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Electrocautery Ablation of High-Grade Anal Squamous Intraepithelial Lesions in HIV-Negative and HIV-Positive Men who have sex with Men

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ABSTRACT:

Background: Anal squamous cell carcinoma (ASCC) incidence has been rising over the past decade, most dramatically in HIV-positive men who have sex with men (MSM). We aimed to identify a novel in-office approach for ablating high-grade anal intraepithelial neoplasia (HGAIN), the believed precursor lesion to ASCC.

Materials & Methods: We performed a retrospective analysis of medical records from a NYC surgical practice, identifying patients with HGAIN treated with electrocautery ablation (ECA) and followed for at least five months with high resolution anoscopy, biopsies and/or cytology. We sought to determine HGAIN recurrence, as well as progression to ASCC after ECA.

Results: 232 MSM, 132 HIV-positive and 100 HIV-negative, with median follow up of 19.0 and 17.5 months respectively met inclusion criterion. In HIV-negative and HIV-positive MSM the probability of curing a lesion after first ECA was 85% and 75% respectively. Over follow up, 53% of HIV-negative and 61% of HIV-positive patients recurred. After first and second ECA HIV-positive MSM were 1.28 times ($p=0.16$) and 2.34 times ($p=0.009$) more likely to recur than HIV-negative MSM. The majority of recurrence was due to development of additional lesions at untreated sites (metachronous recurrence). One patient (0.4%) developed ASCC. At last visit, 83% of HIV-negative and 69% of HIV-positive patients were HGAIN free.

Conclusion: ECA is an effective treatment for HGAIN, with fewer patients progressing to ASCC than predicted with expectant management. HIV-positive patients are significantly more likely to recur than HIV-negative patients.

Keywords: high-grade anal dysplasia, electrocautery, HIV, HPV, anal cancer, men who have sex with men

INTRODUCTION:

Over the last 15 years there has been an increase in the incidence of anal squamous cell carcinoma (ASCC), most dramatically in men who have sex with men (MSM)[1]. According to a recent multicenter cohort study, the incidence rate in HIV-positive MSM is 69 per 100,000, nearly five times the rate observed in HIV-negative MSM[2]. Current evidence indicates that ASCC incidence is unlikely to decline in the absence of novel treatment options[3].

High-grade anal intraepithelial neoplasia (HGAIN) is believed to be the ASCC precursor[4-6]. The exact rate of progression of HGAIN to ASCC is not known but is estimated to be 8.5-13%[5-7]. Both anal and cervical cancers develop as a result of infection with oncogenic strains of human papilloma virus (HPV), most commonly HPV 16 and 18[8,9]. To prevent progression to invasive cancer, cervical dysplasia is excised with the surrounding squamous-columnar junction (SCJ), with conization or loop electrosurgical excision (LEEP)[10-12] achieving cure rates of greater than 95% in HIV-negative females[12]. Aggressive screening and treatment of cervical dysplasia has even resulted in a decline in HIV-positive women progressing to invasive cancer[13]. Anal dysplasia, like cervical dysplasia, is most frequently located at the SCJ, but resection of the anal SCJ results in undo morbidity including stricture, anal spasm and dyschezia[7, 14]. As a result, targeted ablation of individual lesions has become the most common management approach. Multiple techniques including: laser, electrocautery ablation (ECA), infrared coagulation (IRC), cryotherapy, or topical agents (imiquimod, tricholoracetic acid (TCA) and 5% 5-Fluoro-uracil cream)[7, 15-23] have been employed.

We previously showed that IRC was an effective in-office treatment in both HIV-negative and HIV-positive patients with individual lesion cure rates after the first ablation of 81% and 72%, respectively[20, 24]. We now endeavored to determine if in-office ECA of intra anal HGAIN was as safe and effective as IRC ablation in MSM[20, 24, 25].

