Esophageal injury during AF ablation

Singh: Esophageal injury during AF ablation

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Total Word Count: 4 794

Subject Code: 22
ABSTRACT

**Background:** It is common practice to empirically limit the radiofrequency (RF) power when ablating the posterior left atrium (LA) during atrial fibrillation (AF) ablation to avoid thermal injury to the esophagus. The objective of this study was to determine whether RF energy delivery limited by luminal esophageal temperature (LET) monitoring is associated with a reduction in esophageal injury compared to a strategy of RF power limitation alone.

**Methods and Results:** Eighty-one consecutive patients undergoing AF ablation followed by esophageal endoscopy (EGD) were included in this observational study. All patients underwent extra-ostial electrical PV isolation using an electro-anatomical mapping system and irrigated RF ablation. All RF applications on the posterior LA were limited to 35 Watts. A commercially available, single-thermocouple esophageal probe was used to monitor LET in a subset of patients (n=67). In these cases, applications were promptly interrupted when LET was ≥38.5°C; further applications were performed at reduced power to obtain a LET <38.5°C. EGD was performed 1-3 days post-procedure. Ablation-related esophageal ulcerations were identified in 9/81 (11%) patients. All patients were asymptomatic. Of these 81 patients, LET monitoring during ablation occurred in 67 (83%) of patients. Esophageal injury was observed more frequently (36% vs. 6%, p< 0.006) in the group without LET monitoring.

**Conclusions:** These data suggest that LET monitoring may be associated with a reduction in esophageal injury compared to power limitation alone.

**Key Words:** catheter ablation; atrial fibrillation; complications
INTRODUCTION

Radiofrequency (RF) catheter ablation of atrial fibrillation (AF) has become a common ablation procedure performed worldwide (1). The cornerstone of this procedure is the placement of ablation lesions around the pulmonary vein (PV) ostia to isolate AF triggers. RF lesions extending beyond the atrial myocardium may result in collateral damage to adjacent structures, including the esophagus (2-7).

Left atrial-esophageal (LA-Eso) fistula formation is now a well-recognized complication of percutaneous AF ablation with an estimated incidence of ~0.1%. Although less prevalent than reported in the surgical literature (8), this complication remains devastating, with significant morbidity and mortality (1, 4-7). While the pathophysiology is not fully understood, it is clear that thermal injury to the esophagus during ablation of the LA posterior wall plays a crucial role in triggering the cascade of events which eventually result in the development of LA-Eso fistula (8-10).

Currently, the most commonly employed clinical strategy to minimize esophageal thermal injury during AF ablation involves limiting the magnitude of power (25-35 Watts), as well as the duration (< 30 seconds), of RF applications placed along the posterior wall of the LA (11-13). A major limitation of this approach is that it fails to account for the variability in the thickness of the posterior LA wall and the presence of peri-esophageal connective tissue – important determinants of esophageal heating (7, 14, 15). Thus, empirically limiting the power and duration of RF applications may be insufficient to prevent esophageal thermal injury in all
patients. The aim of this study was to determine whether RF power delivery during AF ablation guided by luminal esophageal temperature (LET) monitoring is associated with less frequent esophageal injury compared to a strategy of power limitation alone.

METHODS

Patients:

Eighty-one consecutive patients with symptomatic, drug-refractory AF, undergoing AF ablation followed by a post-procedural, non-symptom driven, esophageal endoscopy (EGD) within 3 days of the ablation procedure, were included in this observational study. Patients were identified between October 2006 and November 2007 at the Massachusetts General Hospital, Boston, MA and the Saint John's Health Center, Santa Monica, CA. All patients provided verbal and written consent for both procedures, according to institutional guidelines. The study was approved by the research ethics board of each institution.

Patient demographics (age, sex, body-mass index), disease characteristics (paroxysmal AF, normal heart, ejection fraction (EF), LA size, previous AF ablation), and medication use (current use of anti-arrhythmic drugs [AAD], aspirin, and proton pump inhibitor [PPI] or histamine-2 receptor antagonist [H2RA]) were obtained.

Monitoring esophageal temperature:

In patients undergoing LET monitoring, a 9-Fr single thermocouple esophageal temperature probe (Vital Temp, Vital Signs Colorado Inc.) was inserted nasally, and advanced into the esophagus, under fluoroscopic guidance, to a position directly posterior to the LA. The position
of the tip of the temperature probe was continuously verified by fluoroscopy throughout the procedure, and was adjusted in a cranio-caudal fashion to the level of the ablation catheter prior to the application of each ablation lesion to ensure that the thermometer tip was positioned as close as possible to the RF ablation catheter tip (Figure 1). Continuous real-time esophageal temperature monitoring was performed and recorded throughout each case.

