Esophageal Deviation in Atrial Fibrillation Ablation

A Prospective Single-Arm Study

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July 18, 2019

Version 14.0

NCT#: 03261973

Table of Contents:

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2 ABSTRACT

Catheter ablation with pulmonary vein (PV) isolation is a commonly performed strategy employed for the treatment of atrial fibrillation (AF). However, ablation in the posterior wall of the left atrium can cause thermal injury to the esophagus. Thermal injury is very common and occurs in up to 40% of AF ablations per some studies. When significant thermal injury to the esophagus occurs, two significant complications can arise: 1) the formation of an atrio-esophageal fistula, and 2) gastrointestinal dysmotility. While the occurrence of fistula is rare, it is a very important complication since it is often fatal. Currently luminal esophageal temperature monitoring is the most commonly employed modality to prevent such injury. However, there are

limitations to its use, and atrio-esophageal fistulas continue to be a major problem in AF ablation even when using esophageal temperature monitoring. Esophageal deviation using either a Transesophageal echocardiogram (TEE) or Esophagogastroduodenoscopy (EGD) probe has been described in the literature, but the effectiveness and practicality of these techniques are suboptimal, and have therefore precluded their use in routine clinical practice. Recently, esophageal deviation using off-the-shelf equipment (a soft thoracic tube and endotracheal stylet) was tested in the randomized double-blind multicenter study “Deviating the Esophagus in Atrial Fibrillation Ablation (DEVIATE-AF)”. In that study the standard practice (i.e., use of luminal esophageal temperature monitoring) was compared to esophageal deviation using off-the-shelf equipment. The results were very encouraging showing that esophageal deviation allowed for significant reductions in esophageal temperature and proportion of premature ablation terminations. Importantly, esophageal deviation allowed the isolation all PVs in the treatment group, which was not the case in the control group. One major limitation in the DEVIATE-AF trial was that off-the-shelf equipment tool was challenging to use. The aim of the Esophageal Deviation in Atrial Fibrillation Ablation study is to test the feasibility and safety of moving the esophagus using a specialized esophageal deviation tool (DV8, Manual Surgical Sciences, Minneapolis, MN).

3. STUDY OBJECTIVE

Catheter ablation is a commonly performed procedure employed for the treatment of drug resistant atrial fibrillation (AF). For paroxysmal AF, the ablation typically involves pulmonary vein (PV) isolation, and in cases of persistent AF often involves additional linear ablation lesions, ablation of sites of complex fractionated atrial electrograms (CFE), and ablation of drivers of AF. However, when ablation lesions are placed in the posterior left atrial (LA) wall during the above-mentioned steps, these lesions can cause thermal injury to the adjacent esophagus. This can result in 1) esophageal erosions and/or ulcers – which can culminate in fatal atrio-esophageal fistula formation, and 2) gastrointestinal dysmotility such as gastroparesis as a result of damage to the peri-esophageal vagal plexus.

To minimize the chance of these complications, electrophysiologists employ different strategies to minimize esophageal injury. A widely accepted and recommended strategy is to deploy a transnasal or transoral temperature sensing probe into the esophagus to detect esophageal heating during ablation; this allows the physician to either modulate the level of energy used or to terminate any individual ablation lesion that results is inappropriate heating of the esophagus. While this approach has been shown to reduce esophageal injury, it is clear that this is an imperfect tool as evidenced by the reporting of both ulcerations and fistula formation in patients with no detectable temperature rise. In addition, even if the detection of esophageal temperature rise is identifiable in all cases, this still necessitates that the operator stop ablation and wait for the temperature to passively cool before applying another ablation lesion. This adversely impacts procedure time, and (by allowing time for tissue edema to form between lesion applications) might even impact on the long-term durability of the PV isolating lesion set.

Recently, the randomized double-blind multicenter study “Deviating the Esophagus in Atrial Fibrillation Ablation (DEVIATE-AF) demonstrated that the esophagus can be successfully displaced in patients undergoing AF ablation using off-the-shelf equipment (a soft thoracic tube and endotracheal stylet. One major limitation in the DEVIATE-AF trial was that off-the-shelf equipment tool was challenging to use. The aim of the Esophageal Deviation in Atrial Fibrillation Ablation study is to test the feasibility and safety of moving the esophagus using a specialized esophageal deviation tool (DV8, Manual Surgical Sciences, Minneapolis, MN).

