Lethal Tissue Temperature During Cervical Cryotherapy with a Small Flat Cryoprobe

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Background. Some female patients, especially those with cervical intraepithelial neoplasia III (CIN III), are not successfully cured following cervical cryotherapy, for which a small flat cryoprobe tip is commonly used. The thermodynamic effect produced in the cervical tissue by this device has not been previously described. This study examined the capability of a small flat cryoprobe tip to generate a lethal temperature during thermocouple-monitored cryosurgery of the cervix.

Methods. A thermocouple was placed in the cervix 5 mm from the cryoprobe margin, and a pyrometer indicated temperatures generated by nitrous oxide cryosurgery. Iceball lateral spread of freeze was measured with a cryosurgical iceball gauge.

Results. A minimum temperature of −2C° was generated at the termination of freeze ($6\frac{1}{2}$ minutes). The maximum lateral spread of freeze at termination was 6.2 mm. A lethal zone of 4.2 mm was estimated based on a 2-mm recovery zone.

Conclusions. When compared with morphometric studies of cervical dysplasia depth of involvement, an estimated 12.5% of CIN III would be inadequately treated based on our in vivo data. A small flat cryoprobe is incapable of eradicating all severe premalignant cervical disease deep within the glandular clefts. An alternative treatment method, such as electrosurgical loop excision of the cervical transformation zone (ELECTZ), therefore, may be the preferred treatment modality for CIN III.

Key words. Cryosurgery; cervix diseases; cervix neoplasms; cervix dysplasia. (*J Fam Pract 1994; 38:153-156*)

Cryosurgery is frequently used by physicians to treat histologically confirmed premalignant disease of the cervix.[1] The objective for all treatment modalities of cervical premalignant disease, including cryosurgery, is to effectively remove or destroy entirely the diseased lesion and the complete transformation zone. Many studies have documented cure rates of 75% to 90% for cervical cryosurgery.[2–5] Cervical cryotherapy treatment failure is more common in women with cervical intraepithelial neoplasia III (CIN III) than with less severe premalignant cervical disease.

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Treatment outcome variability depends on anatomy,[6,7] pathology,[2–6] technique,[6,8] the surgeon's skill,[9] and the type of equipment.[6,10] Ablative treatment outcome measures have been based primarily on follow-up cytologic evaluation and colposcopic examinations limited to superficial epithelial evaluation. In contrast, excisional treatment methods may be additionally evaluated by histologic examination of the margins of the surgically excised specimen. Ablative[6] and excisional[11] treatment failures correlate inversely with the depth of tissue destruction. Postoperative regenerated normal superficial squamous epithelium may bury residual diseased tissue within gland clefts if an insufficient depth of treatment is surgically obtained. Subsequent cytologic and colposcopic examinations may then fail to detect residual disease.

The evolution of the proper technique for cervical cryosurgery is largely based on the same limited outcome measures. The technique has progressed from a single

timed freeze, to a variably timed freeze-thaw-freeze approach, to the recommendation for a 3- to 5-mm lateral spread of freeze past the lesion. Early cervical cryosurgery studies did not document either lethal tissue temperatures generated by cryosurgery or subsequent cryonecrosis patterns observed histologically. The absence of meticulous cryosurgery analysis may be why there is ambiguity concerning a uniform treatment standard for an adequate iceball lateral spread of freeze.[12] In this case, uncritical acceptance of medical innovation[13] without a full understanding of tissue thermodynamics may contribute to the lack of a universally accepted therapeutic norm.

A morphometric analysis of patients with cervical intraepithelial neoplasia (CIN) has determined the maximum depth of extension of CIN III into epithelium gland crypts of 4.8 mm.[7] Boonstra et al[6] performed a sophisticated retrospective histopathologic tissue analysis of cervical conization tissue collected 24 hours following cryosurgery. This analysis revealed that only when a lethal zone of 5 mm beyond the probe tip was generated were all women with premalignant disease, regardless of cervical location, effectively cured. Clinically, such a lethal zone would be equivalent to a 7-mm iceball lateral spread of freeze including a 2-mm recovery zone. Thus, the rationale for a suggested 7-mm iceball treatment standard is scientifically clear.[9]

A 19-mm flat cryoprobe tip is commonly advocated for cervical cryosurgery.[14] The rationale for use of this cryoprobe is based on the theories that the flat probe, when compared with the cone-shaped probe tip, will not reposition the squamocolumnar junction within the endocervical canal following cryosurgery and that cervical stenosis will be minimized. Therefore, satisfactory colposcopy visualization of the squamocolumnar junction following cryosurgery will be maximized and the risk of infertility minimized. Regardless of these issues, complete eradication of disease is of primary importance and the ultimate goal of cryosurgery.[1]

The purpose of this study was to document in vivo the capability of a small flat cryosurgery probe to effectively generate an appropriate iceball during thermocouple-monitored cryosurgery.