**PV isolation:**

Conscious sedation or general anesthesia was available for each case, and was utilized according to the patient’s preference and physician’s discretion. Ablation procedures were performed by operators with experience in atrial fibrillation ablation (AD, SD, TM and VR). All patients underwent a pre-procedural computed tomography (CT) or magnetic resonance imaging (MRI) scan of the LA. A trans-esophageal echocardiogram was performed on the day of the procedure when clinically indicated. Double trans-septal punctures were performed in all patients. Intravenous unfractionated heparin was administered in boluses immediately prior, and subsequent to the trans-septal punctures, followed by an infusion to maintain an activated clotting time of 250-350 seconds. Intra-cardiac echocardiography (ICE) (AcuNav, Siemens) was frequently employed to guide trans-septal puncture. An electro-anatomic map of the LA and PVs was created with the CARTO (Biosense Webster) or NavX/ESI (St. Jude Medical) navigation systems. Of note, in no case was the image of the esophagus obtained on a pre-procedural CT or MRI segmented or displayed.

Radiofrequency pulses were delivered circumferentially around each vein pair, approximately 1cm from each PV ostium; additional linear lesions and ablation of fractionated potentials were performed at the operator’s discretion. RF energy was delivered with a 3.5-mm externally
(Thermocool, Biosense Webster) or 4mm internally (Chili, Boston Scientific) irrigated catheter. The RF Generator (Stockert, Biosense Webster) was set to deliver lesions up to 35W and 40°C.

Based on our prior experience with LET monitoring during atrial fibrillation ablation prior to the study period, RF applications were terminated when the LET exceeded 38.5°C in patients with LET monitoring. Subsequent lesions in adjacent areas were performed with reduced power to avoid further temperature elevation. The maximal LET for each patient was documented with the average power and duration of ablation for the corresponding RF lesion.

**Esophageal evaluation / Follow-up:**

All patients underwent a non-symptom driven EGD between 1 and 3 days post procedure. Ulceration was attributed to AF ablation if it was located on the anterior wall of the mid-esophagus (approximately 20-30cm from the incisors) and was adjacent to the pulsating heart. These findings were confirmed by the gastroenterologist performing the EGD (who were blinded to the use of LET monitoring). All patients with ulcerations were treated with high dose proton-pump inhibitor therapy for at least one week and all underwent repeat endoscopy at 1 week to ensure ulcer healing. Any additional follow-up was scheduled at the discretion of the gastroenterologist.

Typically, the day following the procedure, patients were discharged on anticoagulation with warfarin (target INR of 2.0 to 3.0) for at least 3 months post-ablation. Pre-ablation AAD were generally maintained for four weeks following the procedure. Patients were seen in the outpatient clinic for follow-up at 6 weeks and 3 months post-procedure. AF recurrences were documented with electrocardiograms, holter and/or trans-telephonic monitoring. The presence
of esophageal ulceration, post-procedure pericarditis or pericardial effusion, and AF recurrence at 3 months was ascertained for each patient.

Statistical Analysis:

Patients were divided into two groups: those with and without LET monitoring. The primary end-point of the study was the presence of esophageal ulceration on EGD. Continuous variables were reported as mean ± standard deviation (SD), distribution of discrete variables as percentages (%) for each group. Means of continuous variables were compared with the Student’s t-test. Two by two contingency tables were created for discrete variables and frequencies compared with Fisher’s exact test when any cell within the table contained a value ≤5; the Chi squared test was used in all other cases. The strength and direction of the association between LET and RF power applied was quantified using Pearson’s correlation coefficient. P values <0.05 were considered significant. All statistical analyses were performed with SAS version 9 (SAS institute, Cary NC, USA). The authors had full access to the data and take responsibility for its integrity. All authors have read and agree to the manuscript as written.

RESULTS

Patient characteristics:

The mean age of the cohort (81 patients) was 58 ± 11 years, 74% were male, 44% had paroxysmal AF with an average duration of AF of 5±4 years. The mean EF and LA size were 60±8% and 43±9mm, respectively. The CARTO and NavX/ESI mapping systems were employed in 78% and 22% of patients, respectively.
Sixty-seven patients (83%) underwent AF ablation with LET monitoring. Fourteen (17%) did not undergo LET monitoring: five (36%) due to difficulties in placing the LET probe within the esophagus and nine (64%) due to the operator’s preference. LET monitoring was employed with equal frequency throughout the study period and amongst all operators.