4 INTRODUCTION, RATIONALE, PRELIMINARY DATA

Introduction and Rationale:

Role of catheter ablation: Atrial fibrillation (AF) is a disorder affecting more than 3 million Americans. The likelihood of developing AF increases with age. Three to five percent of people over 65 have AF. Given the aging population, it is important that effective therapeutic strategies are available. Non-pharmacologic approaches to maintaining sinus rhythm with catheter ablation offer an alternative approach for control of AF and avoid the toxicity of anti-arrhythmic drugs. Several randomized controlled trials have demonstrated the superiority of catheter ablation over medical treatment for AF, in terms of maintenance of sinus rhythm and improved symptoms (1,2,3,4,5). PV isolation is a procedure that involves placing circumferential and importantly transmural lesions around all the PVs to electrically isolate the veins from the rest of the left atrium (LA). This procedure alone is successful for 70–90% of patients with paroxysmal AF (6), the effectiveness largely depending on the contiguity and transmurality of these circumferential lesions around the PV. Catheter ablation of persistent AF on the other hand usually involves a hybrid strategy, incorporating PV isolation with further ablation, typically in the form of linear lesions, complex fractionated electrogram ablation, and/or ablation of drivers of AF that need to be performed in various locations in the LA including the posterior wall of the LA (7,8) which lies in close proximity to the esophagus.

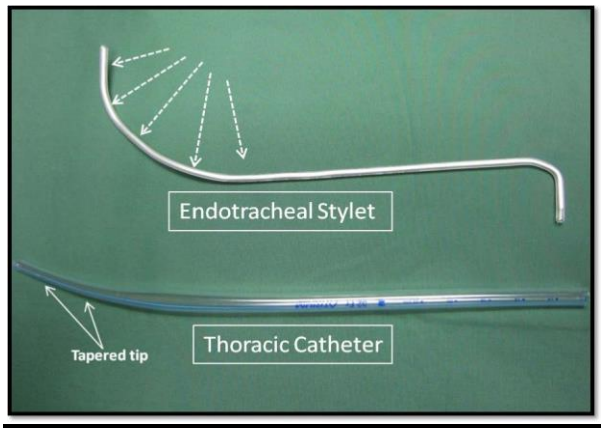
Gastro-esophageal injury: While the overall complication rates of catheter ablation of AF have decreased (major complication rates in large centers are in the 2-3% range) with advancements in technique and technology of catheter ablation, the threat of gastro-esophageal damage due to thermal injury from ablation remains. In fact, the risk of atrio-esophageal fistula formation remains one of the most dreaded complications of catheter based AF ablation today.

Thermal injury during AF ablation can occur in the form of esophageal erythema, hemorrhage, erosions, ulceration, gastro-esophageal motility disorders or rarely atrio-esophageal fistulas. These occur consequent to the use of thermal based ablation applied to the posterior wall that often lies immediately adjacent to the esophagus (9,10). It is thought that this thermal energy extends beyond the posterior LA wall and reaches the adjacent esophagus causing damage that manifests as described above. In patients undergoing radiofrequency (the most common thermal based energy source) catheter ablation of AF, the reported incidence of any esophageal injury varies from 2.2% - 48%. The incidence of the often catastrophic atrio-esophageal fistula however, is much lower at around 0.04% (11). Typically, the clinical presentation of such fistulae occurs late after the procedure (usually within the first 2 weeks) (9,10). The symptoms are usually nonspecific, including fever, neurological abnormalities, gastrointestinal bleeding, and sepsis. This condition is often fatal. The mechanism of esophageal injury is thought to be to thermal injury (9,10,12,13). The degree of variation in the reported incidence of esophageal damage (2.2- 48%) is likely accounted for by differences in the frequency of use of esophageal protection (e.g. - temperature monitoring probe), use of general anesthesia versus conscious sedation, magnitude of power, duration and contract force during ablation and finally the method of assessment of esophageal injury. An effective strategy to reduce gastro-esophageal injury is therefore of significant clinical importance.