MATERIALS & METHODS:

Identification of Subjects

With IRB approval from Mount Sinai Medical Center Investigational Review Board and in accordance with health insurance portability and accountability act regulations, we performed a retrospective chart review on all MSM patients who underwent ECA of intra anal HGAIN from Jan 2006 to April 2010 at a surgical practice (SG) specializing in treatment of anorectal HPV related disease. It was at this time that we began to use electrocautery ablation almost exclusively for treatment of HGAIN. For inclusion subjects were required to have a history of biopsy confirmed HGAIN treated with ECA during the study period as well as at least five months follow up after ECA. Patients were excluded if they had ever received IRC treatment, or participated in vaccine trials. MSM who had prior HGAIN treatment by laser ablation in the operating room were eligible for inclusion if recurrent disease was treated in-office with ECA. Lesion size was not measured and lesions could be confluent. Only lesions within the anal canal, proximal to the anal verge were included in the analysis. Circumferential disease was not treated in office but instead ablated in the operating room as were patients with extensive condyloma. As previously described, evaluation included anal cytology followed by digital rectal examination and standard anoscopy[26]. Cytology was obtained with a wetted Dacron® swab, and reported as squamous cells within normal limits (benign), atypical squamous cells of undetermined significance (ASCUS), atypical cells cannot rule out high-grade dysplasia (ASC-H), low-grade squamous intraepithelial lesion (LSIL) and high-grade squamous intraepithelial lesion (HSIL). Patients with abnormal cytology, and/or visible lesions on standard anoscopy underwent high-resolution anoscopy (HRA) in accordance with the technique of Jay et al.[27] Lesions suspicious for HGAIN were biopsied, and fixed in 10% formalin and processed for histology diagnosis with results reported in accordance with the Bethesda classification of normal or benign, low-grade anal intraepithelial neoplasia (LGAIN), HGAIN and ASCC[28].

Patients with HGAIN amenable to in-office treatment were most often treated at a subsequent visit after biopsy confirmation of disease. Lesions were re-identified during HRA and infiltrated with either 0.5% bupivicaine or 1% lidocaine with epinephrine to achieve local anesthesia. The anesthetic was infiltrated just distal to the lesion and minimal amounts were used to avoid lesion distortion. Later in the

series patients with larger volume disease were offered in office anesthesiologist delivered monitored sedation to alleviate discomfort from multiple injections of local anesthetic. Approximately 50% of patients chose monitored sedation.

The lesion was ablated with The Hyfrecator® 2000 (ConMed® Corporation, Utica, New York) on 13-15 watts. A 6" UltraClean® Blade with Extended Insulation (ConMed® Corporation, Utica, New York) was passed down the anoscope to make contact with the lesion. Using a gentle brushing technique the lesion was ablated by moving the blade lightly across the surface like a gentle paint-brush. The char was swept away with the blade or removed with blunt dissection utilizing the end of the anoscope. Thick lesions were debrided with a Baby Tischler Biopsy Punch (CooperSurgical, Inc. Trumbull, CT) to the level of submucosal vessels. Hemostasis was achieved with the hyfrecator. The hyfrecator smoke plume was removed with a Porta PlumeSafe 604 smoke evacuator (Buffalo Filter, Lancaster, New York) held in place by an assistant. All procedures were performed by SG. It is not our practice to ablate flat LGAIN but we routinely ablate condyloma, and these lesions are not included in the analysis.

Follow up consisted of regular 3-6 month evaluations including a history of postsurgical complications and digital rectal exam. At three months post ablation patients would also have standard anoscopy to access healing and gross recurrence. Given the high recurrence rates with IRC, at 6 months patients would have cytology and simultaneous HRA to rule out recurrence. If no lesion was found then the patient would be evaluated at 12 months with cytology and standard anoscopy. Patients with an observed lesion on standard anoscopy or abnormal cytology were always referred for HRA. Patients with HGAIN on biopsy were classified as having recurrent disease and offered repeat ablation. Patients with benign cytology or without HGAIN on HRA maintained regular follow up. The screening and treatment algorithm is depicted in Figure 1.