Materials and Methods

A single subject with histologically confirmed moderate dysplasia of the cervix volunteered for the study. The lesion was confined to the ectocervix and limited to one quadrant. No contraindications to cryosurgery were identified. The procedure was performed midway through the subject's menstrual cycle.

The necessary equipment included: a nitrous oxide cryosurgical unit and pyrometer/thermocouple attachment[10] (Wallach Surgical Devices Inc, Milford, Conn); a colposcope[15] and video system[16] (Cabot Medical, Langhorne, Pa); and a cryosurgical iceball gauge[9] (Colpo Educational Technology, Evans, Ga). A full and completely regenerated nitrous oxide 20-lb cylinder ensured maximal cryosurgery performance.

The cervix was fully visualized by colposcopic examination. A cryosurgical iceball gauge (CIG) was placed around a nitrous oxide cryogun barrel, and a 19-mm flat cryoprobe was attached to the distal barrel. A small amount of water-soluble gel was applied to the cryoprobe surface. The intact CIG/cryoprobe unit was inserted into the vagina, and the probe, at ambient temperature, was placed on the moistened cervix. A thermocouple needle was placed and secured through an aperture in the CIG 5 mm from the cryoprobe margin and into the cervical epithelium at a depth of 1 mm. The thermocouple was placed at the one o'clock position relative to the cervical os. Nitrous oxide cryosurgery was initiated, and sequential temperature measurements from the thermocouple and cryoprobe were recorded by a digital pyrometer every 30 seconds. The corresponding iceball lateral spread of freeze was video recorded and simultaneously measured under colposcopic magnification using the CIG as a standard reference.

The documented pyrometer temperatures, the iceball lateral spread of freeze CIG measurements, and corresponding time intervals were used to plot the cryosurgical performance curves for the 19-mm flat cryoprobe. The maximal extent of the iceball lateral spread of freeze, which was used to estimate a lethal zone, was compared with cervical intraepithelial neoplasia morphometric data.[7]

Results

Thermocouple-monitored cryosurgery results for the small flat cryoprobe are depicted in the Figure. The values indicate temperatures recorded 5 mm from the cryoprobe margin within the superficial epithelium. The characteristic curve demonstrates an ideal, rapid, initial freeze phase, a temporary equilibrium at 0°C, then a flattened terminal phase curve representing equilibrium between tissue and cryoprobe. The freeze required nearly 5 minutes to produce an iceball of 5 mm. More important, the minimum temperature generated (−2°C) at the termination of freeze ($6\frac{1}{2}$ minutes) did not equate with a lethal temperature of −20°C.

The maximum lateral spread of freeze at termination of 6.2 mm is equal to an approximate lethal zone of 4.2

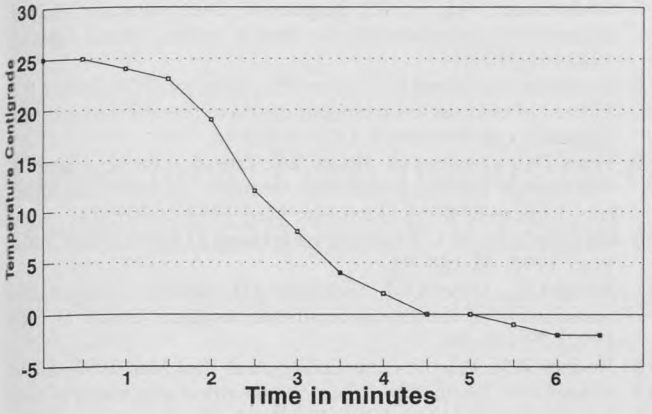

Figure. Thermocouple-monitored cryosurgery using a 19-mm flat cryoprobe. Temperatures were recorded at 30-second intervals 5 mm from the cryoprobe margin in the superficial epithelium. Tissue temperatures of −20°C or less are necessary for effective treatment. Therefore, at $6\frac{1}{2}$ minutes of freezing, the temperature at 5 mm from the cryoprobe margin was insufficient to achieve tissue destruction.

