Cryotherapy Precision

Clinician's Estimate of Cryosurgical Iceball Lateral Spread of Freeze

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Objective: To examine physicians' ability to estimate the lateral spread of freeze (LSF) of a cryosurgical iceball using three techniques.

Design: A nonrandomized control trial of in vitro nitrous oxide cryosurgical procedures.

Setting: Primary care residency training programs.

Participants: A convenience sample of 80 resident and faculty physicians from four family practice residency programs and one obstetrics and gynecology residency program.

Interventions: After performing cryosurgery with standard naked-eye and colposcopic-assisted techniques, subjects used a new experimental cryosurgical iceball gauge (CIG) to estimate the LSF during cryotherapy.

Main Outcome Measures: LSF estimations reported by physicians were compared simultaneously with those measured by an observer.

Results: The mean (±SD) LSF estimation errors at the termination of freeze were as follows: 2.62±2.42 mm for the colposcopy technique, 2.00±2.16 mm for the naked-eye method, and 1.28±0.87 mm for the CIG technique. The range of maximum error was 6.5 to 11 mm for the colposcopic technique, 5.5 to 12.5 mm for the naked-eye method, and 3.0 to 4.0 mm for the CIG technique.

Conclusions: Overestimation of the LSF, which increases the risk of undertreatment and residual disease, was more common than underestimation. The CIG minimized perceptual error and provided the best cryosurgical precision.

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C RYOSURGERY IS commonly used by physicians to treat premalignant cervical disease following appropriate colposcopic evaluation.[1] This ablative procedure begins with the generation of an iceball or frozen volume of tissue. An area of tissue cryonecrosis results, provided a temperature of at least $-20°C$ is induced.[2]

Because the procedure is nonexcisional, the true extent and margins of cryonecrosis can only be estimated. Cryosurgery should not be timed to determine a therapeutic end point, but actual measurement of the iceball is visually estimated. The lateral spread of freeze (LSF) observed on the tissue surface roughly equates to the important depth of freeze, and so, imprecisely guides the cryotherapist.[3] The interface, or 0° isotherm, representing the iceball leading edge, serves only as a reference point for the cryotherapist.

The most peripheral 2-mm rim (approximate) of the iceball is known as the *recovery zone*. Tissue within this area "recovers" from the freeze and retains viability. The remaining more centrally positioned portion of the iceball constitutes the lethal zone where temperatures exceed $-20°C$ and cells do not survive the cryoeffect. The cryotherapist cannot visually distinguish between the area of eventual cryonecrosis and the recovery zone margin of tissue. Thus, cryosurgery, based on these thermophysical characteristics, is an inexact procedure.

Cervical cryotherapy success is determined by five factors: patient anatomy, pa-

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MATERIALS AND METHODS

Physicians from four family practice residency programs and one obstetrics and gynecology residency program (Department of Family Medicine and Department of Obstetrics and Gynecology, Medical College of Georgia, Augusta; Anderson [SC] Family Practice Center; Department of Family Medicine, Morehouse School of Medicine, Atlanta, Ga; and the Memorial Family Practice Residency Program, Savannah, Ga) volunteered to participate in the investigation. The inclusion criteria were faculty or resident physicians, with or without previous cryosurgical experience. The exclusion criteria were severe psychomotor impairment, significant visual acuity deficits, and nonphysicians.

A colposcopy model (Colpo Educational Technology, Evans, Ga), used to simulate vaginal spatial limitations, was modified at the "cervical" end by the addition of a bracket that held a 10-cm² Petri plate. The Petri plates were filled to a depth of 7 mm with 2% clear agar. Nonviable biologic materials with similar osmolality and water content to human tissue are frequently used to simulate thermophysical properties during cryobiologic research.[10] The clear media allowed essential simultaneous observer measurement of the iceball formation. Two commercially available cryosurgical units (Wallach L1100, Wallach Surgical Devices Inc, Milford, Conn, and Leisegang LM-900, Leisegang Medical Inc, Boca Raton, Fla) with 19-mm flat cryoprobe tips were used for all procedures. Two metric rulers attached perpendicularly to the model adjacent to the Petri plate enabled observer LSF measurements. The cryosurgical iceball gauge (CIG) (**Figure 1**) consisted of a plastic sleeve positioned over the shaft of the cryogun, an attached proximal handle to permit gauge alignment, and a ruler. The clear metric ruler was attached perpendicular to the dis-

tal sleeve and extended beyond the edge of the cryoprobe tip. Subjects performed three in vitro cryosurgical procedures. In phase I, the subject estimated the iceball LSF by "naked-eye" examination. In phase II, cryosurgery was repeated, but subjects viewed the iceball through a colposcope set at a low power magnification. In phase III, subjects estimated the LSF using the CIG while viewing through the colposcope.