Study Definitions

Treatment success following ECA was defined as no evidence of HGAIN on HRA or benign cytology if a follow up HRA was not performed. Recurrence was defined as either cytologic or biopsy proven HGAIN after treatment. Overall recurrence was defined as identification of HGAIN at any point during follow-up, in either the treated location, or at a new site. Persistence is recurrence of disease at the treatment site. A metachronous recurrence is HGAIN found at a site not previously treated. Time to recurrence was measured from ECA to the date recurrent HGAIN was diagnosed.

Statistical Analysis

Statistical analyses were performed with SAS (SAS Institute Inc., Cary, NC). Chi-squared tests were used to compare proportions and Student's t-tests to compare means, as appropriate. The Cox proportional hazards model was used to compute risk ratios (equivalent of odds ratios) and confidence intervals after adjusting for other covariates. Recurrence rates were estimated using Kaplan-Meier product limit method with comparison between the HIV-positive and HIV-negative groups evaluated with log-rank statistic.

RESULTS

A total of 100 HIV-negative and 132 HIV-positive MSM met enrollment criteria, with a median age of 49 (range 27-74) years and 42 (range 21-70) years respectively ($p<0.0001$). Mean length of follow-up was 21.1 (range 6.1-43.9) months and 20.0 (range 5.4-46.0) months for HIV-negative and HIV-positive MSM ($p=0.40$). HIV-positive MSM had significantly more lesions treated at their first ablation than HIV-negative MSM; in total 375 lesions were treated at first treatment in the HIV-positive MSM vs. 226 in the HIV-negative MSM ($p=0.006$). Following HGAIN diagnosis, 90 percent of patients had ECA by 1.5 months for HIV-negative vs. 1.8 months in the HIV-positive patients.

HGAIN recurrence after ECA

Table 1 details the overall recurrence rates observed for HIV- negative and HIV-positive MSM. In both the HIV- positive and HIV-negative groups, more patients recurred after first electrocautery than remained disease free. In the HIV-negative group 53 (53%) patients recurred after first ablation with a

mean of 1.6 lesions over a mean of 8.2 months, whereas, 47 (47%) patients did not recur over a mean of 18.1 months. For HIV-positive patients, 80 (61%) recurred after first ablation with a mean of 1.9 lesions over a mean of 9.1 months, whereas 52 (39%) did not recur over a mean of 16.0 months. Mean number of recurrent lesions for both HIV-positive and HIV-negative MSM was never greater than two. In both the HIV-negative and HIV-positive patients there was no statistically significant decrease in overall recurrence rates with continued ECA. Lesion burden was observed to affect recurrence rates only in the HIV-positive patients. Patients with one HGAIN on first ECA were 55% (p=0.008) and 73% (p<0.0001) less likely to have recurrence than patients with two or three lesions, respectively.

Table 2 depicts HGAIN persistence after treatment in HIV-positive and HIV-negative MSM. Following ablation, persistent HGAIN was identified in 27 (27%) of HIV-negative MSM, but 226 lesions were treated once, and 35 persisted yielding an individual lesion cure rate of 85%. In the HIV-positive patients, 55 (42%) had persistent HGAIN after their first ablation, but 375 lesions were treated once, and 93 persisted yielding an individual lesion cure rate of 75%. In the HIV-negative patients, the persistence rate after ECA of refractory HGAIN was 3.03 ([1.32, 6.93]; p=0.009) times greater than the persistence rate following initial electrocautery of index lesions. Similarly, in the HIV-positive patients, the persistence rate for lesions following third ECA was 3.08 ([1.58, 5.99]; p=0.0009) and 2.98 ([1.34, 6.65]; p=0.008) times greater than following 1st and 2nd electrocautery respectively. Increased persistence between 1st and 2nd ECA's was observed but not statistically significant.

