Optimising cryosurgery technique

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Background

Cryosurgery is an effective, simple and inexpensive treatment used extensively in general practice and dermatology. It is used most commonly for actinic keratoses and warts; however, a large number of benign, premalignant and malignant skin diseases can also be treated.

Objective

The objective of this article is to help readers improve their cryosurgery technique.

Discussion

Application of the cryogenic agent (most commonly liquid nitrogen) to the skin induces rapid freezing followed by slow thawing. This produces cell injury, vascular stasis and occlusion, and inflammation. The quantity of cryogen delivered onto the skin (dose), technique, duration of thawing and amount of surrounding tissue frozen are dependent on the body region and type of lesion. If clinical diagnosis is not possible, either a skin biopsy or referral to a dermatologist is recommended. We strongly discourage blind treatment of undiagnosed skin lesions.

Cryosurgery is an effective, simple and inexpensive treatment for a number of common skin lesions.[1] It is an established technique that remains particularly popular in general practice for the treatment of actinic keratoses and warts. The treatment of multiple actinic keratoses is one of the most commonly used item numbers on the Medicare Benefits Schedule (MBS) in general practice, with an increase in the number of treatments from 247,515 to 643,622 between 1994 and 2012.[2] Cure rates with cryosurgery for actinic keratoses are reported to be between 86% and 99%.[3,4] Therefore, a review of the indications, perioperative considerations and technique of cryosurgery is a valuable tool for all general practitioners (GPs).

A number of advantages of cryosurgery, compared with other surgical treatments, are listed in Box 1. Cryosurgery is not suitable when histological confirmation or complete excision is required. Cryosurgery can be problematic for patients with Fitzpatrick skin types III–V because of post-inflammatory hyperpigmentation and hypopigmentation. Extra care is also required when treating skin lesions on hair-bearing skin because of the risk of alopecia.

The aim of cryosurgery is to induce directed tissue necrosis through skin cooling and cell freezing.[5,6] There is a clear dose-response relationship between the amount of cryogen applied to the skin surface and tissue destruction. The degree of tissue destruction in turn determines cure rate, and also immediate

Box 1. Advantages of cryosurgery

- Low cost
- Safe and simple
- Treatment option on any area of the body
- Suitable for treatment of numerous benign, premalignant and malignant lesions
- Suitable for office and outpatient setting. No need for operating theatre access or anaesthesia
- Suitable for poor surgical candidates, older people, pregnant women, or those unable or unwilling to undergo general anaesthesia
- Most cases require little postoperative care and no leave from work or study

pain and post-procedure healing times. The dose delivered to the skin is determined by the timed spot-freeze technique, and this predicts therapeutic response outcome and morbidity.

The mechanism of action of cryosurgery includes heat transfer between skin and cryogen, cell injury, vascular stasis and occlusion, and inflammation.[7] Tissue freezing results in a number of pathological changes, including formation of ice crystals, disruption of cellular membrane integrity, changes in tissue pH, impairment of homeostatic functions and thermal shock. Tissue thawing enhances tissue damage through failure of the vascular microcirculation and vascular stasis. Intracellular ice formation is maximised through rapid cooling and slow thawing of desired tissue. With repeated freeze–thaw cycles, the underlying stroma provides the framework for wound repair and optimises cosmetic outcome. Acute inflammation in the 24 hours after treatment further contributes to cell death and lesion destruction.[7]

Liquid nitrogen is the most commonly used cryogenic agent. It has the lowest boiling point (–196°C) and greatest tissue-freezing capacity of available cryogens. Other cryogenic agents sometimes used in clinical practice include nitrous oxide, carbon dioxide and fluorinated hydrocarbons. These agents have a higher boiling point, making them more suitable for benign lesions but unsuitable for treatment of skin cancers. Home treatments that contain dimethyl ether and propane may be suitable for warts, but are not effective for treating premalignant and malignant lesions.

Liquid nitrogen is most commonly administered using a closed-system apparatus that allows continuous administration of liquid nitrogen to the target tissue. Tools commonly used in dermatology include handheld units with a spray-tip or a cryoprobe (contact therapy). Depending on the body region, cotton-tipped applicators and crushed carbon dioxide are also used. These techniques do not allow accurate determination of dosage. The optimal dose of cryogen to be applied, optimal technique for application, duration of cooling required and amount of surrounding tissue that should be frozen will be dependent on the nature of the lesion being treated and the location of the lesion on the body.

