

NEWS, VIEWS, AND REVIEWS

Can't Believe It Can Be Cryo'd: Beyond Conventional Applications of Liquid Nitrogen

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INTRODUCTION

Liquid nitrogen cryotherapy is widely used in dermatologic practice, most commonly for verrucae, molluscum contagiosum, seborrheic keratoses, actinic keratoses, and selected low-risk keratinocyte carcinomas.^{1,2} It is inexpensive, portable, most often does not require injectable anesthesia, and, when used appropriately, provides good cosmetic results with minimal wound care.¹ Rapid freezing at rates exceeding -25°C per second induces intracellular ice crystal formation, disruption of cellular membranes and organelles, and osmotic injury related to extracellular ice formation. This primary cellular injury is followed by microvascular thrombosis, tissue ischemia, and delayed necrosis.^{3,4,5}

There is a broad range of less widely recognized conditions for which cryotherapy has been used. These applications take advantage of biologic effects that extend beyond direct tissue destruction. Lower-intensity cryotherapy represents a distinct therapeutic approach. Often termed superficial cryotherapy or "cryostimulation," it is not intended to produce tissue ablation. Instead, its effects may be mediated by reactive vasodilation, improved microcirculation, and local immunomodulation.⁶ This review examines the less common dermatologic uses of cryotherapy and evaluates the evidence supporting these applications.

Kaposi Sarcoma

Cutaneous Kaposi sarcoma (KS) is among the best-supported indications for cryotherapy and is included by the National Comprehensive Cancer Network as a local treatment option when performed by clinicians experienced in cutaneous cancer cryotherapy.⁷ Freezing produces direct tumor necrosis and vascular injury, mechanisms that are particularly relevant to this highly vascular neoplasm. Cryotherapy may also promote tumor antigen release and dendritic cell presentation, providing a rationale for combination therapy with immune-stimulating treatments.⁸

In a series of 30 patients with 125 lesions, two 15- to 40-second freeze-thaw cycles administered over a mean of 3.2 sessions produced complete response without recurrence in 63% of patients.⁹ More recently, a randomized, single-blind study of classic HIV-negative KS cases found a 100% reduction in lesion score with cryotherapy compared to 42.6% with pro-yellow laser treatment ($P=0.008$). The greatest benefit was observed in papular and plaque-type lesions.¹⁰ Cryotherapy was associated with more blistering and delayed healing, while laser treatment was better tolerated. Combination treatment may further improve efficacy: cryotherapy followed by topical imiquimod resulted in complete resolution of 42 of 45 lesions (93%), although the median time to resolution was 30.5 weeks.^{11,12}

Overall, cryotherapy appears to be an effective and accessible option for limited cutaneous KS, particularly for papular or plaque

type lesions. Its principal limitations are blistering, delayed healing, and the need for repeated treatment, and the evidence supporting combination therapy remains limited to small clinical series.

Alopecia Areata

Superficial cryotherapy for alopecia areata (AA) appears to contradict conventional effects of cryosurgery. Although cryotherapy delivered at tissue-destructive intensities can induce alopecia, superficial application with shorter freeze durations may instead promote hair regrowth.¹³ Proposed mechanisms include reactive vasodilation, improved perifollicular circulation, and modulation of follicular inflammation.^{13,14} The largest available study is a 22-year retrospective review of 353 patients with AA, in which 60.9% achieved a clinical response to cryotherapy after 3 months.¹⁴ Response was more likely among patients experiencing a first episode of AA and those treated at intervals of 2 weeks or less, while adverse effects were limited to mild pain and pruritus.¹⁴ A more recent randomized trial of 75 patients with recalcitrant disease found good-to-moderate improvement in approximately 65% to 76% of patients across different freeze durations.¹⁵ Although overall response rates did not differ significantly, greater mean improvement was observed with 8- to 10-second and 13- to 15-second cycles, leading the authors to suggest an 8- to 10-second freeze duration.¹⁵

Across 8 studies, approximately 60% of patients achieved hair regrowth, with efficacy generally comparable to topical or intralesional corticosteroids and potentially lower relapse rates in some cryotherapy groups.¹⁶ These findings suggest that superficial cryotherapy may be a low-cost alternative for localized AA, particularly when corticosteroid injections are unavailable, contraindicated, or poorly tolerated. However, the evidence remains limited by heterogeneous protocols, predominantly retrospective study designs, and insufficient long-term follow-up.