Comparison of HGAIN recurrence between HIV-positive and HIV-negative MSM

Our data demonstrates that HGAIN recurrence was greater among HIV-positive patients than HIV-negative patients (Figure 2). After first ECA, HIV-positive MSM were 1.28 times ([0.91, 1.82]; p=0.1578) more likely to recur than HIV-negative MSM and 2.34 ([1.24, 4.43]; p=0.009) times more likely to recur after second ECA. Similarly the persistence rate after first ECA in HIV-positive patients was double that of the HIV-negative patients (p=0.003).

Of note, at last visit, 83% of HIV-negative and 69% of HIV-positive patients were HGAIN free.

Adverse events

One HIV-positive patient (0.4%) progressed to ASCC despite multiple ECA's. Initially the patient presented with circumferential intra anal HGAIN and was treated with laser ablation in the operating room. At that time, no biopsies indicated ASCC. He developed 4 localized HGAIN recurrent lesions 21 months after surgery and was treated in office with ECA. Five months later he developed a single recurrence retreated with ECA. Six months later multiple recurrent HGAIN's developed, and one lesion that had persisted throughout now appeared raised. Despite the fact that the biopsy was only HGAIN, the lesion was excised instead of ablated and found to have ASCC deep to the HGAIN.

No patients developed other serious adverse events following ECA, including anal stenosis, persistent bleeding, hemorrhage, failure to heal, or infection necessitating antibiotic therapy. Most often pain was the only post-procedure complaint and was adequately controlled by over the counter medication or mild narcotic analgesia, however no post procedure diaries were utilized.

DISCUSSION:

This study represents the largest efficacy analysis of ECA to date. The only other major study published by Chang et al. in 2002 examines ECA for extensive HGAIN disease in the operating room setting. The study reported recurrence rates of 79% in HIV-positive group and 0% in HIV-negative group, but was limited by small size (n=37) and fairly short follow up[21]. In the extended and much larger follow-up series that included these patients, the 0% recurrence did not hold[22]. Our results confirm that ECA is an effective treatment for HGAIN, and can be used safely in-office.

In both HIV-positive and HIV-negative patients, lesions that failed initial ECA were less likely to be successfully ablated on subsequent treatment. This observation has both positive and negative implications. As might be predicted, there does not appear to be any lasting tissue effect following ECA such as scarring or destruction of the transformation zone that could diminish recurrence. Development of persistent lesions may be secondary to inadequate initial lesion ablation or "oncogenic" virus present in adjacent cells activates during wound healing causing a new HGAIN to develop. At this point there is no

way of knowing if the persistent lesion actually resulted from remaining disease left behind or if it developed from a new cell line. The greater difficulty in preventing persistence of a recurrent lesion with successive ablations, however, seems to support the possibility that the lesion was caused by a more oncogenic virus (perhaps HPV 16).

Similarly, HIV-positive patients with less extensive HGAIN, defined by fewer lesions at presentation, had lower recurrence rates than those presenting with multiple lesions. Patients with only one lesion at first ablation were 55% less likely to recur than those with two lesions ($p=0.008$) and 73% less likely than patients with three lesions ($p<0.0001$). Extensive dysplastic tissue may indicate either infection with a more oncogenic virus or a more immune compromised host. Interestingly, we did not see a statistically significant association between disease burden and risk of recurrence in HIV-negative patients. This could result from the fact the HIV-negative patients had fewer lesions and likely a more robust immune response reducing recurrence. If we had more HIV-negative patients with extensive disease we might have seen a difference.

Comparing overall recurrence rates to persistence rates clearly demonstrates that recurrence in non-treated areas (metachronous recurrence) is the major factor preventing patients from achieving disease free status. While our study demonstrates that ECA effectively ablates dysplastic lesions, it also suggests that even with successive treatments recurrence over time remains a problem. Clearly, ablation destroys dysplastic cells but does not eradicate the HPV infection from other cells or prevent re-infection leaving the patient at risk for new foci of dysplasia. It remains to be seen with long-term follow-up for patients in monogamous relationships if risk of recurrence decreases.