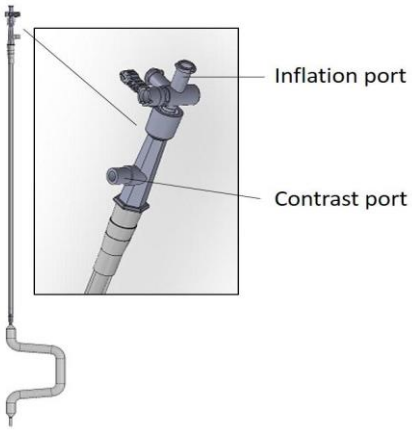
Esophageal protection strategies: Several strategies have been described to help prevent or reduce gastro-esophageal injury during AF ablation. These include luminal esophageal temperature (LET) monitoring (14), determination of the anatomical relationship of the esophagus to the posterior LA with pre-procedural or real time imaging (15,16,17) and modulation of power and duration of radiofrequency lesions (18). The effectiveness of the above approaches, even when applied in combination, has failed to prevent atrio-esophageal fistula formation (17). Moreover, these strategies do not address the need for reduction of other forms of injury, such as gastroesophageal motility disorders that originate from injury of vagal nerves that surround the esophagus. In addition, LET monitoring focuses on the early detection of thermal injury, and both 1) invariably results in a pause in ablation while waiting for passive tissue cooling, and 2) often results in modification of the lesion sets, i.e., by directing the encircling lesions to be either more ostial or further midline in order to avoid temperature rises. Such modifications increase the risk of vein stenosis and the formation of 'gaps' that may reduce the long-term clinical success of the ablation procedure. Frequent premature lesion terminations and power reductions may also compromise chronic PV isolation rates, an endpoint critical to the long-term outcomes of AF ablation.

Autopsy studies (19) have shown that there is loose areolar tissue between the anterior wall of the esophagus and the parietal pericardium of the posterior left atrium. A post-mortem study (19) demonstrated that the esophagus relative to the posterior left atrium could be displaced up to 7 cm. Both these studies indicate that lateral esophageal displacement is a feasible strategy from an anatomic basis. Lateral mechanical displacement of the esophagus along the posterior LA as an esophageal protective strategy has been previously described using either an endoscope (20) or a TEE (21). Both these strategies had significant limitations. In the strategy using the endoscope, i) the actual deviation of the esophagus was unclear since concomitant contrast was not employed to differentiate esophageal deviation from esophageal tenting, ii) the esophagus could not be deviated in 2/12 patients, and most importantly, iii) the deviation could not be maintained in 7 patients to allow uninterrupted lesion delivery. This approach required the active participation of a gastroenterologist and the true extent of deviation achieved was unclear given the lack of barium contrast. On the other hand, in the strategy using the TEE probe, all 3 patients underwent successful displacement that was maintained during ablation, but this was not studied in a systematic fashion. Although thought-provoking, widespread application of these two techniques has not been realized in clinical practice due to attendant limitations. Over the past 2 years the randomized double-blind multicenter study "Deviating the Esophagus in Atrial Fibrillation Ablation (DEVIATE-AF) demonstrated that the esophagus can be successfully displaced in patients undergoing AF ablation using off-the-shelf equipment (a soft thoracic tube and endotracheal stylet) (Figure-1). The study randomized 69 patients and is still ongoing. Interim analysis revealed that esophageal deviation allowed for significant reductions in maximum esophageal temperature rises {1.1±0.7ºC vs 0.26±0.2 ºC, $p<0.0001$} and proportion of premature ablation terminations {38.8±0.3% vs 5.7%±0.1, $p<0.0001$}. Importantly, all PVs were not isolated in 2 controls due to temperature rises. In the deviation arm, total time and RF time for PV isolation was shorter, but did not reach statistical significance. There were challenges however related to the ease of deviation using the off-the-shelf tool, and it was concluded that the technique requires improvement.

Figure-1**:** Off-the-shelf tapered tip (solid arrows) thoracic catheter used for esophageal deviation. Adjacent to that is an endotracheal stylet with a distal curve (dashed arrows)



Because of the logistical difficulties attendant with the off-the-shelf tools and the obvious need that remains in terms of esophageal protection during AF ablation, we sought to evaluate the feasibility and safety of a strategy of mechanical esophageal deviation during AF ablation using specialized equipment (DV8 specialized esophageal retraction tool made by Manual Surgical Sciences, Minneapolis, MN) (Figure-2). **The device is commercially available in the US and is 510(k) exempt. (Regulation Number 878.4800, Registered Establishment Number is 3011596926)** Figure-2: DV 8 esophageal retractor.



