

# Extremity Cooling

## A synthesis of cryotherapy interventions to reduce peripheral neuropathy and nail changes from taxane-based chemotherapy

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**BACKGROUND:** Taxane-based chemotherapies are frequently used to treat solid tumor cancers. Two significant side effects include nail changes and/or peripheral neuropathy. These side effects can cause pain, infections, dose reductions, and treatment delays, all of which negatively affect quality of life.

**OBJECTIVES:** This article synthesizes the literature on efficacy and tolerability of extremity cryotherapy during taxane administration to identify if it is an intervention that can be provided to patients to mitigate these symptoms.

**METHODS:** A literature review was performed using PubMed®, the Cochrane Database of Systematic Reviews, Ovid, Web of Science, and CINAHL®. 46 articles were initially identified, and 10 articles were reviewed (5 related to nail changes and 5 related to neuropathy).

**FINDINGS:** Larger, powered studies are needed on these topics; however, existing data suggest this intervention as a promising low-risk option for mitigating the severity of nail changes and peripheral neuropathy related to taxane chemotherapy.

### KEYWORDS

peripheral neuropathy; taxanes; extremity cooling; nail changes; cryotherapy

### DIGITAL OBJECT IDENTIFIER

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**TAXANES ARE A COMMON CHEMOTHERAPY CLASS** used to treat many solid-tumor cancers (Robert et al., 2015). This class includes paclitaxel, docetaxel, albumin-bound paclitaxel, and cabazitaxel. The most characteristic and potentially dose-limiting side effects include nail changes and peripheral neuropathy (PN) (Robert et al., 2015). Nail changes and PN occur in about 50% of patients receiving a taxane, and the risk increases with the number of treatments received. With the highest rates of PN being from paclitaxel and the highest rates of nail changes being from docetaxel (Eckhoff, Knoop, Jensen, Ejlertsen, & Ewertz, 2013; Minisini et al., 2003). Nail changes can present as darkening or discoloration, bleeding, onycholysis (lifting of the nail from the bed), or oozing, which can lead to pain, functional limitations, or infection. PN can affect a person's ability to carry out routine activities, such as dressing, walking, and other fine-motor tasks, and influences quality of life (QOL) (Sato et al., 2016). In addition, sensory impairments caused by PN, including loss of balance, muscle weakness, and numbness, put patients at a higher risk for falls (Toftthagen, 2010).

The exact pathophysiology of nail changes is unknown; however, those with existing PN are at increased risk (Swenson, Bell, & Nissen, 2013). Researchers have hypothesized that direct cytotoxic effects of the skin can lead to nail lifting or separation (Kadokia, Rozell, Butala, & Loprinzi, 2014) or that the vascular effects of circulating taxanes block blood vessel formation and, therefore, damage the area (McCarthy, Shaban, Gillespie, & Vick, 2013). PN pathophysiology is also unknown, and comorbidities exposing patients to PN, such as peripheral vascular disease and diabetes, increase risk (Scripture, Figg, & Sparreboom, 2006). Hypotheses about why PN occurs in patients receiving taxane chemotherapies include greater exposure to cremophor, a solvent in which paclitaxel is mixed (Gilbar, Hain, & Peereboom, 2009), and that the area where taxanes bind to B-tubulin leads to microtubule disruptions that may cause PN (LaPointe et al., 2013).

With these complications, treatment delays or dose reductions are frequently needed and not ideal for patients with cancer (Griffiths, Kwon, Beaumont, & Paice, 2017). No pharmacologic options are available to prevent nail changes or PN. Effective interventions are needed to mitigate the impact of these side effects on well-being and QOL. To date, no review has been synthesized of all available literature on the use of cryotherapy for these toxicities. This article will review current literature on cryotherapy, a single intervention that may have potential to mitigate nail changes and PN from taxane treatment.