Relevant demographic data were ascertained from each subject. The proper use of the cryosurgical units and the colposcope were reviewed with each subject. The model was then positioned on a table between the subject and the observer (G.R.C.) to enable the observer to record the LSF from the opposite side of the agar. Subjects positioned the probe tip on the agar and maintained perpendicular probe tip–agar contact. Subjects then generated an iceball for 3 minutes and, at 30-second intervals, estimated the iceball LSF. The observer simultaneously recorded the LSF. At the freeze termination, the agar was rapidly removed from the model by the observer and the LSF was measured directly from the agar surface. Subjects were not permitted to use additional measuring devices or given LSF measurement feedback during the three study phases.

Data were analyzed to determine the absolute value of clinician precision when estimating the iceball LSF. Individual clinician estimates for each of the three methods at each interval were subtracted from observer measurements to determine difference scores. Means and variance measures were calculated based on absolute values. Pearson correlation coefficients were computed for subject and observer termination estimates and final direct measurements. Overestimation and underestimation frequencies were determined and means and variance measures were computed for estimation error by method across time. Group differences were compared with Student's t tests. Analyses of variance with Scheffé follow-up tests were used to compare estimation methods.

thology, equipment, technique, and physician skill. The location of the lesion, the vascular supply, and potential crypt involvement induce anatomical variability.[4,5] The lesion size and severity of disease determine pathologic factors.[6,7] Equipment variability results from cryosurgical unit performance differences, refrigerant types, and cryoprobe selection.[5,8] Technique variability has been described for timed procedures, and single- vs double-freeze procedures.[9] Finally, the physician's procedural proficiency affects therapeutic success. Clinician skill and perceptual abilities have not been specifically evaluated.

The purpose of this in vitro study was to determine the clinical precision of physicians to accurately estimate the LSF of a cryosurgical iceball during cryosurgery. Three cryosurgical techniques were evaluated to assess their effect on gynecologic cryosurgery precision.

RESULTS

Eighty physicians participated in the study, and complete data are available for 75 subjects. Data were deleted be-

cause of subject error for three colposcopic-assisted procedures and two CIG procedures. Of the 80 subjects, 58 were resident physicians and 22 were faculty. Thirty-seven percent of subjects had previous cervical cryosurgical experience of more than 10 procedures. No statistically significant differences between groups were noted when the effects of subject experience were compared with LSF estimation accuracy.

Subject estimations of the iceball LSF for each technique at the termination of cryosurgery are shown in **Table 1**. Subjects tended to overestimate the LSF for the naked-eye and CIG techniques. Few (11%) subjects underestimated the LSF with the CIG. An exact LSF was most commonly determined with the CIG and naked-eye techniques, 13% and 10%, respectively. Estimates of the LSF for each technique correlated with the observer LSF measurement at termination as follows: colposcopy viewed, .142; naked-eye observed, .297; and CIG use, .650.

In **Figure 2**, the absolute value of mean differences between the subject LSF estimate and the observer LSF
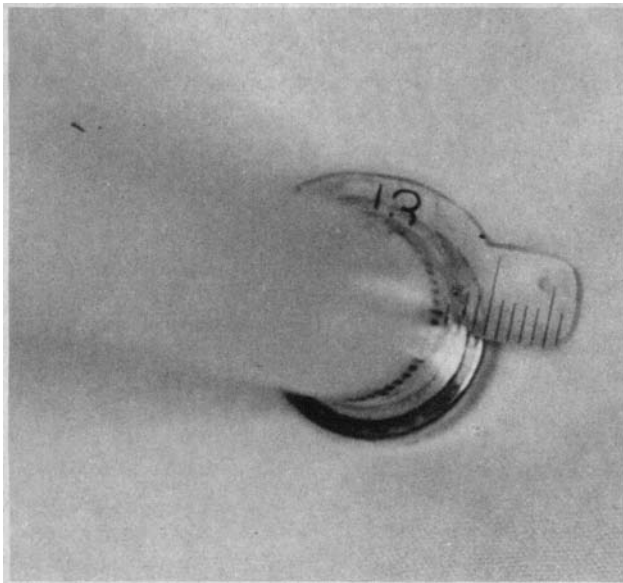
Figure 1. *The cryosurgical iceball gauge.*

measurement for each cryotherapy technique at each interval are reported. The CIG curve demonstrated the smallest mean error at five of six intervals. Significant differences were found at 90 seconds ($P<.05$), 120 seconds ($P<.01$), 150 seconds ($P<.001$), and 180 seconds ($P<.0001$).