Indications and contraindications

There are a number of benign, premalignant and malignant lesions that can be treated with cryosurgery. For many lesions, such as viral warts and actinic keratosis, cryosurgery is the treatment of choice. Cryosurgery is also used as a second-line treatment for patients who do not want surgery, or in patients who have a relative contraindication to surgery, such as allergy to local anaesthesia, needle phobia coagulopathies, or a pacemaker or defibrillator that would interfere with electrocoagulation. Cryosurgery is also used for inoperable tumours and palliative treatment.

Accurate diagnosis is crucial for determining the dose and number of repeat treatments required. If there is diagnostic uncertainty, the patient should be referred to a dermatologist or a skin biopsy should be performed. A punch biopsy from the centre of a lesion will also provide information about lesion thickness. If the diagnosis of melanoma cannot be confidently excluded on clinical assessment, excisional biopsy is required.

More than 50 types of benign lesions can be suitably treated with cryosurgery, some of which are listed in Table 1.[7] Suitable premalignant lesions and in situ malignancies include actinic keratoses, actinic cheilitis, Bowen's disease and erythroplasia of

Table 1. Benign lesions amenable to cryosurgery treatment[7]

Pigmentation and melanocytic lesions
• Melasma – A common condition that affects the forehead, cheeks, nose and upper lips. It is more common in people who tan well or have brown skin. The risk of hypopigmentation is therefore significant and poor cosmetic outcomes are common
• Idiopathic guttate hypomelanosis
• Tattoos – There are much more efficacious treatments available for tattoo removal. Referral to a dermatologist prior to treatment in general practice will minimise the likely risk of scarring associated with cryosurgery
• Lentigo simplex
• Solar lentigo – Given no excisional biopsy is taken, there is a real risk that an in situ melanoma is treated inappropriately. Adverse outcomes of in situ melanoma are reports
Vascular lesions and naevi
• Venous lake
• Cherry angioma
• Angiokeratoma of Mibelli
• Angiokeratoma of the scrotum
• Spider naevus
• Capillary haemangioma
• Cavernous haemangioma
• Pyogenic granuloma (these lesions require biopsy to exclude melanoma prior to any ablative therapy)
Cysts, tumours and naevi (not including melanocytic naevi)
• Acne cyst
• Milia
• Myxoid cyst
• Syringioma
• Trichoepithelioma
• Trichilemmal cyst
• Skin tag
• Dermatofibroma
• Seborrheic keratosis
• Sebaceous hyperplasia
• Adenoma sebaceum
Miscellaneous conditions
• Keloid
• Acne vulgaris and acne scar
• Rhinophyma
• Xanthelasma
• Alopecia areata

Queyrat. The treatment of lentigo maligna with cryosurgery is not approved in the current Australasia melanoma guidelines. Lentigo maligna on the face is commonly mistaken as actinic keratosis. The suggested treatment regime of a number of lesions in general practice are outlined in Table 2.[7–11] Importantly, the common practice of treating actinic keratoses with approximately one to two seconds of cryosurgery is ineffective and likely to lead to further treatment.

Cryosurgery is not suitable for lesions with poorly defined margins, a lesion diameter >2 cm, a lesion depth >3 mm or for lesions that are tethered to underlying structures. Recurrent lesions and lesions on ala nasi, eyelids, nasolabial fold and pre-auricular skin are best treated with surgical excision as this allows histological examination of the margins and confirmation of complete histological clearance.

Caution must be taken when undertaking cosmetic procedures using cryosurgery in general practice. Poor cosmetic outcomes are common and cosmetic procedures should only be attempted if appropriate training has been completed and with consideration of medico-legal implications.

Relative contraindications to cryosurgery relate to lesion selection and site. It is usually best to avoid treating lesions in beard areas, and lesions in patients with pigmented skin because of the risks of permanent alopecia and depigmentation respectively. Absolute contraindications are generally due to premorbid illness, including agammaglobulinaemia cryoglobulinaemia, blood dyscrasias of unknown origin, cold intolerance, cold urticaria, Raynaud's disease, pyoderma gangrenosum, and collagen and autoimmune disease.[7] Deeply invasive and aggressive lesions should be referred for specialist opinion and treatment rather than treatment with cryosurgery.

