CLINICAL COMPENDIUM
The HeartLight® Endoscopic Ablation System
Putting a New Level of PVI Precision Close at Hand

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Published results noted below may include references to both on-label and off-label usage of the HeartLight Endoscopic Ablation System.

INTRODUCTION
The HeartLight System has been successfully used in more than 4,500 patients and featured in more than 80 peer-reviewed publications and abstracts. The clinical data demonstrates that:

- Efficacy of the HeartLight System compares well to other atrial fibrillation (AF) ablation modalities.
- The quality and durability of lesions produced by the HeartLight System are highly reproducible and well suited for establishing chronic pulmonary vein isolation (PVI).
- HeartLight allows for targeted and flexible energy titration strategies that accommodate significant variability in pulmonary vein (PV) tissue thickness.
- HeartLight is able to address wide-ranging PV variant anatomies, allowing for high rates of PV isolation without separate touch ups required.
- HeartLight represents a new paradigm in ablation of cardiac arrhythmias as it enables direct visualization and titratable laser energy on a universal, compliant balloon platform.

COMPARATIVE STUDIES
Efficacy of the HeartLight System compares well to other atrial fibrillation (AF) ablation modalities.

Pulmonary Vein Isolation Using the Visually Guided Laser Balloon: A Prospective, Multicenter and Randomized Comparison to Standard Radiofrequency Ablation

- In this study, 353 patients with a history of paroxysmal AF (PAF) (178 HeartLight, 175 Irrigated Radiofrequency [RF]) were randomized across 19 highly experienced RF clinical sites.
- Efficacy was defined as freedom from: documented symptomatic AF, ablation-induced LA flutter or atrial tachycardia, failure to isolate all PVs, use of any anti-arrhythmic drug or additional intervention for AF was assessed through 12 months along with adverse events.
- Despite minimal prior experience, the efficacy and safety with HeartLight proved to be noninferior (similar) to RF. Efficacy rates were 61.1% for HeartLight and 61.7% for RF. Primary adverse event rate was 11.8% for HeartLight and 14.5% for RF.
- HeartLight demonstrated a statistically significant lower rate of reconnection in comparison to RF.
- When analyzing results of physicians who had performed a minimum of 15 procedures, HeartLight outcomes start to appear even more favorable.
- The results also compare well to the US Pivotal Trial with the CryoBalloon, which demonstrated 1-year efficacy of 49.7% in the STOP AF study.

Key Takeaway
In a randomized clinical trial, HeartLight demonstrated excellent efficacy and safety despite a significant difference in physician experience with the two modalities under evaluation.
Comparison of Balloon Catheter Ablation Technologies for Pulmonary Vein Isolation: The Laser Versus Cryo Study

- In this study, 140 patients with a history of PAF were randomized to treatment with HeartLight (Gen 1) or CryoBalloon (Gen 1) in a 1:1 fashion and followed for 12 months in a single-center evaluation.
- Efficacy was defined as documented AF recurrence freedom from documented AF recurrence ≥ 30 seconds between 90 and 365 days post procedure.
- At 12 months, 73% of the HeartLight group achieved the efficacy endpoint compared to 63% of the CryoBalloon group. The HeartLight group demonstrated a significantly lower fluoroscopy time (15 minutes) versus 21 minutes with the CryoBalloon. Procedural times were similar, 144 minutes with HeartLight compared to 136 minutes with the CryoBalloon.

Key Takeaway
In a randomized clinical trial as compared with the CryoBalloon, the HeartLight System demonstrated excellent safety and efficacy with lower fluoroscopy times.

LONG-TERM RESULTS – SINGLE CENTER EVALUATIONS
Long-term results with the HeartLight System have shown consistently to be durable.

Visually guided laser ablation: a single-centre long-term experience

- In this study, 194 patients with a history of PAF or persistent AF (PsAF) were treated with HeartLight and followed for up to four (4) years to assess rates of freedom from AF.
- Recurrence of AF was defined as any documented AF episode of greater than 30 seconds.
- Follow-up demonstrated high and durable rates of AF freedom with 82% PAF patients free of AF at one year, 76% free at two years, 76% free at three years and 75% free at four years.
- Patients with PsAF demonstrated 75% freedom from AF at one year. Additional follow up on PsAF patients was not yet available as these patients were addressed much later in this clinical evaluation.
- Over the course of the site’s experience, both procedure and fluoroscopy times improved substantially with mean procedure times of 150 minutes and mean fluoroscopy times of 13 minutes in its most recent cohort of patients.