The range of maximum overestimation error was most uniformly consistent and minimal with the CIG device (3.0 to 4.0 mm) and wide for the naked-eye estimate (5.5 to 12.5 mm) and the colposcopy technique (6.5 to 11.0 mm) (**Figure 3**). The error for the naked-eye and colposcope technique increased as the LSF size increased. Underestimation errors were smaller for all techniques. The mean ($\pm$SD) estimation error at the termination of freeze was smaller with the CIG technique (1.28 ± 0.87 mm) than for the colposcopy technique (2.62 ± 2.42 mm) and the naked-eye technique (2.00 ± 2.16 mm).

The mean observer LSF measurement at the completion of all cryotherapy procedures was 5.5 mm. The mean error of LSF estimate for the naked-eye, colposcopy, and CIG techniques, when compared with the actual mean observer LSF measurement, represents the percentage of cryotherapy error: 34.5%, 46.0%, and 8.9%,

respectively. Mean scores of the CIG were significantly different from both colposcopy and naked-eye techniques ($P<.0001$).

The mean observer LSF measurement (5.5 mm) and the mean subject LSF estimate for each cryotherapy technique are plotted over the linear extent and depth of cervical intraepithelial neoplasia (CIN) based on morphometric data.[4] The colposcope and naked-eye LSF overestimates of greater than 7 mm equate to clinically unsatisfactory cryotherapy for a significant proportion of CIN III disease located within the recovery zone. In other words, cryotherapy may have been prematurely terminated at the 7-mm point using the colposcope and naked-eye techniques (**Figure 4**).

COMMENT

Medically effective cervical cryosurgery eradicates the entire pathologic lesion and results in the absence of detectable residual disease postoperatively. Equipment, patient anatomy, pathology, technique, and physician skill influence the outcome. Equipment variability may be controlled and technique standardized for maximum effectiveness. Anatomical variability may be minimized by use of anatomically conforming cryotherapy probes or by the limitation of treatment when therapeutically inappropriate. Pathologic severity affects outcome only when the abnormality is not sufficiently removed or rendered nonviable. Excisional procedures provide for scrutiny of the specimen margins to optimize outcome and minimize treatment failure. Ablative procedures depend on the physician's skill of estimating or predicting the eventual surgical margin. Only by careful posttreatment examination can cryotherapy failure be determined. Unfortunately, patients' failure to follow up[11] often negates this necessary component of the complete treatment plan.

Physicians demonstrated a significant and variable error in accurately estimating the LSF when performing cryosurgery. A certain amount of error existed for each cryotherapy technique used. Magnification by the colposcope technique likely accentuated the gross overestimation of the LSF by physicians. The amount of error did not correspond with levels of previous cervical cryosur-

Table 1. Subject Estimation of the Iceball Lateral Spread of Freeze (LSF) for Each Technique at Termination of Cryosurgery (N=80)

Cryotherapy Technique*	LSF Estimation, No. (%)†			
	Underestimation	Overestimation	Exact	Missing
Naked eye	31 (39)	41 (51)	8 (10)	0
Colposcopy	37 (46)	36 (45)	4 (5)	3 (4)
Cryosurgical iceball gauge	9 (11)	59 (74)	10 (13)	2 (2)

*Cryotherapy viewed by naked-eye examination, with colposcopic magnification or with colposcopic magnification and use of the cryosurgical iceball gauge.
†Subject estimation compared with an accurate measurement by an observer.
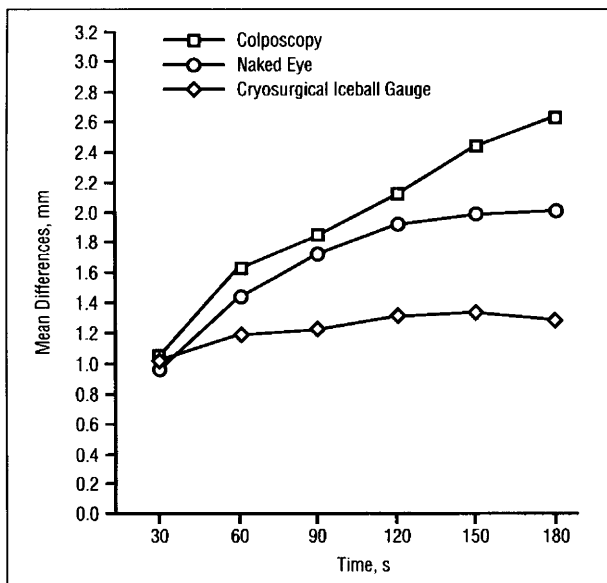
Figure 2. *The absolute value of mean differences between subject lateral spread of freeze (LSF) estimates and observer LSF measurements for each cryotherapy technique at each interval.*

gical experience. The error was greatest at the critical termination of freeze or maximum LSF distances.