mm when a 2-mm recovery zone is considered.[10] When the generated lethal zone of 4.2 mm is compared with the known morphometric maximal depth of the CIN III lesion, the extent of which is calculated at 4.8 mm,[7] the diseased tissue located beneath the lethal zone would be temporarily frozen but would remain viable within the 2-mm recovery zone. This volume of viable tissue represents 12.5% of the total extent of CIN III. Hence, based on the documented performance of the small flat nitrous oxide cryoprobe, 12.5% of the CIN III lesion would not be effectively ablated by this technique because of the inability to freeze to a sufficient depth.

Discussion

The results from this study indicate that the small flat cryoprobe may have limited potential for effectively treating severe premalignant disease of the cervix (CIN III) with gland cleft involvement. In association with CIN III, gland cleft involvement would result in residual or recurrent disease.[17] With maximum freeze, a lethal zone of only 4.2 mm could be generated. Based on correlation with available morphometric data of premalignant disease, 12.5% of women with CIN III theoretically would be ineffectively treated. According to reports in the literature, the mean failure rate (residual disease) for cryosurgery of CIN III is approximately 15.7%,[9] which is strikingly similar to our in vivo estimate of the predicted theoretical failure rate of 12.5%.

The basis for insufficient treatment is further supported by reported statistically significant smaller cryosurgery failure rates of 6.1% and 7.4% for cervical intraepithelial neoplasia I and II, respectively.[9] These failure rates may represent an overall constant baseline of error caused by anatomy, technique, or surgeon ability. Cryosurgical equipment performance limitations combined with the extent of severe disease may be the chief reason for the contrast in CIN I, II, and III failure rates. The small flat cryoprobe appears to produce a marginal "heat sink" to adequately treat some CIN III lesions. Physician tendency to overestimate the lateral spread of freeze, particularly at the maximal extent of freeze or termination, also may explain the contrasting failure rates.[9] In addition, as the goal of cryosurgery is to ablate the lesion and transformation zone, the small flat cryoprobe used in a single freeze can accomplish this goal in an area measuring approximately 27 mm in diameter without overlapping treatment. This diameter may be adequate except for some young women with a large cervical ectropion.

The findings of this in vivo study are consistent with the retrospective in vitro data of Boonstra et al,[6] in which the small flat cryoprobe produced an inadequate cryolesion for 41.7% of women treated twice with a 5-mm iceball lateral spread freeze. In comparison, the small cone probe and the large flat and large cone probes reduced the percentage of inadequate cryolesions and appeared to be superior to the small flat cryoprobe. The small flat cryoprobe treatment results also varied as to the location of the lesion in the cervix. Sixty-five percent of the lesions located at the 3 and 9 o'clock positions were inadequately treated in contrast to 30% when the lesions were located at the 6 and 12 o'clock positions. The placement of our thermocouple at the 1 o'clock position helped to maximize the in vivo therapeutic results. The effective lethal zone would be smaller at the lateral cervical positions because of the rich vascular supply from the cervical branch of the uterine artery found in those regions. Boonstra et al[6] also demonstrated that a lethal zone of 5 mm or a total lateral spread of freeze of 7 mm generated by a small cone cryoprobe was 100% successful in generating an adequate histologically confirmed cryolesion, regardless of lesion location.

The following conclusions about cryosurgery with a small flat cryoprobe are clinically relevant. First, use of this cryoprobe should be limited to treating CIN I and II or small CIN III lesions without gland cleft involvement. Second, excision techniques, such as electrosurgical loop excision of the cervical transformation zone (ELECTZ), should be used to treat CIN III and carcinoma in situ, particularly when gland crypt involvement is noted in the pretreatment histology report. Third, use of the small flat cryoprobe should be limited to treating small lesions and only those located on the ectocervix. Finally, the small

flat cryoprobe must be used aggressively and accurately, since a prolonged freeze duration is essential for generating maximal lateral spread of freeze and treating low-grade diseases.

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