Lichen Simplex Chronicus

Lichen simplex chronicus (LSC) is sustained by an itch-rub cycle that produces persistent lichenified plaques. Standard treatment relies on potent topical corticosteroids and behavioral measures, although recurrence is common when friction to the area persists. Superficial cryotherapy has therefore been studied as an adjunct in refractory disease. Rather than ablating a discrete lesion, brief freezing may reduce sensory nerve signaling and thin the hyperkeratotic epidermis, thereby improving lesion appearance and mitigating symptoms.¹⁷

A meta-analysis of 12 randomized trials involving 1,066 participants found that cryotherapy-containing regimens improved clinical response compared with conventional therapy alone (RR 1.25; $P=0.005$).¹⁷ Importantly, the benefit was confined to combination regimens: cryotherapy added to topical treatment was effective,

whereas cryotherapy as monotherapy was not superior to other interventions.¹⁷ These findings support superficial cryotherapy as an adjunct for localized, treatment-resistant LSC rather than a replacement for topical corticosteroids.

Prurigo Nodularis

Prurigo nodularis (PN) is a chronic neuroimmune dermatosis in which intensely pruritic nodules perpetuate neural and inflammatory signaling through an ongoing itch-scratch cycle. Lesion-directed cryotherapy may interrupt this cycle by reducing nodule burden and local sensory signaling.

Evidence is limited to a small intra-patient randomized study of 11 patients. A single session of two 5- to 10-second freeze cycles produced 75% to 100% clearance on the cryotherapy-treated side in all patients, compared with 3 patients treated with clobetasol.¹⁸ Cryotherapy was preferred by 63.6% of patients.¹⁸ Although these findings suggest that cryotherapy may rapidly improve individual lesions, the very small sample size and limited follow-up preclude conclusions about durability or broader efficacy. Cryotherapy is therefore best considered an adjunct for a limited number of recalcitrant nodules rather than a treatment for widespread disease.

Granuloma Annulare

Localized granuloma annulare (GA) is another inflammatory dermatosis that often resolves spontaneously; however, cryotherapy may be considered for persistent or cosmetically bothersome lesions. Lesion-directed freezing is thought to disrupt the granulomatous infiltrate and induce local tissue remodeling.¹⁹

In a prospective study of 31 patients, all treated lesions resolved after contact cryosurgery, with 80.6% clearance after a single freeze-thaw cycle.¹⁹ Among the 11 patients followed for more than 2 years, only one experienced recurrence, and cosmetic outcomes were rated good or excellent in 90% of evaluable patients.¹⁹ These findings, although limited, suggest that cryotherapy can produce durable clearance. Universal blistering and the risks of dyspigmentation and atrophic scarring further restrict its use, particularly in patients with darker skin phototypes.

Keloids

Cryotherapy has been adapted as a fibrolytic treatment for keloids, where controlled freezing promotes vascular injury, necrosis, and collagen remodeling. Technique influences efficacy: intralesional cryotherapy generally achieves greater improvement with fewer sessions than spray or contact methods.²⁰

Cryotherapy is most commonly used as part of combination therapy. Cryotherapy followed by intralesional triamcinolone reduced scar volume by 34.3% and height by 41.3% after 4 monthly treatments.²⁰ In another randomized comparison, cryosurgery plus triamcinolone produced greater height and volume reductions than CO₂ laser plus triamcinolone.²¹ Shaving followed by contact cryosurgery achieved at least 50% volume reduction in 71% of scars, with 20% recurrence at 12 months.^{21,22}

These findings suggest that cryotherapy is most useful as an adjunct to corticosteroid injection or surgical debulking rather than as monotherapy. Pain, atrophy, and hypopigmentation remain important limitations, particularly in darker skin phototypes, and outcomes appear most favorable in younger, smaller lesions.^{20,22}

CONCLUSION

Liquid nitrogen cryotherapy is more versatile than conventional indications suggest. Its effects vary with treatment intensity: ablative freezing produces direct cryonecrosis and vascular compromise, whereas superficial treatment may influence microcirculation, sensory signaling, and local immune activity. These mechanisms help explain its use across otherwise distinct conditions, from debulking Kaposi sarcoma and remodeling keloids to promoting hair regrowth in alopecia areata.

The strength of evidence, however, varies considerably by indication. The evidence is strongest for its use in local treatment for limited cutaneous KS and as an adjunct in keloids and LSC, while evidence for AA, PN, and GA remains limited by small or uncontrolled studies. Its affordability, portability, and repeatability may make it particularly useful when laser, surgery, injections, or systemic therapy are unavailable or poorly tolerated. Procedural pain, blistering, delayed healing, and pigmentary alteration remain important constraints, especially in patients with darker skin phototypes. Future studies should aim to standardize treatment protocols and evaluate durability, comparative efficacy, and patient selection.

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