Table 1 displays the characteristics of the two groups. There were no significant differences between each group, with the exception that individuals without LET monitoring had a lower BMI, used more AAD, and underwent ablation more frequently with general anesthesia.

**Esophageal ulceration:**

Overall, 9 patients (11%) in the cohort had esophageal ulceration on EGD (Figure 2 and 3). Esophageal ulceration was more prevalent in the group without LET monitoring (36% versus 6%, P<0.006). Ulcer formation was not clustered at any time during the study period or with a specific operator. Qualitatively, ulcerations in patients without LET monitoring appeared longer and linear (vertical) compared to ulcerations observed in patients with LET monitoring which was discrete with diameter between 3-10mm. All patients with ulceration were asymptomatic, treated with high-dose proton pump inhibitor, and demonstrated ulcer healing on follow-up EGD at 1 week. No patient developed a LA-Eso fistula.

**Esophageal temperature:**

Esophageal temperature recordings for 67% (45/67) of patients with LET monitoring were recorded and reviewed. Despite stopping RF energy when the LET was 38.5°C, the LET continued to rise to $\geq 39^\circ$C at least once in over half of the study cohort (24/45 (53%); maximum recorded LET = 41.9°C). There was no clear relationship between the maximal esophageal
temperature recorded (Figure 4) or number of elevated LET recording (Figure 5) in the patients with and without esophageal ulceration. A trend towards more esophageal ulceration was noted in patients with maximal LET $\geq 39^\circ$C (75% vs. 54%, $P=0.4$).

**RF power and LET:**

No correlation was observed between LET and the average RF power applied to the corresponding lesion ($r=0.1$, $P=0.2$; Figure 6). In patients requiring reductions in RF power, elevated LET often continued to be present with subsequent RF applications. Of all applications resulting in an LET $\geq 38.5^\circ$C ($n=101$), 34% occurred at a power of $\leq 20$W, including 8% at a power $\leq 10$W.

**Other adverse events:**

A statistically significant difference was not observed between the two groups in the incidence of post-procedure pericarditis and/or pericardial effusion and AF recurrence at 3 months. No complications associated with LET probe placement were observed in the cohort of patients undergoing LET monitoring.

**DISCUSSION**

This study suggests that temperature monitoring during AF ablation may be associated with a reduction in esophageal injury.

**Esophageal injury associated with AF ablation:**
The mechanism of esophageal injury during RF ablation is not clear, but hypothesized to be secondary to thermal injury related to conductive heating (11-13). It has been suggested that the muscular layer of the esophagus absorbs the majority of heat and is most susceptible to injury (8, 12). Injury to this area may result in reduced esophageal elasticity producing symptoms of dysphagia (4).

Aupperle et. al. (12) systematically evaluated esophageal injury in sheep undergoing AF ablation. Twenty-four (62%) sheep demonstrated histological evidence of post-AF ablation esophageal injury, which occurred predominantly in the peri-esophageal and outer esophageal muscular layers. Only 1 animal had visible evidence of esophageal injury.

To our knowledge, three human studies have attempted to evaluate the presence of esophageal injury associated with AF ablation. Cummings et. al. (13) performed an EGD on 16 patients undergoing AF ablation with an 8mm non-irrigated catheter, with power titration guided by microbubbles formation on ICE. No patient demonstrated esophageal injury on EGD within 24 hours post ablation. Marrouche et. al. (16) examined 28 patients with EGD post AF ablation (14 underwent AF ablation with an irrigated tip catheter and 14 with an 8mm non-irrigated catheter). Overall, 13 patients (48%) demonstrated EGD evidence of esophageal injury—5 (18%) developed ulceration and 8 (29%) erythema. Nakagawa et. al. (17) reported EGD findings on 16 patients who underwent AF ablation under general anesthesia with power limitation to 20-25W in areas near the esophagus; nine patients (56%) developed esophageal ulceration. Thus, the rate of AF related esophageal ulceration during AF ablation is variable.

The Use of Esophageal Temperature Monitoring during AF Ablation:
Continuous evaluation of the intra luminal esophageal temperature during the ablation procedure may prevent thermal injury. However, this approach has several limitations as 1) accurate intra-luminal temperature monitoring depends on optimal contact between the probe and esophageal wall, which is difficult to ensure during the procedure, and 2) intra-luminal esophageal temperature underestimates intramural thermal damage to the muscular layers of the esophagus. In addition, the complex anatomy of the esophagus (including the presence of transverse folds) and mal-alignment of the LET probe at the region of ablation may result in a slow rise in temperature, with ensuing esophageal injury occurring at otherwise acceptable LETs.