The DV8 Retractor™ Esophageal Balloon (DV8 Retractor) is a non-sterile, single-use, disposable esophageal balloon retractor. It is deployed orally and inflated inside the esophagus. The retractor gently and effectively retracts the esophagus to create a stable operating field. The DV8 Retractor has a marker band located at the proximal waist and double marker bands located at the distal waist of the balloon, which are distinguishable from each other under fluoroscopic visualization. When the procedure is completed, the device is deflated and removed. Each balloon inflates to its stated diameter and length at 4-8ATM of pressure. The balloon diameter is ± 10% at the nominal pressure. The Rated Burst Pressure (RBP) is 16

atmospheres (ATM). The DV8 Retractor is designed with a silicone sleeve and balloon coupled to a fitting that can attach to a syringe with a pressure gauge. The DV8 Retractor also has a fitting that allows attachment of a syringe to inject contrast medium directly into the esophagus. The device is 61 cm in length and the balloon is 15 cm balloon length. When inflated, the balloon diameter is 14mm. The detailed steps for deployment are as follows:

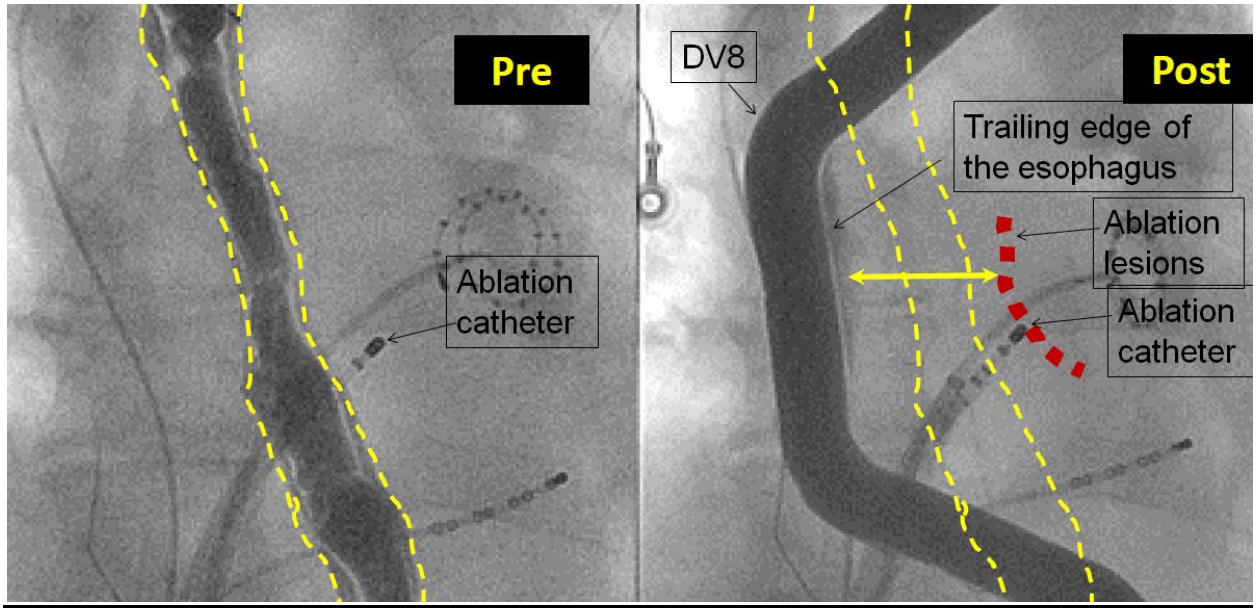
Insertion and Inflation:

- The DV8 Retractor Esophageal Balloon is removed from its package. The Inflation Syringe is filled with pressure gauge with an appropriately diluted (25-50%) contrast medium (Gastrografin).
- The Luer-tip Inflation Syringe is attached with pressure gauge into the DV8 Retractor balloon inflation stopcock.
- Lubricant is applied to the balloon and device shaft. The DV8 Retractor is directed into the esophagus using fluoroscopic guidance.
- The balloon is positioned in the appropriate location with the distal marker band at the level of the lower esophageal sphincter.
- The balloon is inflated with contrast medium with 4-8 ATM of pressure as indicated on the Inflation Syringe (Figure-3).

Deflation and Withdrawal:

- The balloon is deflated prior to withdrawing from the esophagus.
- The deflated DV8 Retractor Balloon is withdrawn from the esophagus using a smooth, gentle, steady motion.

Figure-3: X ray images of the DV8 retractor before and after inflation.