Procedure techniques and variations

Timed spot freeze open-spray technique

The most commonly used and most reliable and reproducible technique used for cryosurgery is the timed spot freeze open-spray technique. It involves the use of a liquid nitrogen spray gun with a spray-tip attachment (Brymill Cryac Gun, Owen Galderma, Fort Worth, Texas, US), the choice of which depends on the size of the lesion. A 'D' nozzle is generally suitable for

Table 2. Treatment regime for skin conditions in general practice

Lesion	Technique	Time, number of freeze–thaw cycles (FTC)	Margin	Sessions, interval	Expected response
Viral warts	Flat lesions: FTC Plane: open-spray technique (OS) – E-tip Plantar: OS – B or C nozzle Filiform/digit: OS – needle probe *Should be pared to remove excess hyperkeratosis prior*	Flat: 10 seconds, x 1 Plane: 3–5 seconds, x 1 Plantar: 10–20 seconds, x 1 Filiform/digit: 10 seconds, x 1 Recalcitrant lesions may require a double FTC	1 mm	2 sessions, 2 weeks	45–85% Response rate is dependent on the number of lesions, user and technique
Spider nevus	Cryoprobe (P)	10 seconds, x 1	1 mm	3 sessions, 6 weeks	Good
Seborrheic keratosis	OS, cotton-tipped dipstick (D) or P	Ice formation, x 1	1 mm	Usually single treatment	Excellent
Skin tag	OS or forceps	5–10 seconds, x 1	1 mm	Usually single treatment	Excellent
Actinic keratosis	OS	15 seconds, x 1	1 mm	Single session, healing within 10 days	86–99%
Solar lentigo	OS	5 seconds, x 1	1 mm	Single session	
Bowen's disease	OS	15–30 seconds, x 1	3 mm	Single session	Excellent (up to 98%)
Basal cell carcinoma	OS (appropriate lesions only)	30 seconds, x 2	5 mm		
Dermatofibroma	P or OS	20–30 seconds, x 1	2 mm	2 sessions, 8 weeks apart	
Pyogenic granuloma	OS	15 seconds, x 1	1 mm	Single session	
Cherry angioma	P	10 seconds, x 1	1 mm	Single session	

D, dipstick; OS, open-spray; P, cryoprobe

most benign lesions. The spray gun administers the most even flow of liquid nitrogen when the canister is two-thirds filled.

A fine spray of liquid nitrogen is administered at a 90° angle and distance of 1 cm from the skin surface. The centre of the lesion is sprayed until the lesion and desired margins are involved. Frozen skin will turn white immediately as an ice ball forms. As the lesion freezes, the margins may become difficult to ascertain. For this reason, marking the desired lateral margin prior to freezing is useful. The depth of the freeze will roughly equal 1.5 times the radius of the ice ball.[12] When the desired radius is achieved, palpate the ice ball that has formed over the lesion to ensure the entire lesion has been frozen. When the clinician is satisfied with the degree of ice formation, continue freezing for the appropriate additional treatment time for the type of lesion. Importantly, the actual freeze time commences at the time of formation of a satisfactory ice ball and not from the time the spray gun is applied. The ice ball may remain for many seconds after the trigger is released, meaning the total freeze time is extended. Through controlled continuous spraying into the centre of the lesion, the size of the ice field should be held constant. This is achieved by adjusting the pressure on the trigger. If repeat freeze–thaw cycles are required, allow the lesion to thaw completely (generally >60 seconds) before re-freezing. To ensure there is no existing ice ball, palpate the lesion between the thumb and finger and wait for the disappearance of white surface.[7]

Variations of the open-spray technique exist for treatment of large lesions or lesions that require a superficial freeze. The paintbrush method involves spraying the entire lesion by moving up and down across the lesion. The spiral method involves spraying the lesion from the centre and in increasingly larger circles until the desired margin is achieved.[7]

Cotton-tipped dipstick

The cotton-tipped dipstick is a largely outmoded technique for using liquid nitrogen. It involves dipping a cotton wool bud in a cup of liquid nitrogen before applying it directly onto the skin surface. A homemade wooden stick with a wrapped wool tip holds more liquid nitrogen than prepackaged cotton buds. The cotton bud is applied to the lesion firmly until a narrow halo of ice forms around the bud.[7] Applying pressure to the lesion increases the surface area of tissue frozen and increases the fall in temperature because of the emptying vasculature. Decanting a small volume of liquid nitrogen from a larger vessel into an individual polystyrene cup for each patient is recommended. Adenovirus and other viruses are capable of contaminating entire stores of liquid nitrogen if strict disposal is not observed. The dipstick technique is commonly used for verrucae warts.