Despite the fact that patients required multiple treatments to ablate HGAIN and recurrence remained high, morbidity was minimal. The mean time to recurrence in both groups approached a year. Moreover, the mean number of recurrent lesions did not exceed two so repeat ablations were localized and not extensive. This could translate into less pain with more rapid healing.

Comparison of ECA to other treatments

We previously reported IRC as an effective in-office treatment modality for HGAIN with individual lesion cure rates after the first IRC of 81% in HIV-negative and 72%, in HIV-positive patients[20, 24] and are not significantly different than what we now report for ECA. Moreover there was no difference in overall recurrence or metachronous lesion recurrence between patients treated with IRC versus ECA[20, 24] (Table 3). Of note, in the IRC study, both the HIV-negative and HIV-positive groups were younger with mean age of 38 & 41 years as compared to 42 and 49 years respectively ($p<.0001$, $p=0.02$) in this EC study. In addition, in the IRC study the mean number of lesions at first treatment in HIV-positive patients was 1.6 versus 2.2 lesions in this study ($p= 0.0005$). In light of previously described relationship between disease burden and recurrence in the HIV-positive patients we might expect that these differences would cause increased recurrence in the current EC trial, but this was not the case. The IRC data we reported is also consistent with 2 other studies of HIV-positive MSM that reported individual lesion cure rates of approximately 65%[14, 23]. Therefore given that IRC and ECA have similar outcomes when treating HGAIN, the choice of modality should be based on clinician comfort and preference. ECA does require smoke evacuation that is best handled with an assistant while IRC does not. It is, however, our belief that whether these minor surgical procedures are performed with IRC or ECA, an assistant should a problem could arise even in the best of circumstances. Although not measured, in our hands the overall impression was that EC seemed faster, more hemostatic and allowed more extensive disease to be treated in office than the IRC.

Topical agents for treating HGAIN have also been studied. Imiquimod was recently evaluated in a double blind randomized controlled trial[19]. In the treatment group of 28 patients, Imiquimod demonstrated a 61% cure rate over 36 months. While Imiquimod could be a promising non-surgical treatment, it required three times weekly application for four months. That withstanding the treatment was tolerable with only a few patients discontinuing treatment. TCA has also been used for topical ablation in patients with limited disease with 73% and 71% individual lesion cure rates for AIN1 and AIN2-3, respectively[18]. Limited follow-up and disease burden make direct comparison with ECA difficult.

Some clinicians advocate a more conservative approach monitoring HGAIN closely and only treating if early ASCC develops or if lesions become palpable or grossly visible[29]. Their rational is that many patients with HGAIN will not progress to cancer and those that do will be caught early when lesions can be cured by excision. However, recent studies by Ortholan et al. looked at recurrence rates after treatment of T1 or T1S anal cancer, and found that excision alone for T1S had a 33% local recurrence rate requiring radiation therapy[30]. Patients with invasion into the submucosa (T1), who failed local treatment, required abdominoperineal resection. These outcomes are associated with significant morbidity and decreased quality of life. Treatment of HGAIN aims to reduce incidence of anal cancer and requirements for large surgical resection or radiation, and chemotherapy. Although unfortunate, one patient developed ASCC while managed with ECA. To date, HGAIN treatment series document a 0-1.2% progression to ASCC which is far lower than retrospective studies which report an 8.5 to 13% progression without intervention[5-7, 20, 22, 24]. Based on these estimates the incidence of anal cancer would be predicted to be much higher in our cohort had HGAIN not been ablated.

There are several limitations to this study besides the fact that it is retrospective with a relatively short follow-up. While HRA is the gold standard in detection of HGAIN, it requires human interpretation, which allows for the possibility that lesions can be missed and recurrence under-diagnosed. In addition, patients with benign cytology and negative standard anoscopy were considered non-recurrent which might further underestimate recurrence rates. The study was performed only on males, which could limit applicability to women. Moreover, patients were excluded from in-office management if their disease was judged too extensive and these results may not be generalizable to patients with large volume HGAIN. In addition post-treatment diaries were not performed, which would have provided data quantifying post-procedural pain. It remains to be seen if identical results would be achieved in a larger and longer prospective trial with men and women. Moreover, all procedures were performed by a single clinician (SG) very experienced in identification and treatment of HGAIN. It remains to be seen if similar results are reported by others.