Preliminary data:

The esophagus was successfully displaced using the DV8 retractor in over 200 patients worldwide. Eleven cases have been performed at MGH. No complications have been reported with its use. In a cohort study at Mt. Sinai Medical Center in New York, 47 patients underwent esophageal deviation using the DV8 tool and were compared with 114 patients who underwent deviation using the off-the shelf stylet. All procedures were performed under general anesthesia. The extent of deviation, as measured by the distance between the trailing edge of the esophagus and the ablation points, was significantly larger with the DV8 tool (Figure-4). Moreover, the incidence of esophageal temperature rises was higher with the off-the-shelf technique compared to the DV8 retractor (Figure-5). Another preliminary study was conducted by the Mt-Sinai group in order to assess the optimal distance for esophageal movement that eliminates the chance of heating. It showed that if the esophagus is moved by an average of 2 cm from the ablation site, no significant heating occurs (Figure-6)

Figure-4: Comparison of the extent of deviation between the DV8 retractor and off-the-shelf stylet.

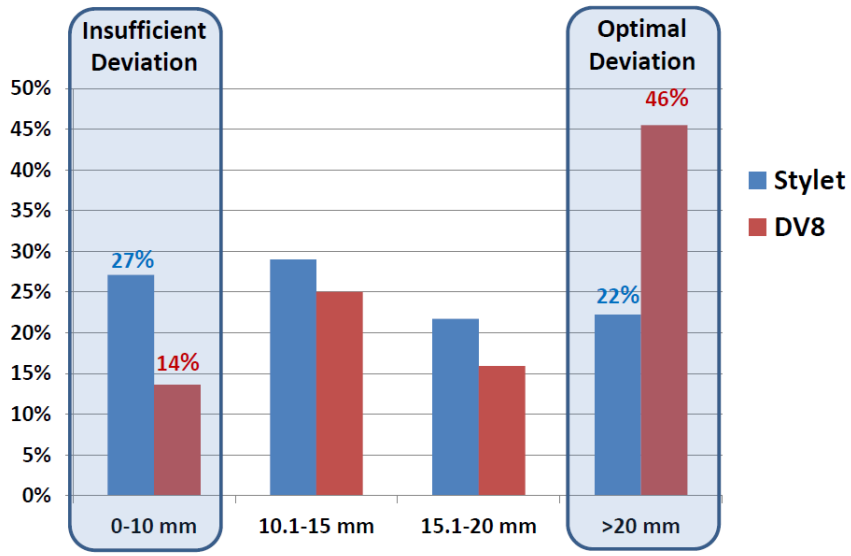


Figure-5: Comparison of the incidence of esophageal temperature rise between the DV8 retractor and the off-the-shelf stylet.

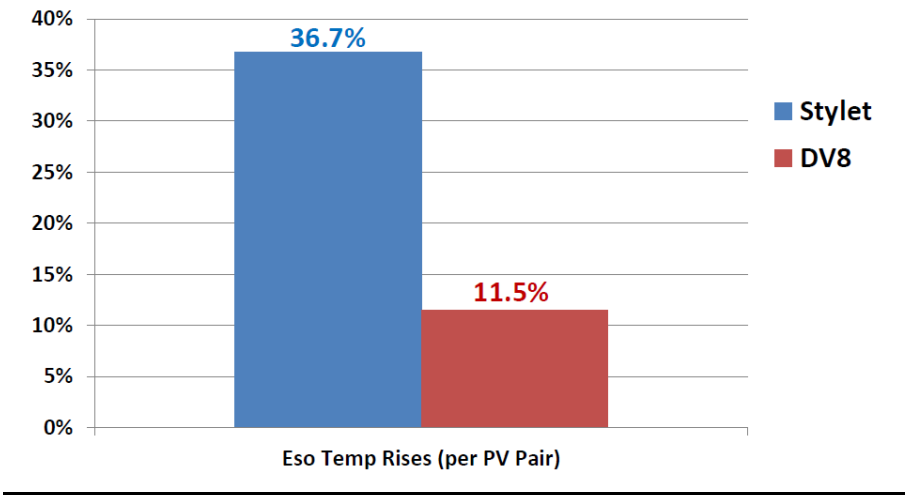
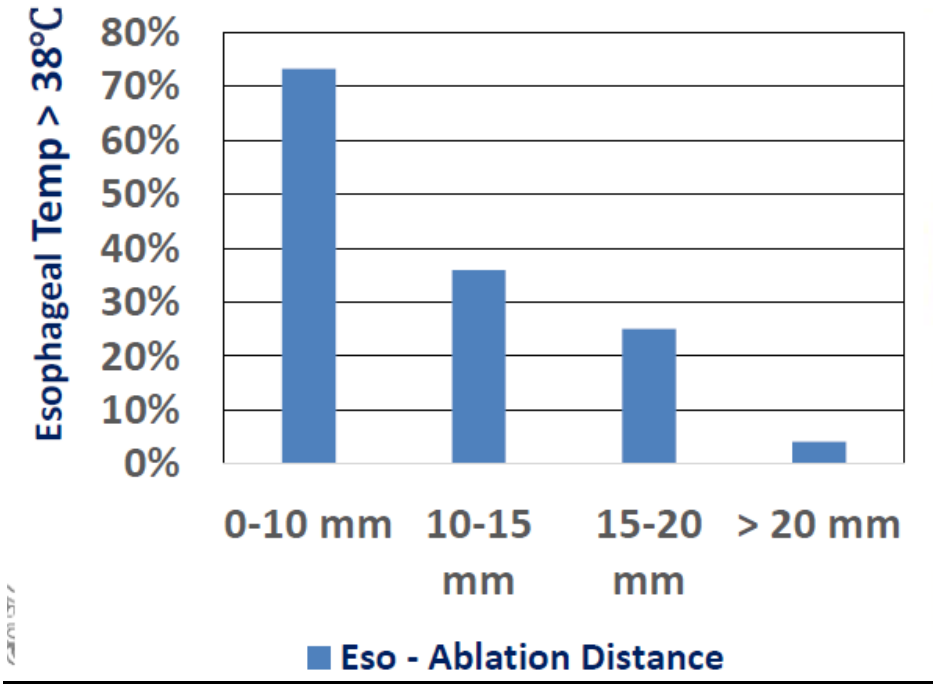


