests a likelihood of the cancer recurring or metastasizing (spread to other parts of the body). Pain, which can vary in type and severity, is often

described as deep-seated, burning, or shooting.

Potential issues with the accuracy and consistency of PNI reporting arise due to:

- Variability in biopsy techniques.
- Differences in detection methods.
- Limited case studies.
- Insufficient follow-up timeframes.
- Lack of a universally accepted definition.

Using imaging to detect PNI/PNS poses challenges, as the literature displays inconsistencies and disagreements about its prognostic value.



The patient presented with inflamed infraorbital and cheek region for about 3 weeks, no prior history of malignancy. The patient presented with inflamed infraorbital and cheek region for about 3 weeks, no prior history of malignancy. Diagnosed squamous cell carcinoma of the maxillary sinus with orbital and ethmoidal extension. Bone window axial computed tomography scans (A, B, C, D) show direct tumor invasion of pterygopalatine fossa and sphenopalatine fissure (ellipse), as well as invasion of the inferior orbital fissure and foramen rotundum (rectangle). The tumor also invades the right hard palate with the

enlargement of the greater (arrow) and lesser (arrowhead) palatine canals, and the infraorbital canal (triangle), compared to the normal left one. Axial T2-weighted image (E) shows the right PPF, pre- and retroantral fat obliteration (ellipses) versus the normal left side. T1-weighted fat-saturated coronal image (F) with contrast medium demonstrates the contrast enhancement of the right Meckel's cave (dashed arrow), not seen on CT, suggesting the involvement of the trigeminal ganglion. Credit: Bosnian Journal of Basic Medical Sciences

The study by Romanian scientists found:

1. Phases of Muscular Denervation: Muscles, particularly those innervated by the mandibular nerve, undergo different phases when the nerves affecting them are compromised. These changes can be best seen on MRI scans, and understanding them can help distinguish between normal muscular changes and those caused by tumor invasion.

a. Acute (

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