Because of the inherent limitations of LET monitoring, LET was not employed to titrate power up in our study. Rather, LET was used simply to insure that the employed power settings thought to be safe would not result in undesired high esophageal temperatures. Thus, intra-luminal esophageal profiles were used to interrupt RF applications prematurely if high esophageal temperatures (≥38.5°C) were detected at a given power, and subsequently titrate power down with additional RF applications. In this regard, this study is important as it suggests that LET monitoring may confer additional protection from esophageal thermal injury as compared to a strategy of power limitation alone. This is of particular importance as 34 of 101 RF applications with resulting LET ≥38.5°C occurred despite a reduction in power to ≤ 20 watts, as shown in Figure 6. High LETs were also noted despite power applications of <10 watts, suggesting that in certain patients, thermal injury may occur despite significant reductions in RF power. These findings suggest value for LET monitoring during AF ablation.
In patients undergoing LET monitoring, a clear relationship between the maximum LET and number of LET $\geq 38.5^\circ$C was not observed in those with and without ulceration. Despite this finding, we suspect that the protective benefit of LET monitoring still lies in its ability to detect elevated LET. We hypothesize that empiric ablation of the posterior LA at a constant RF power of 35W may result in frequent undetected elevations of LET with ensuing esophageal thermal injury, whereas prompt identification of elevated LET during RF ablation in the posterior LA with subsequent down-titration of power to avoid continuous elevated LET, may minimize this injury. Although difficult to prove, the presence of longer linear ulcerations in patients without LET monitoring, compared to the discrete ulcerations in patients with LET monitoring, supports this hypothesis.

Advantages and Limitations of LET:

Compared to alternative approaches to minimize esophageal injury, LET monitoring is straightforward, inexpensive, well tolerated, and may provide information on the risk of esophageal thermal injury independent of the RF application settings used during ablation. The optimal LET threshold to avoid injury has not been defined, and must account for limitations in proper LET probe positioning, thermal latency and the underestimation of mural temperatures with luminal recordings (18). A LET cut-off of $38.5^\circ$C was empirically selected in this study based on our prior experience with LET monitoring during AF ablation. While patients with a LET $\geq 39^\circ$C had a trend toward ulceration, we are unable to suggest a specific LET cut-off to end ablation lesions as the maximal LET recorded is frequently higher than the LET at which ablation
is terminated. Similar to conclusions obtained by other investigators (11, 13), no relationship between RF power and LET was present.

Theoretically, the use of an LET probe is associated with its own risks, including traumatic insertion (with hematoma formation or perforation), aspiration, and patient intolerance. While no complications of LET monitoring were noted in this study, probe placement was not possible in 5 patients. However, with increasing experience, it is possible to properly place the LET probe in the vast majority of patients.

Titrating power and limiting ablation duration to rises in LET may result in the administration of short, low power RF lesions, which may theoretically reduce the efficacy of AF ablation. This was not supported in this study, as no difference in the rate of AF recurrence was noted at 3 months in both groups. Thus, a strategy of power titration guided by esophageal temperature monitoring does not sacrifice efficacy for safety.

**Alternative esophageal protective strategies:**

Alternative strategies described to avoid esophageal injury during AF ablation have included visualization of the esophagus with an enteral feeding tube, barium paste or electroanatomic mapping (19, 20), cooling of the esophagus to counter RF ablation-associated increases in esophageal temperature (21), and using cryoablation rather than radiofrequency energy (22). However, the effectiveness of these approaches on minimizing esophageal injury has not been thoroughly studied.

**Study Limitations:**
Our study has several limitations. First, this was an observational, non-randomized study and hence unmeasured confounding factors may be present and not be accounted for. Second, the sample size was small and unbalanced between the two groups thereby reducing the statistical power to ascertain the role of additional clinical and procedural factors (such as the use of general anesthesia) in the development of esophageal injury. However, this is the largest series of its kind assessing the use of LET during AF ablation as well as systematically evaluating for esophageal injury post ablation. Moreover, despite the small sample size, our results are statistically significant. Third, the end point of visible esophageal mucosal injury may result in an underestimation of true incidence of esophageal injury, which may be microscopic (12) or limited to the muscular layer (8, 12). Estimating peri-esophageal and muscular injury to the esophagus can only be adequately performed at autopsy which is not feasible for a human study of this nature. In addition, we believe that the outcome of interest (i.e. visible endoscopic esophageal injury) is clinically relevant. Fourth, the distance between the left atria and the esophagus was not accounted for in this analysis. While total tissue thickness between the esophagus and LA is an important factor determining esophageal injury (15), CT analyses have suggested an intimate relationship of the posterior LA and esophagus in virtually all patients (23). Moreover, adjusting for patient BMI, did not result in any additional protection from esophageal ulceration.