Figure-6: Incidence of esophageal temperature rise at different distances from the area of ablation.



These data demonstrate the feasibility and safety of the novel technique of esophageal deviation that facilitates uninterrupted energy delivery to the posterior wall during AF. It also demonstrated that the esophagus needs to be moved by an average of 2 cm in order for heating not to occur. Although the results have been very encouraging with respect to safety and efficacy, we believe that there is value in an additional study to prove the reproducibility of the findings.

We propose a prospective single-arm study to confirm the safety and feasibility of this novel deviation tool.

5 ENDPOINTS

5.1 PRIMARY CLINICAL ENDPOINT

The following primary endpoint will be assessed:

1) The extent of esophageal deviation as measured by the incidence of successfully moving the esophagus to achieve a minimum distance of 1 cm between the ablation line for the ipsilateral PV pairs and the trailing edge of the esophagus.

5.2 SECONDARY CLINICAL ENDPOINTS

The following secondary endpoints will be assessed:

1. The extent of esophageal deviation as measured by the incidence of successfully moving the esophagus by an average of 2 cm from the ablation line for the ipsilateral PV pairs.
2. The incidence of esophageal laceration as assessed by a Barium swallow study performed within 1-3 days of the procedure.
3. Incidence of PV reconnection at 30 min post-ablation
4. Fluoroscopy time
5. Procedure duration
6. Time from start of ablation to last ablation lesion for pulmonary vein isolation

The deviation distance was based on the preliminary study mentioned above, showing that if the esophagus is moved by an average of 2 cm, no significant heating occurs.

6 STUDY SUBJECTS

6.1 INCLUSION CRITERIA

A maximum of up to 64 patients will be enrolled in this prospective single-center single-arm study. Patients undergoing AF ablation (including paroxysmal and persistent AF) will be included in this study. Consistent with the current definitions, paroxysmal AF are episodes that will self-terminate in less than 24 hours. Persistent AF, is defined as ≥1 documented AF lasting >1week in duration or lasting less than 7 days but requiring electrical or pharmacological cardioversion to sinus rhythm.

- Age >18 - Age < 80 yr
- Documentation of atrial fibrillation (AF)
- General anesthesia
- All patients must understand and adhere to the requirements of the study and be willing to comply with the post study follow-up requirements.

6.2 EXCLUSION CRITERIA

- Any reversible cause of AF (post-surgery, thyroid disorder, etc.)
- INR > 4.0 at the time of the procedure
- H/o of severe esophageal ulcers, strictures, varices, bleeding, laceration or perforation, esophagitis
- Severe GERD
- H/o esophageal surgery or any esophageal banding or cautery
- History of chest radiation
- Significant abnormality on Swallowing Impairment Score
- Mental impairment precluding signing consent or completing follow up
- Patients with any other significant uncontrolled or unstable medical condition
- Women who are known to be pregnant or have had a positive β-HCG test within 7 days prior to procedure
- Presence of left atrial thrombus

7 ANALYTICAL PLAN

7.1 SAMPLE SIZE CALCULATION

A single arm design is proposed. The primary endpoint will be the incidence of successfully moving the esophagus by a minimum of 1 cm from the ablation line for the ipsilateral PV pairs. We believe that 64 patients need to be enrolled in this single-arm study to achieve this endpoint. With 64 enrolled patients in this single-arm trial, if the true success rate is at least 90% then the statistical power will be 83% to detect such a performance by ruling out a poor success rate of <=75% using exact Binomial test at a two-sided 5% type-1 error rate. The test will reject the null hypothesis H0: Success Rate <=75% in favor of the alternative hypothesis H1: Success Rate>=95% if there are seven or fewer failures among 64 patients.