Cryoprobe

The cryoprobe technique uses a flat, pre-cooled metal tip attached to a liquid nitrogen spray gun. The metal tip is firmly placed on the lesion and conducts heat from the skin to cool the lesion. Direct pressure on the lesion affects the depth and lateral spread of freeze. Given this mechanism of action, freezing times are generally longer (15–20 seconds for benign lesions and up to several minutes for malignancies). A small amount of petroleum jelly may be used to facilitate contact and allow removal of the probe on thawing.[7] When ice is formed, the probe is slowly retracted from the skin to prevent further damage to surrounding tissues. Lesions amenable to cryoprobe technique include venous lakes, haemangiomas, dermatofibromas, mixoid cysts, xanthelasma, and basal and squamous cell carcinomas.[13]

Thermocouple device

The use of a thermocouple device is generally reserved for the treatment of malignant lesions, where the same volume of tissue must be frozen that would otherwise be removed through local excision. A thermocouple needle is a temperature probe attached to a thermometer, which is implanted following local anaesthesia of the target site. The entire tumour is frozen using a spray technique or cryoprobe in one session using a double freeze–thaw cycle. The spray of liquid nitrogen is usually confined within a cone that is held against the skin (confined-spray technique). The liquid nitrogen is sprayed into the cone until a temperature between –50°C and –60°C is achieved. The recommended freeze time is approximately 45 seconds for a 1 cm lesion. This technique is generally recommended for specialist practitioners, given the high-risk lesions amenable to this form of treatment.

Considerations

If the lesion is particularly thick or raised, its bulk may hinder the progression of the ice ball and limit appropriate depth involvement. It is beneficial to de-bulk with a curette, scissors or electrosurgery. Haemostasis must be achieved prior to cryosurgery.

Larger lesions should be treated with overlapping treatment margins. This ensures uniform treatment of the entire lesion and does not affect wound healing or cosmetic outcome. Some lesions may be treated in segments on the same day or during subsequent visits.

The injection of local anaesthetic below the lesion may be used to lift the lesion from underlying tissue or superficial neurovascular structures. This may be particularly useful for warts and actinic keratoses on the finger or head and neck.

Postoperative care and patient advice

Postoperative care depends on the lesion type, location, and depth and cycles of freeze. Most benign lesions treated in general practice require minimal postoperative care. Patients can generally return to work and exercise on the day of the procedure. Patients should be advised that a shallow eschar will develop and fall off spontaneously within 10 days. Watery exudate or granulation tissue may develop beneath the eschar. This can be treated by washing with soap and water, debridement with

curettage or application of antibiotic ointment. Patient education about the formation of 'blood blisters' and signs of localised infection is important to promote appropriate re-presentation. Prolonged wound healing may occur on the lower legs and shins of patients with poor circulation. Cryosurgery in these areas should be approached with caution because of the potential for a non-healing ulcer to form.

Complications

Cryosurgery is associated with a number of potential short-term and long-term complications (Table 3). Complications relate to unexpected outcomes (eg haemorrhage, infection), poor cosmetic result (eg hypertrophic scar formation) or as a result of excessive response to freezing (eg hypopigmentation). Burning pain is experienced during freezing, and throbbing pain, which is generally more severe, is experienced during thawing phases. Pain is particularly severe in the periungal areas and scalp.[7]

Pigmentation changes are common cosmetic complications following cryosurgery. Temporary hyperpigmentation, a result of melanocyte sensitivity to cold temperatures, is common in people with olive-coloured skin. These changes are prolonged but usually temporary (two to four months). Hypopigmentation occurs with longer freeze times (eg 20–30 seconds) and results from increased sensitivity of melanocytes to freezing. Advising patients to adhere to strict sun protection reduces the risk of temporary hyperpigmentation. Loss of pigment can be a permanent complication of cryosurgery, and generally occurs as a result of applying large doses of liquid nitrogen. It is more common on the face. Care should be taken in patients with dark-coloured skin and a test patch should precede treatment. Alopecia is also usually permanent.

Scarring and wound contracture are complications when liquid nitrogen doses are applied for >30 seconds. Underlying fibroblasts and collagen fibres are cold-resistant up to 30 seconds, leading to preservation of the fibrous matrix structure.[14] Collagen is similarly cryoresistant, meaning that ears and nose can receive cycles of up to 30 seconds without distortion of shape.[15]

Nerve damage is common when freezing overlying superficial nerves, including the sides of fingers, postauricular or the peroneal nerve. The extent of neuropathy is related to the length of the freeze time. Light touch, temperature and pain sensation are all affected, and may take up to 18 months to recover completely (if at all). Patients must be counselled about these side effects if treating sensitive areas.

Table 3. Immediate, short-term and long-term complications of cryosurgery

Topics	Questions
Immediate complications	• Pain • Haemorrhage • Headache • Syncope • Oedema/blister formation
Short-term complications	• Infection • Haemorrhage and 'blood blister' formation • Pyogenic granuloma (rare) • Prolonged wound healing (in areas of poor circulation)
Long-term complications	• Nerve damage • Pigmentary changes • Hypertrophic scarring • Permanent nail dystrophy • Recurrence of lesion • Alopecia • Ectropion • Notching of eyelid, vermilion border or ear

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