The strengths of this study include its size (which is the largest study of its kind to date), complete follow-up, the simple intervention examined, and clinically relevant endpoint reported.

**Clinical Implications:**
Although limiting RF power titration and ablation duration in response to esophageal temperature \( \geq 38.5^\circ C \) does not eliminate AF ablation-associated esophageal injury, these data suggest that it may be associated with reduced esophageal injury. As the frequency of LA-eso fistula is \(~0.1\%\), it would be extremely difficult to prove that this strategy reduces this complication; however, the reduction of collateral damage to the esophagus remains significant.

**Conclusion:**

These data demonstrates an association between esophageal temperature monitoring and a reduction in esophageal injury during AF ablation and is suggestive of a potential role for LET monitoring during AF ablation. Further studies are needed to confirm these findings as this intervention may be beneficial during AF ablation.
References:


Acknowledgements:

We would like to thank Steve K. Singh, MSc, MD for his assistance with statistical analysis of the data.

Funding sources:

Dr. S. M. Singh is a recipient of a Detweiler Traveling Fellowship from the Royal College of Physicians and Surgeons of Canada, Ottawa, Ontario, Canada.

Disclosures:

The authors do not have any conflicts of interest to disclose.

This work was presented in part at the 2008 Annual Sessions of the Heart Rhythm Society, San Francisco, CA, May 15–17, 2008, and published in abstract form (Heart Rhythm. 2008;5:S15).
Table 1: Univariate analysis comparing patients with and without luminal esophageal temperature (LET) monitoring.

Table 1: Abbreviations

SD = standard deviation, % = percent, AF = atrial fibrillation, LA = left atrial, mm= millimeters, AAD = anti-arrhythmic drugs, ASA = aspirin, PPI = proton pump inhibitor, H2 = Histamine 2 receptor, CT = computed tomography, MRI = magnetic resonance imaging.
### Esophageal injury during AF ablation

<table>
<thead>
<tr>
<th></th>
<th>LET Monitoring (N=67)</th>
<th>No LET Monitoring (N=14)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic information</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
<td>57±11</td>
<td>61±11</td>
<td>0.2</td>
</tr>
<tr>
<td>Male (%)</td>
<td>70</td>
<td>86</td>
<td>0.2</td>
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<tr>
<td>Body Mass Index</td>
<td>31±6</td>
<td>28±3</td>
<td>0.05</td>
</tr>
<tr>
<td>History of gastro-esophageal reflux disease (%)</td>
<td>9</td>
<td>14</td>
<td>0.62</td>
</tr>
<tr>
<td><strong>Disease characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Paroxysmal AF(%)</td>
<td>42</td>
<td>50</td>
<td>0.6</td>
</tr>
<tr>
<td>Duration of AF in years ( mean ± SD)</td>
<td>5±4</td>
<td>4±4</td>
<td>0.5</td>
</tr>
<tr>
<td>Structurally normal heart (%)</td>
<td>66</td>
<td>64</td>
<td>0.7</td>
</tr>
<tr>
<td>Ejection fraction (%, mean ± SD)</td>
<td>60±9</td>
<td>61±7</td>
<td>0.8</td>
</tr>
<tr>
<td>LA size (mm, mean ± SD)</td>
<td>44±9</td>
<td>42±5</td>
<td>0.3</td>
</tr>
<tr>
<td>Redo AF ablation (%)</td>
<td>21</td>
<td>14</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Medication use</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current number of AAD</td>
<td>1.6±0.8</td>
<td>2.1±0.8</td>
<td>0.02</td>
</tr>
<tr>
<td>ASA (%)</td>
<td>33</td>
<td>36</td>
<td>0.8</td>
</tr>
<tr>
<td>PPI or H2-antagonist (%)</td>
<td>21</td>
<td>14</td>
<td>0.8</td>
</tr>
<tr>
<td><strong>Procedural characteristics</strong></td>
<td></td>
<td></td>
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<tr>
<td>General anaesthesia (%)</td>
<td>13</td>
<td>43</td>
<td>0.01</td>
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<tr>
<td>Pre-procedural trans-esophageal echocardiography (%)</td>
<td>15</td>
<td>14</td>
<td>1.0</td>
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<tr>
<td>Intracardiac echocardiography (%)</td>
<td>93</td>
<td>93</td>
<td>0.9</td>
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<tr>
<td>Pre-procedure CT or MRI (%)</td>
<td>97</td>
<td>100</td>
<td>0.7</td>
</tr>
<tr>
<td>Duration of RF ablation (seconds, mean ± SD)</td>
<td>3530±1420</td>
<td>4030±2240</td>
<td>0.3</td>
</tr>
<tr>
<td><strong>Post procedure complications</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Esophageal ulcer (%)</td>
<td>6% (4/67)</td>
<td>36% (5/14)</td>
<td>0.007</td>
</tr>
<tr>
<td>Pericarditis / Pericardial Effusion (%)</td>
<td>9</td>
<td>0</td>
<td>1.0</td>
</tr>
<tr>
<td>AF recurrence at 3 months (%)</td>
<td>31</td>
<td>43</td>
<td>0.5</td>
</tr>
</tbody>
</table>
Figure 1: Location of luminal esophageal temperature probe in relation to ablation catheter.