The significance of these estimation errors equates to undertreatment of disease when physicians overestimate the LSF, and excessive treatment when physicians underestimate the LSF and prolong treatment. Physicians in this study overestimated the LSF more often than they underestimated the LSF. Consequently, physician measurement perceptions were flawed and, in practice, clinically significant treatment failure may result. Physician distance estimates may be insufficiently accurate for cryotherapy procedures.

Cervical intraepithelial neoplasia may extend approximately 4.8 mm into endocervical epithelial crypts.[4] Therefore, a minimal LSF of 7 mm—2-mm recovery zone[8] and 5-mm lethal zone—may be clinically necessary to satisfactorily treat some disease. Benedet et al[12] clinically confirmed the importance of this practice in a study of patients treated by laser vaporization. Among patients who had vaporization to a depth of 5 mm or less, only 80% were cured, whereas 95.5% of patients were cured if the
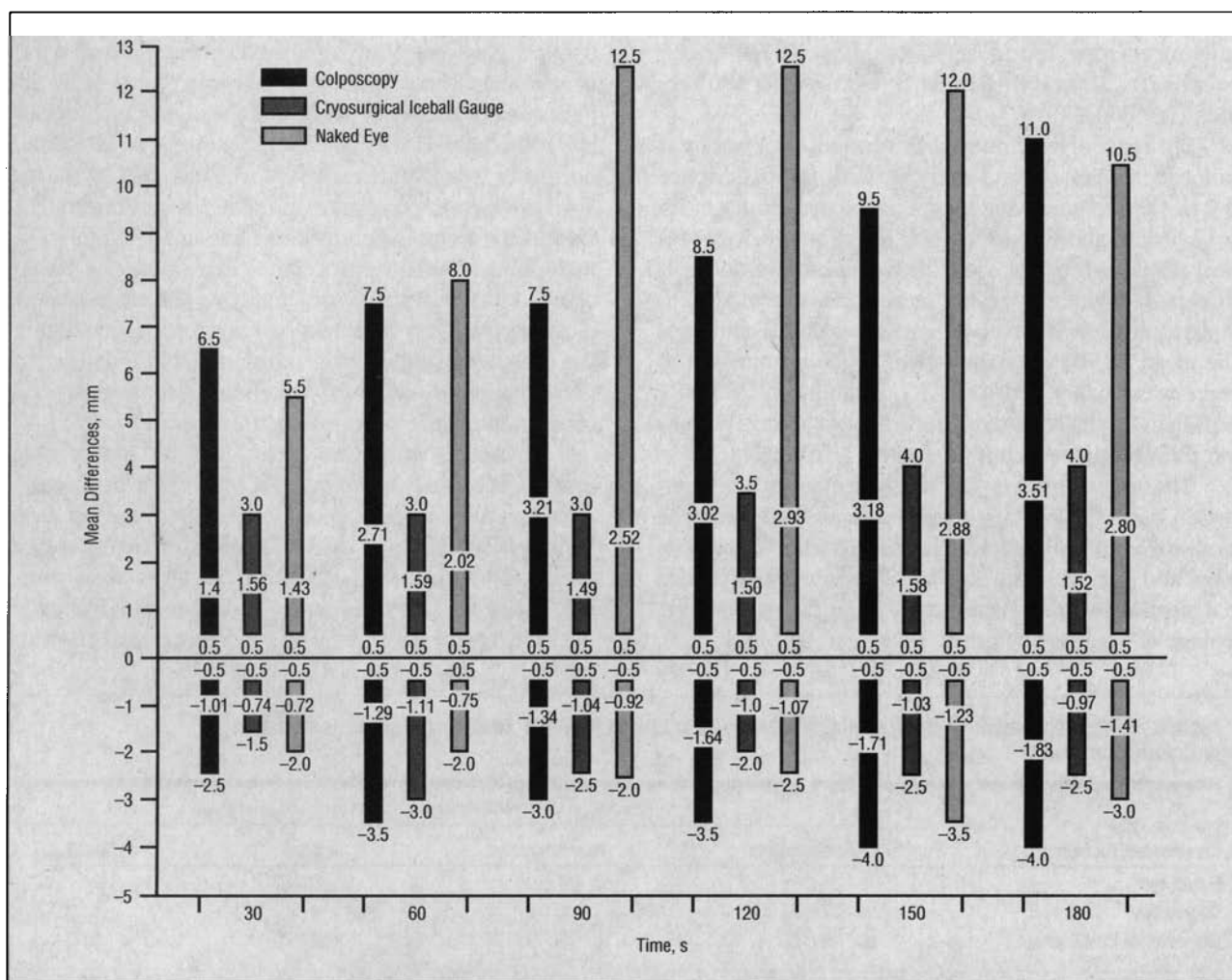

