

Editorial Letter



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Ultrasound-Guided Neuromodulation in the AI Era: Toward a Precision in Chronic Pain Management

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Dear Editor-in-Chief

Chronic pain (CP) is defined as pain that regularly limits work or daily life and is regarded as one of the most common and costly complaints in modern medicine. Globally it has an incidence of 8.5% among older adults and women; in the USA its incidence rose from 20% to 24.3% between 2019 and 2023 [1]. Conventional therapies used to treat CP include systemic opioids and nonsteroidal anti-inflammatory drugs, which are able to control acute and chronic pain and cancer-related pain. However, they carry well-documented side effects, including renal and hepatic toxicity, cognitive impairment, and reduced fertility—making localized alternatives essential [2-4]. Ultrasound (US)-guided regional anesthesia provides a safer and targeted alternative. They allow real-time nerve visualization, deliver precise perioperative and post-traumatic

analgesia, and significantly reduce reliance on systemic opioids [2]. Nevertheless, they remain limited by operator dependency, temporary signal blockage, and the inability to address central sensitization and cortical reorganization. Both are primary neural players that sustain their effects long after the healing of CP tissue [5]. AI-driven US neuromodulation directly bridges this gap by transforming static, temporary nerve blocks into precise, dynamic, and centrally targeted therapies [6]. Pain is usually conveyed via peripheral nociceptors and travels through peripheral nerves and the spinal dorsal horn to ascend to the thalamus, where it is conveyed to cortical and limbic regions, which translate it to sensory, affective, and cognitive dimensions. CP reflects sensitization or reorganization at one or more points along this route; that is why a single peripheral procedure is rarely enough to resolve it [1]. Figure 1 maps this pathway and shows where each of the technologies discussed below intervenes.

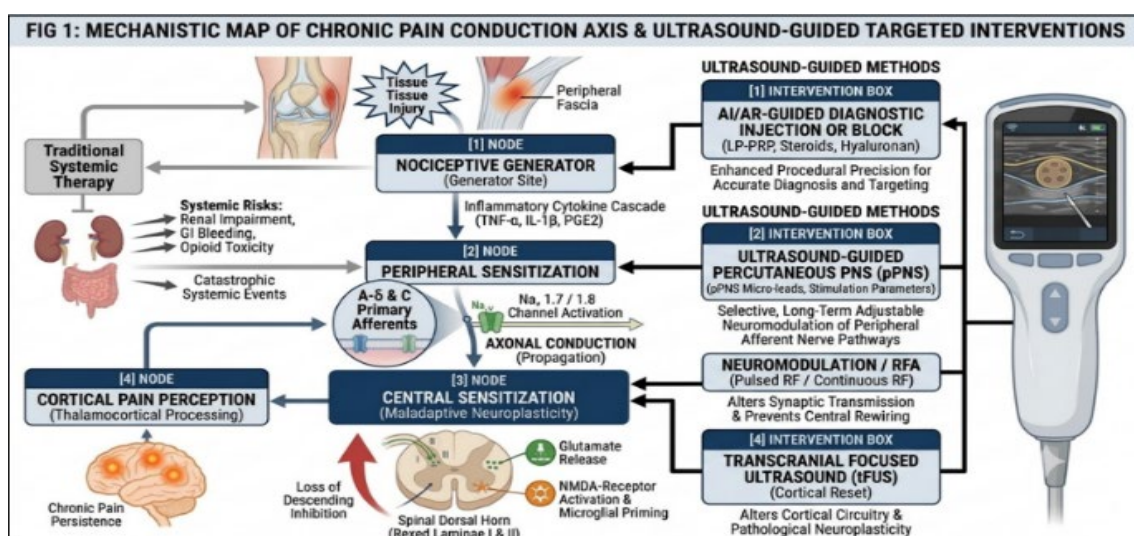


Figure 1: The mechanistic map of chronic pain conduction and how ultrasound guided intervention fit into that map.

Three AI modalities map onto this CP axis at different levels:

Artificial Intelligence and Augmented Reality (AI/AR) that sharpen intervention at the nociceptive generator and

peripheral nerve, **percutaneous Peripheral Nerve Stimulation** (pPNS), which modulates peripheral sensitization directly, and **Transcranial Focused Ultrasound** (tFUS) reach central and cortical processing non-invasively [7]. Artificial intelligence (AI) is