CONCLUSION:

ECA of HGAIN is a safe and effective office based procedure comparable to other available treatments. Cure rates of individual lesions are excellent but patients continue to develop metachronous recurrence making continued follow-up important. While we documented a single progression to ASCC (0.4%), rates are far lower than series advocating a "watch and wait" approach.

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FIGURE CAPTIONS:

Figure 1.

Figure 1. Anal neoplasia screening and treatment algorithm.

[…]

(*) If no abnormal cytology or gross lesion is identified HIV+ MSM should be rescreened in 12 months and HIV- MSM should be rescreened in 24-36 months.

(**) If no HGAIN lesion is identified on HRA following an HSIL cytology result, a repeat HRA is performed in 3 months to rule out a missed lesion.

Figure 2.

Figure 2. Kaplan-Meier curves for development of recurrent lesions after EC treatment.

[…]

(a) The hazard ratio comparing the risk of recurrence after 1st EC between HIV positive and negative patients is 1.28 [0.91, 1.82]; p=0.1578.

(b) The hazard ratio comparing the risk of recurrence after 2nd EC between HIV positive and negative patients is 2.34 [1.24, 4.43]; p=0.0090.

Table 1. Overall recurrence rates in HIV-negative and HIV-positive patients

	HIV- Negative		HIV-Positive	
	Recurrence n (%)	No recurrence n (%)	Recurrence n (%)	No recurrence n (%)
After 1st EC Treatment				
Number of Patients	53 (53%)	47 (47%)	80 (61%)	52 (39%)
Median months after EC[a)]	7.0	17.3	6.8	13.0
Mean # of Lesions	1.58		1.88	
Range of Lesions	[1-6]		[1-4]	
After 2nd EC Treatment[(b)]				
Number of Patients	14 (38%)	23 (62%)	34 (63%)	20 (37%)
Median months after EC[(a)]	6.2	13.3	6.5	6.9
Mean # of Lesions	1.57		1.62	
Range of Lesions	[1-2]		[1-4]	
After 3rd EC Treatment[(c)]				
Number of Patients	5 (63%)	2 (37%)	11 (50%)	11 (50%)
Median months after EC[(a),]	6.2	8.5	6.1	7.5
Mean # of Lesions	1.4		1.64	
Range of Lesions	[1-3]		[1-4]	
After 4th EC Treatment[(d)]				
Number of Patients			3 (75%)	1 (25%)
Median months after EC[(a),]			6.3	11.7
Mean # of Lesions			1	
Range of Lesions			[1 – 1]	

a) For those who recurred this is the number of months from electrocautery ablation (ECA) to time new high grade anal intraepithelial neoplasia (HGAIN) and for those who did not recur it is the follow up time in months to their last visit.

b) HIV-negative patients: 9 of the 53 patients did not have their HGAIN treated with electrocautery and 7 of the 53 patients had their 1st recurrence on their last visit and thus could not be followed for further recurrence. HIV-positive patients: 11 of the 80 patients did not have their recurrent HGAIN treated with electrocautery and 15 of the 80 patients had their 1st recurrence on their last visit.

c) HIV-negative patients: 3 of the 14 patients did not have their 2nd recurrence treated with electrocautery and 4 of the 14 patients had their 2nd recurrence on their last visit. HIV-positive patients: 8 of the 34 patients did not have their 2nd recurrence treated with electrocautery and 4 of the 34 patients had their 2nd recurrence on their last visit.

d) HIV-positive patients: 2 of the 11 patients did not have their 3rd recurrence treated with electrocautery and 5 of the 11 patients had their 3rd recurrence on their last visit.