Figure 3. *The range of error and mean error for lateral spread of freeze (LSF) overestimation and LSF underestimation for each cryotherapy technique at each interval.*
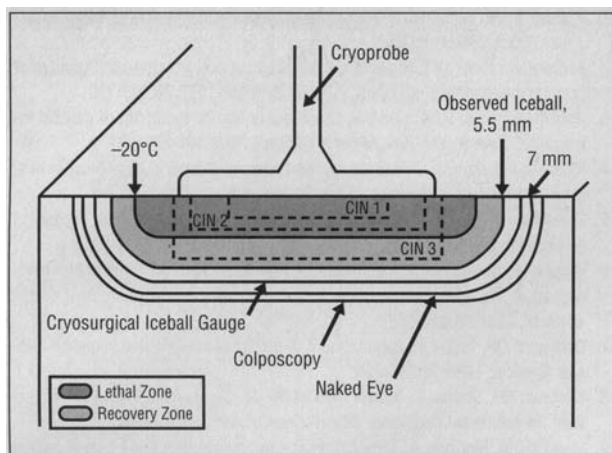
Figure 4. *The clinical consequence of lateral spread of freeze (LSF) overestimation for the naked-eye and colposcopic technique.*

vaporization exceeded 6 mm. The mean error of overestimation for the naked-eye and colposcopic-assisted procedures at termination of freeze was greater than 3 mm for a mean iceball of 5.5 mm. If one applied this same in vitro physician estimation error to clinical cryosurgery, a clinically significant treatment failure rate would result with CIN III lesions (Figure 4). The treatment failure rate for CIN II lesions, which demonstrate a crypt depth involvement of 3.06 mm,[4] would be substantially less.

A review of the reported cryosurgery treatment failure rates for CIN is seen in **Table 2**.[13-18] The rate of residual disease for CIN III is twice that for CIN I and CIN II. Why should this difference exist? All grades of CIN initially evolve deeply near the basement membrane, remain confined to the epithelium, and represent only premalignant, noninvasive disease. Either cryosurgery is technically unable to consistently destroy tissue to a depth of 5 mm or the surgeon is unable to accurately determine satisfactory ablative margins. Our reported increasing estimate error by physicians for increasing iceball size suggests that treatment failure, particularly in the case of severe disease, may be due to the imprecision of the surgeon who overestimates the depth of the freeze and thus undertreats the patient. These published studies provide evidence to support this premise (Table 2).

The results of this study indicate that physicians' measurement perceptions of relatively small but very critical distances are variable and inaccurate. The range of error appeared correspondingly extreme. The CIG minimized perceptual error by more than 50% and provided the greatest cryosurgical precision, reliability, and least variability of error. The margin of error was consistent and uniform for iceball size, including maximal LSF distances. The consistently small CIG error may be explained by the parallax phenomenon of aligning the CIG zero point with the edge of the cryoprobe. Excessive treatment was infrequently observed with the CIG, which may minimize the possibility of postoperative cervical stenosis.[19] The depth of excision for cervical cold knife conization, laser coniza-

tion, and electrosurgical loop excision of the cervical transformation zone (ELECTZ) procedures is routinely measured with a surgical rule. Incorporation of comparable measurements during cervical cryotherapy would help to suitably document the ablative effect. Further research to evaluate the clinical use and therapeutic value of the CIG appears appropriate. The CIG may serve as a valuable tool for teaching cryosurgical technique.

The study results may be limited by three factors. First, a simulated study design was necessary to permit simultaneously recorded clinician and observer measurements. Perceptual errors may differ during actual clinical cryotherapy. Not all subjects were experienced cryotherapists, but estimation errors were similar for different levels of experience. Finally, we did not assess subject's knowledge of adequate cervical cryotherapy. Certainly, misconceptions of effective cryosurgery are found in the medical literature. As a consequence, reported actual treatment failures may be a result of inappropriate technique in addition to perceptual error.

In summary, physicians demonstrated significant error in estimating the iceball LSF when performing cryosurgery. Overestimation of the LSF was more common than underestimation of the LSF, which would then increase the risk of undertreatment and residual disease. The CIG minimized perceptual error and provided the best cryosurgical precision. Use of a CIG may minimize cryotherapy failure, particularly for severe cervical premalignant disease.

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