increasingly built into the US systems and is used by clinicians. Deep learning models are integrated into the device to overcome US operator decadency and to assist in segmenting nerves and surrounding structures on-screen and tracking the needle as it advances, so anatomy is read confidently and highlighted automatically [5,6]. This assistance narrows the gap between novice and expert, helping less-experienced clinicians identify target nerves, vessels, and safe insertion angles while standardizing image interpretation across operators—potentially extending advanced pain procedures to hospitals that currently lack subspecialists. Still, these models are trained on narrow, non-diverse datasets. Their performance can be hindered by poor image quality or atypical anatomy, and the regulatory frameworks for AI-assisted decisions need further maturation [8]. Poor image quality or atypical anatomy can hinder performance, and the regulatory frameworks for AI-assisted decisions require further maturation [8]. Poor image quality or atypical anatomy can hinder performance, and the regulatory frameworks for AI-assisted decisions require further maturation [8]. In Artificial Intelligence (AI) and Augmented Reality (AR), the AI sharpens what the clinician sees on a flat screen, and AR changes how that information is experienced in space. In 2026 Augmented Reality, Real-time Volumetric Imaging in Ultrasound (AR-VIU) was introduced; it couples real-time three-dimensional US with a mixed-reality headset (Varjo XR-4) to render the US volume as a point cloud registered directly onto the patient, with overlay accuracy of 1.3–3 mm across surfaces [9]. In practice, this technology is translated into improved object identification and less localization error than conventional 2D viewing. Moreover, like AI guidance, this technology reduces skill disparities between beginners and experts [7]. Although AR-VIU was originally tested for vascular access, its spatial benefits apply equally to deep targets like the brachial plexus and to the precise lead placement needed for pPNS. For this reason, AR simulators are already entering regional anesthesia and emergency medicine training [10]. Still, routine clinical use, however, is hindered by many obstacles, including the fact that research systems currently operate at low frame rates (1–2 Hz). However, many obstacles hinder routine clinical use, one of which is that research systems currently operate at low frame rates (1–2 Hz). Two: physical limitations, which include headset weight, cabling, and calibration, which kept AR out of live pain-neuromodulation procedures until now [7]. The natural next step in CP management once a peripheral nerve has been located with precision is to modulate it rather than simply block it, which is the foundation of US-guided percutaneous peripheral nerve stimulation (pPNS) [11]. In pPNS, an electrode is placed adjacent to a target nerve under US guidance and connected to an external pulse generator that brings low-level stimulation to dampen nociceptive transmission. Consensus guidelines already place pPNS as a targeted option for focal neuropathic pain, such as the shoulder, knee, or tibial distribution [12]. The results are optimistic; short, time-limited courses of 2-month protocols have produced long-term relief following total knee arthroplasty, while in other patients' implantable systems delivered sustained analgesia for 2 years [7,8]. The pPNS directly benefits from what both AI

and AR guidance offer because efficacy relies on placing the lead as close as possible to the nerve without causing dysesthesia. This approach makes pPNS a logical next step whenever pain recurs in spite of well-executed blocks or when repeated pharmacologic escalation is not desired [11]. Peripheral modulation is hindered by the inability to reach pain that has become centrally maintained, where the transcranial focused ultrasound becomes needed (tFUS). The latter delivers low-intensity, focused acoustic energy through the intact skull to excite or inhibit activity in specific brain areas, depending on the parameters used [13]. The tFUS can reach deep pain-relevant structures, i.e., the thalamic nuclei and the cingulate cortex, which are accessible only via invasive surgery. Early-phase trials and case reports already reported optimistic pain reduction in neuropathic conditions [14]. Ongoing research is testing focused US in deep brain stimulation; unlike surgical neuromodulation, tFUS is non-invasive, repeatable, and has the capacity of the highest precision without ablating tissue [18]. The trade-off is entirely relying on MRI- or CT-based neuronavigation rather than US—so the peripheral end of this continuum does not transfer automatically to central applications; thus, the supporting evidence remains largely speculative [15]. Taken together, these technologies describe a single escalating pathway rather than competing options. AI and AR sharpen the precision of image-guided blocks at the peripheral, plexus, and spinal level; that same accuracy underlies pPNS, which brings adjustable neuromodulation at the peripheral axon; and when pain persists in spite of accurate peripheral intervention, tFUS delivers a non-invasive route into central circuits that peripheral techniques cannot reach [6,13]. Additionally, this process offers diagnostic potential. If the AI-assisted nerve gave temporary relief, then make the area eligible for peripheral nerve stimulation (PNS). Conversely, if pPNS produced diminished results, the clinician should consider the central treatment option. Precision pain medicine, in this framing, does not choose the single best technology, but it matches the level of intervention to the level at which a given patient's pain is actually maintained. Turning this AI-assisted framework into standard practice will require future validation against conventional US guidance to measure block success and complication rates rather than technical precision alone. Currently, both pPNS and tFUS results come mostly from case series and feasibility studies. Larger, multicenter randomized trials are needed to prove their efficacy, not to mention that most personalized neuromodulation is still theoretical. Rigorous cost-effectiveness studies are also needed. Finally, a prospective study must evaluate a unified protocol from AI-assisted blocks to central neuromodulation, rather than studying each technology separately. In conclusion, AI, AR, pPNS, and tFUS each solve a different piece of the same CP puzzle, but their real significance lies in how closely they integrate to track pain anatomy, from peripheral nerve to spinal cord to brain. Treating these tools as a continuum, rather than as a collection of separate tools, provides a realistic framework for managing chronic pain (CP) that ensures precise invasiveness.

Keywords: AI era; Chronic pain; Neuromodulation; Management; Ultrasound-guided.

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