Table 2. Persistence in HIV-negative and HIV-positive patients.

	HIV-negative		HIV-positive	
	Persisted N (%)	Not Persisted N (%)	Persisted N (%)	Not Persisted N (%)
After 1st EC Treatment				
Number of Patients	27 (27%)	73 (73%)	55 (42%)	77 (58%)
# HGAIN Lesions Persisted	35 (15%)	191 (85%)	93 (25%)	282 (75%)
Mean # of Lesions	1.30		1.69	
Range of Lesions	[1-3]		[1-4]	
After 2nd EC Treatment[(a)]				
Number of Patients	6 (35%)	11 (65%)	11 (31%)	25 (69%)
# HGAIN Lesions Persisted	7 (33%)	14 (67%)	12 (21%)	46 (79%)
Mean # of Lesions	1.17		1.09	
Range of Lesions	[1-2]		[1-2]	
After 3rd EC Treatment[(b)]				
Number of Patients	0 (0%)	4 (100%)	5 (63%)	3 (38%)
# HGAIN Lesions Persisted			5 (56%)	4 (44%)
Mean # of Lesions			1	
Range of Lesions			[1-1]	

a) HIV-negative patients: Among the 27 patients who had at least 1 lesion persist, 17 had electrocautery ablation (ECA) a 2nd time with adequate follow up. Of those 17 patients, there were 21 persistent lesions treated and followed a 2nd time with ECA and of those 21 lesions only 7 persisted after the 2nd ECA treatment. HIV-positive patients: Among the 55 patients who had at least 1 lesion persist after their 1st ECA, 36 patients were treated with electrocautery a 2nd time with adequate follow up. Among those 36 patients, there were 58 persistent lesions treated and followed a 2nd time with ECA and only 12 persisted after the 2nd ECA treatment.

b) HIV-negative patients: Of the 6 patients that had a persistent lesion after 2nd electrocautery, 4 patients were retreated with a 3rd electrocautery treatment after which no patient was observed to have persistence. HIV-positive patients: Among the 11 HIV-positive patients who had at least 1 lesion persist after their 2nd ECA treatment 8 had that (those) persistent lesion(s) treated a 3rd time with ECA (and could be followed). Of those 8 patients, there were 9 persistent lesions treated and followed a 3rd time with ECA and 5 persisted after the 3rd ECA treatment.

Table 3. Comparison of electrocautery vs. IRC series

	IRC						EC						IRC vs. EC	
	HIV-positive[a]			HIV-negative[b]			HIV-positive			HIV-negative			P-value	
	N	SD or Event#	Mean or %	N	SD or Event#	Mean or %	N	SD or Event#	Mean or %	N	SD or Event#	Mean or %	HIV +	HIV -
Mean Age	68	6.95	41 (29-62)	75	10.72	38 (20-72)	132	8.76	49 (27-74)	100	10.88	42 (21-70)	<0.0001	0.0166
Mean number of lesions, 1st treatment	68	0.84	1.56 (1-5)	75	0.41	1.5 (1-3)	132	1.35	2.2 (1-7)	100	1.11	1.7 (1-6)	0.0005	0.1393
# lesions at 1st treatment	165			113			375			226				
Proportion not persistent at 1st treatment	165	119	72%	113	92	81%	375	282	75%	226	191	85%	0.4508	0.4691
Recurrence after 1st treatment	68	44	65%	75	40	53%	132	80	61%	100	53	53%	0.5714	0.9649

a) Goldstone SE, Kawalek AZ, Huyett JW. Infrared coagulator: a useful tool for treating anal squamous intraepithelial lesions. Dis Colon Rectum 2005;48:1042--54.

b) Goldstone SE, Hundert JS, Huyett JW (2007) Infrared coagulator ablation of high-grade anal squamous intraepithelial lesions in HIV-negative males who have sex with males. *Dis Colon Rectum* 50:565–575