Power	N	Proportion Given H0 (P0)	Proportion Given H1 (P1)	Target Alpha	Actual Alpha	Beta	Reject H0 If ≤ R | ≥ R
0.8321	64	0.7500	0.9000	0.0500	0.0410	0.01679	33 I 47

7.2 STOPPING CRITERIA

STOPPING CRITERIA

We propose as a stopping criterion the occurrence of 1 case or more of esophageal laceration based on the finding of the Barium Swallow.

8 PATIENT ENROLLMENT AND WITHDRAWAL

Patients meeting the study inclusion criteria will be identified in the outpatient setting by one of the study staff.

The study will typically be described (including the risks and benefits) during the clinic visit. Consent will typically be obtained at the time of the initial assessment if it is clear that the patient truly understands the nature of the study. Alternatively, the patient will be allowed to take a copy of the consent form home to contemplate whether they would like to be enrolled in the study. Only patients who voluntarily provide consent will be included in this study. Consent will be obtained prior to undergoing the ablation procedure. Patients will be able to withdraw from the study at any point without compromising their medical care.

Since there is minimal additional follow-up beyond routine clinical care in this study, we expect to achieve > 95% rate of follow-up.

9 STUDY PROCEDURES

All aspects of the study (including pre- and post- care) are currently undertaken during the care of patients undergoing traditional catheter ablation procedures for AF.

9.1 PRE- AND ABLATION PROCEDURE

9.1.1 PRE-PROCEDURE TESTING

The following tests and procedures will occur before the ablation:

- Baseline swallowing impairment score
- Collect any pre-procedural imaging of left atrium (if performed): MRI/CT within 6 months of procedure
- Baseline CBC-Platelets, PTT/PT-INR

9.1.2 ABLATION PROCEDURAL DETAILS

- Patients will be brought to the electrophysiology laboratory in a fasting state.
- General anesthesia will be used for all cases, which is routine practice for all AF ablations at MGH.
- Venous ± arterial access, number of transseptal punctures performed, and catheter selection (coronary sinus catheter, right atrial catheter, intra-cardiac echocardiography (ICE), and ablation catheter) will be left to the discretion of the operator.
- Any 3D Mapping system can be used
- Any thermal based ablation system can be used for the procedure.
- Insertion of the DV8 tool will be performed at the beginning of the procedure. The esophagus will be then moved with a goal of deviation of 2 cm from the ablation sites.
- Circumferential pulmonary vein (PV) isolation will be performed next.
- Bidirectional block in and out of the PV must be demonstrated after PV isolation (again, this is usual clinical practice).
- Use of adenosine to assess for dormant conduction is required.
- Per usual practice of the clinical site, Isoproterenol may be used at the end of the study protocol to assess for PV reconnection
- After performance of PV isolation on both sides additional LA ablation is left to the discretion of the electrophysiologist

9.2 POST-PROCEDURE

9.2.1 POST-PROCEDURE TESTING

- Swallowing impairment score: next morning

- Preferably the next day but up to 3 days after the procedure: Barium swallow to be performed on all patients.

9.2.2 POST-PROCEDURE FOLLOW UP

- 2 week and 3-month phone follow up: Repeat swallowing impairment score (to be obtained trans-telephonically)

9.2.3 POST-PROCEDURE MEDICATION MANAGEMENT

- All medications are left up to the discretion of the investigator.
- Visualization of any esophageal injury should prompt proton pump inhibitors for 2 weeks (per usual practice of the clinical site), CT scan of the chest, and referral to the gastroenterology service.
- Therapeutic anticoagulation (example warfarin or equivalent agent) is at the discretion of the patient's electrophysiologist.

9.2.4 POST-PROCEDURE DATA COLLECTION

- At the end of the case a copy of the Barium swallow (coded) will be obtained on CD/DVD and stored.
- Coded fluoroscopy/CINE images from the procedure.
- Coded electroanatomical mapping data.