Key Takeaway
In a large consecutive series of patients with long-term follow, HeartLight demonstrated impressive long-term results out to four years.

Electrical Isolation of Pulmonary Veins Using Laser Catheter in the Treatment of Paroxysmal and Persistent Atrial Fibrillation. One-year Results

- In this study, 71 patients with a history of PAF or PsAF were treated with HeartLight and followed for one year to assess rates of freedom from AF.
- Rates of AF freedom were 88% and 70% in the PAF and PsAF groups respectively with a mean follow up of 420 days.
- Isolation was possible in 275 of 278 pulmonary veins (99%).
- Procedure and fluoroscopy times improved through the course of the site’s experience. Mean procedure time was 145 minutes and mean fluoroscopy time was 24 minutes in the final cohort of patients.
- Authors believe that positive results may be attributed to the routine use of higher energy in areas at higher risk of electrical reconnection, particularly at the ridge between the left atrial appendage and the left pulmonary vein.

Key Takeaway
In this single center initial series of patients with a mean follow up of 420 days, HeartLight demonstrated positive results with 88% of PAF patients remaining AF free.
LESION QUALITY
The quality and durability of lesions produced by the HeartLight System are highly reproducible and well suited for establishing chronic PVI.

Unmasking the Dormant Pulmonary Vein Conduction with Adenosine Administration after Pulmonary Vein Isolation with Laser Energy

- This study assessed the quality of lesion creation with HeartLight through application of adenosine in 26 symptomatic paroxysmal AF patients.
- 97% of ablated PVs were acutely isolated followed by adenosine administration to assess reconnection induction. Only 6 PVs (6.7%) could be induced into reconnection by the adenosine administration.
- Studies of PV conduction recovery with adenosine provocation using conventional RF ablation catheters consistently report results of PV recovery that are approximately 4 times higher than HeartLight in this study.
- At 6 months, 81% of patients remained arrhythmia free.
- PVs that demonstrated reconnection during adenosine provocation had worse PV occlusion and a lower amount of energy delivered.

**Key Takeaway**
HeartLight results in very effective acute lesion formation that demonstrates durability even under adenosine provocation.

The Durability of Pulmonary Vein Isolation Using the Visually Guided Laser Balloon Catheter: Multicenter Results of Pulmonary Vein Remapping Studies

- This study consisted of a multicenter evaluation of HeartLight’s PV isolation durability. 56 patients were evaluated with PVs acutely and chronically assessed.
- 98% (202 of 206) PVs were acutely isolated and 86% (162 of 189) PVs remained isolated during remapping at an average of 105 days in the 52 patients who underwent remapping. As part of the remapping procedure, un-isolated PVs could be re-isolated.
- Using powers higher than 5.5W / 30 seconds was associated with a lower reconnection rate during follow-up.
- For those operators who had performed at least 10 procedures, the rate of persistent PVs isolated at the time of remapping was 89.4%.
- The drug-free rate of freedom from AF or atrial tachycardia in the 52 patients that underwent remapping at an average of 12 months was 71.2%.

**Key Takeaway**
In this multicenter PV isolation remapping study, HeartLight demonstrated impressive lesion durability and AF freedom at one year.

MRI Evaluation of Radiofrequency, Cryothermal, and Laser Left Atrial Lesion Formation in Patients with Atrial Fibrillation

- This study consisted of an assessment of seventeen (17) AF patients who underwent PVI using Laser (n=5), RF (n=7), or Cryo (n=5) with a goal of comparing baseline to post-procedural change in left atrial (LA) scar burden.
- Assessments were made prior to, at 24 hours and at 3 months after PVI using Late gadolinium enhancement magnetic resonance imaging (LGE-MRI).
- While differences did not achieve statistical significance (low sample size), Laser demonstrated numerically a lower scar burden than RF and Cryo.
- Qualitatively, laser energy caused focused, discrete lesions compared to the diffuse lesion sets associated with RF and Cryo ablation as seen on three months images attained in the laser group.