ICE = intra-cardiac echocardiography catheter, LET = luminal esophageal temperature probe, CS = coronary sinus catheter, QUAD = reference quadrapolar catheter placed in the coronary sinus for NavX (St. Jude Medical), ABL = ablation catheter, LASSO = 20mm Lasso catheter (St. Jude Medical), LSPV = left superior pulmonary vein.
Figure 2: Esophageal ulceration in patients with luminal esophageal temperature (LET) monitoring.
Figure 3: Esophageal ulceration in 4 of 5 patients without luminal esophageal temperature (LET) monitoring:

Note: images available for 4 of 5 patients. The fifth patient’s ulcer was located at 30cm from the incisors and 5-6mm in diameter.
Figure 4: Maximum luminal esophageal temperature recording (n=45 patients with documented luminal esophageal temperatures).

\[ ^\circ \text{C} \] – degrees Celsius
Figure 5: Number of elevated luminal esophageal temperature recordings ≥38.5°C in 45 patients with documented luminal esophageal temperatures. (Note: 13 patients did not have a maximum LET ≥38.5°C and thus have 0 LET ≥38.5°C)
Figure 6: Correlation between average power applied and luminal esophageal temperature for maximum esophageal temperature >38°C (136 temperature points in 45 patients)

r = correlation coefficient, P = p-value.
<table>
<thead>
<tr>
<th>Patient</th>
<th>A:</th>
<th>B:</th>
<th>C:</th>
<th>D:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Max. Temperature</td>
<td>36.5°C</td>
<td>39.2°C</td>
<td>39.6°C</td>
<td>40.6°C</td>
</tr>
<tr>
<td># of T &gt;38.5°C</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Location of ulcer</td>
<td>26cm from incisors</td>
<td>29cm from incisors</td>
<td>25-30cm from incisor</td>
<td>30-35cm from incisors</td>
</tr>
<tr>
<td>Lesion description</td>
<td>3 mm in diameter</td>
<td>3 mm in diameter with red spot on wall opposite to the ulcer</td>
<td>small ulceration</td>
<td>Patchy mucosal ulceration and erythema</td>
</tr>
<tr>
<td>Patient</td>
<td>A:</td>
<td>B:</td>
<td>C:</td>
<td>D:</td>
</tr>
<tr>
<td>---------</td>
<td>----</td>
<td>----</td>
<td>----</td>
<td>----</td>
</tr>
<tr>
<td>Location of ulcer</td>
<td>30cm from incisors</td>
<td>17-23cm from incisors</td>
<td>35cm from incisors</td>
<td>30cm from incisors</td>
</tr>
<tr>
<td>Lesion description</td>
<td>Linear superficial ulcer with white exudates</td>
<td>Linear ulcer</td>
<td>Linear ulcer</td>
<td>Linear ulcer</td>
</tr>
</tbody>
</table>
mean max. LET = 39.0 ± 1.4 °C

mean max. LET = 39.0 ± 1.8 °C
No Ulcer

Mean # of LET
≥ 38.5°C = 2.2 +/- 3.2

Ulcer

Mean # of LET
≥ 38.5°C = 1.8 +/- 1.7