**Key Takeaway**
Laser energy caused focused, discrete lesions at three months compared to the diffuse lesion sets associated with RF and Cryo ablation.
Visual Balloon-Guided Point-by-Point Ablation Reliable, Reproducible, and Persistent Pulmonary Vein Isolation

- This study consisted two components: (1) an acute porcine assessment with 15 subjects and (2) a single-center clinical feasibility evaluation with 27 PAF patients.
- 97% (29 of 30) of PVs in animal subjects were found to be electrically isolated in acute and chronic phases. Histologically, lesions were shown to be circumferential in all cases (120 of 120 PV sections) and consistently transmural (116 of 120 sections).
- Mean atrial wall thickness was 3.0 mm ± 1.0 in the acute porcine evaluation and 5.1 mm ± 0.9 in the chronic evaluation.
- In the separate, second phase clinical evaluation, all PVs were able to be isolated with the HeartLight System and at 3 months 90% remained electrically isolated.

**Key Takeaway**
HeartLight produces lesion sets that are reproducibly contiguous, circumferential, transmural and durable, supported both by animal and human evaluation.

Pulmonary Vein Isolation Using a Compliant Endoscopic Laser Balloon Ablation System in a Swine Model

- This study evaluated HeartLight PVI ablation in comparison to standard RF ablation in a swine model. Eight HeartLight subjects were treated and two RF subjects were treated.
- Evaluation of a lesion set was based upon a quantitative histopathologic assessment, incorporating a composite determination of circumferential and transmural lesion creation.
- Acute isolation was achieved in all subjects, although there was one audible steam pop in one of the RF subjects.
- Quantitative histopathologic assessment was completed approximately 30 days after initial treatment. Results showed that lesions with HeartLight were a composite of 99.9% circumferential and transmural in comparison to a composite score of 93.1% with RF.
- While the RF lesions were shown to be 100% circumferential, they were not transmural in all sections.

**Key Takeaway**
HeartLight produces lesion sets that are reproducibly circumferential and transmural with histologic confirmation.

**DOsing / energy titration**
HeartLight allows for targeted and flexible energy titration strategies that accommodate significant variability in pulmonary vein (PV) tissue thickness.

The influence of varying energy settings on efficacy and safety of endoscopic pulmonary vein isolation

- This study assessed the influence of varying energy settings on the outcomes of PVI with the HeartLight System.
- A total of 30 patients were included in the assessment (10 in each of three groups). Group A was treated with 5.5 W and 7.0 W, Group B with 7.0 W and 8.5 W and Group C with 8.5 W and 10.0 W along the posterior and anterior portion of each PV, respectively.
- The rate of PVI was significantly higher in group C than in group A (p=.025) and group B (p=.045). There was no difference in the detection of esophageal thermal lesions.
- Authors concluded that the use of higher energy settings increases the acute efficacy of HeartLight without compromising safety.

**Key Takeaway**
Study concluded that high dose laser ablation has superior outcomes.
Energy titration strategies with the endoscopic ablation system: lessons from the high-dose vs. low-dose laser ablation study

- This study assessed the effects of low-dose and high-dose ablation on acute and chronic success in patients with AF with the HeartLight System.
- Sixty (60) patients were divided into two groups (30 patients each). The low dose (LD) group was treated with 5.5 – 8.5 W and the high dose (HD) group was treated with more than 8.5 W.
- Acute and chronic efficacy was shown to be higher in the HD group.
- High dose laser balloon ablation allowed for an acute PVI rate of 89% and a chronic AF-free rate of 83% after a single procedure.

**Key Takeaway**
High dose laser ablation has superior outcomes compared with low dose laser ablation and can be enabled by suitable tissue contact.

**LEARNING CURVE STUDIES**
New HeartLight operators consistently demonstrate the ability to become highly proficient with the system through a short learning curve.

**How to Learn Pulmonary Vein Isolation with a Novel Ablation Device: Learning Curve Effects Using the Endoscopic Ablation System**

- In this study, 150 patients with a history of PAF or PsAF were treated with HeartLight with their results analyzed in sequential tertiles of 50 patients in each cohort.
- Users were able to have positive outcomes from the beginning with the technology, demonstrating 96% of all PVs isolated acutely in the first tertile.
- Learning curve effects were also demonstrated with numeric improvements seen in procedure times, fluoroscopy times, adverse event rates and AF free rates at 12 months.
- In the third tertile, procedure times averaged 123 minutes, fluoroscopy times: 12 minutes, AF-free rate of 86% at 12 months and zero complications.

**Key Takeaway**
New operators can obtain very positive outcomes initially and experience improvements in procedural efficiency and outcomes as they gain more experience.

**Visually Guided Sequential Pulmonary Vein Isolation: Insights into Techniques and Predictors of Acute Success**

- In this study, 35 patients with a history of PAF or persistent AF were treated with HeartLight and results analyzed to understand predictors of acute isolation.
- Results showed that both degree of PV occlusion (higher occlusion score correlated with higher likelihood of isolation) as well as the number of catheter repositionings (less repositioning correlated with higher likelihood of isolation) were predictors of acute isolation.
- Conduction gaps were detected at sites were there was suboptimal vessel occlusion as well as esophageal temperature elevations.
- Learning curve effects were also demonstrated with a statistically significant improvement in procedure time demonstrated between the first 12 cases (175 minutes) and the last 12 cases (138 minutes).

**Key Takeaway**
New operators can become facile with the HeartLight system quickly, reducing procedure times and potentially improving PV occlusion and catheter repositioning, which could be drivers of better outcomes.
ADDRESSING ANATOMIC VARIABILITY
HeartLight is able to address highly variable wide-ranging pulmonary vein (PV) variant anatomies, allowing for high rates of PV isolation without separate touch ups required.

Impact of pulmonary vein anatomy assessed by cardiac magnetic resonance imaging on endoscopic pulmonary vein isolation in consecutive patients
- In this study, the impact of variant PV anatomy on outcomes with the HeartLight System was evaluated in 51 patients with a history of paroxysmal AF.
- A total of 195 PVs were assessed by pre-interventional cardiac magnetic resonance imaging (CMRI).
- PV anatomy was found to be widely variable in terms of: number of PVs; separate vs common anatomy; PV diameter; round vs oval PV shape; level of first PV branching; and the level of insertion of the right inferior PV into the left atrium.
- PV isolation was achieved exclusively with the HeartLight System in 192 of 195 (98%) PVs. Isolation was achieved irrespective of variable PV anatomy.

Key Takeaway
Study validates the HeartLight system’s universal balloon design, demonstrating that a single balloon can be used in highly variable PV anatomies, achieving a very high rate of isolation without the requirement of additional ‘touch ups’.

Anatomical Predictors for Successful Pulmonary Vein Isolation using Balloon-Based Ablation Technologies
- Authors evaluated the correlation between pulmonary vein (PV) anatomy and acute and long-term success with HeartLight (Gen 1) and CryoBalloon (Gen 2).
- 100 consecutive patients with paroxysmal AF were analyzed in two equal groups (50 patients each) – and received either HeartLight or CryoBalloon ablation.
- Using multi-detector CT imaging, variant anatomy was discovered in 40% of the HeartLight group and 32% of the CryoBalloon ablation group.
- Peri-procedurally 194 of 206 PVs (94%) were successfully isolated with HeartLight alone and 193 of 199 PVs (97%) were successfully isolated with CryoBalloon alone.
- At 12 month follow-up, 84 percent of HeartLight patients remained AF free compared to 76% of CryoBalloon ablation patients.
- Of patients who presented with AF occurrence 38 percent treated with HeartLight were found to have PV conduction gaps and 52 percent treated with Cryoablation were found to have conduction gaps.

Key Takeaway
Study shows vast majority of PVs can be addressed with HeartLight balloon technology with positive long-term AF free results.
The article further highlights procedural considerations, preclinical studies and initial clinical evaluations prior to randomized studies.

The registry demonstrates an acute PV isolation rate of 98.1%, an average procedure time of 133 minutes and an average fluoroscopy time of 25 minutes.

**Key Takeaway**
HeartLight repeatedly demonstrates positive clinical outcomes based on a unique feature set with improvements seen over a short learning curve.

### Endoscopic Ablation Systems


- This review article provides an in-depth description of the HeartLight technology, its components and how the system works functionally.
- The article further highlights procedural considerations, preclinical studies and initial clinical evaluations prior to randomized studies.
- The article also comments on ways in which the HeartLight System might undergo further development.

**Key Takeaway**
The HeartLight system offers unique, novel features, which resulted in positive outcomes during its initial clinical evaluation.