9.3 SAFETY

With the data from the preliminary study, and the 200 cases performed worldwide including MGH, we anticipate no significant injury to the esophagus. Instrumental to the safety, is a prerequisite for proctoring and education of each study staff with regards to the appropriate and safe use of the esophageal deviation procedure. In this regard, each study staff should have completed training on the use of the device. All documentation for the training will be kept in the regulatory binder.

The swallowing impairment scores performed the day after the procedure and over the phone in 2 weeks will assess for symptoms including dysphagia that can potentially occur as a result of esophageal manipulation.

Patients will report symptoms to the study coordinator and investigators during the follow-up period.

The Principal Investigator will oversee the safety of the study.

Adverse events and Serious adverse events will be monitored and reported to the IRB.

9.3.1 ADVERSE EVENTS

The incidence of serious adverse events over the course of the study will be recorded. An adverse event is any undesirable clinical occurrence in a study patient, whether or not it is related to the study intervention. Any condition that was recorded as pre-existing is not an AE unless there is a change in the nature, severity or degree of the condition.

9.3.2 SERIOUS ADVERSE EVENTS

Serious adverse events are defined as any experience that results in a fatality or is life threatening; results in significant or persistent disability; or represents other significant hazards or potentially serious harm to research subjects or others, in the opinion of the investigators.

9.3.3 EVENT RECORDING

Protocol-defined adverse events will be captured throughout the period of trial participation.

9.3.4 CAUSALITY

The investigator will assess the relationship of an adverse event to the intervention. The investigator should distinguish the relationship between the event and (a) ablation procedure (i.e. AF ablation procedure or other concomitant procedures), and (b) the esophageal deviation. Causality will be defined as follows:

Probable

Adverse events that, after careful medical evaluation, are considered with a high degree of certainty to be related to the intervention (AF ablation ± esophageal deviation). The following characteristics will apply:

- A reasonable temporal relationship exists between the event and the intervention, and
- The event is a known reaction to the intervention, and cannot be explained by an alternative etiology commonly occurring in the population/individual.

Possible

Adverse events that, after careful medical evaluation, do not meet the criteria for a probable relationship to the intervention, but for which a connection cannot be ruled out with certainty. The following characteristics will apply:

- The event occurs after intervention, and
- The event is not a known reaction to intervention, but cannot be explained by a commonly occurring alternative etiology

Unlikely

Adverse events that, after careful medical evaluation, do not meet the criteria for a possible or probable relationship to intervention and for which a connection is unlikely. The following characteristics will apply:

- The event does not follow a reasonable temporal sequence from administration of the intervention, or
- May have been produced by environmental factors, and there is no apparent pattern of response to the intervention.

9.3.5 REPORTING OF SERIOUS ADVERSE EVENTS

All investigators must report unanticipated problems involving risks to subjects or others including adverse events within 5 working days/7 calendar days of the date the investigator first becomes aware of the problem, as dictated by the specific IRB policy.

9.4 RISKS

As the protocol described is standard to an AF ablation procedure, the risks of the procedure include that of a standard AF procedure, which are:

Common:

- Discomfort at the site of venous access
- Groin hematoma

Uncommon:

- Discomfort in the throat region
- Cardiac Perforation requiring drainage or surgery
- Pulmonary venous stenosis / occlusion
- Thrombus formation / stroke
- Injury to adjacent structures (phrenic nerve, esophagus, lung, cardiac valves)
- Bleeding

- Congestive heart failure
- Renal dysfunction
- Vascular complications (including pseudoaneurysm, AV fistula requiring surgical intervention)
- Myocardial infarction
- Esophageal deviation risks include dental injury and esophageal injury similar to that of TEE
- Radiation burns
- Ventricular arrhythmias or QT prolongation
- Pneumonia and/or sepsis
- Anaphylaxis
- Death

Additional risks unique to the protocol are

- Sore throat
- Aspiration pneumonia from barium sulfate or Gastrografin.
- Difficulty or painful swallowing
- Bleeding from the mouth area or from the food pipe
- Perforation—a tear or hole in the esophagus (the “tube” that connects your mouth to your stomach”) or heart
- Infection
- Failure to protect the esophagus from heat related injury.
- Nausea
- Abdominal pain
- Atrio-esophageal fistula- An abnormal connection between the atria of the heart and the esophagus in which they fuse together

9.5 DATA HANDLING

Information about patients will be kept confidential and managed according to the requirements of the United States of American Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed patient authorization informing the patient of the following:

1. What protected health information (PHI) will be collected from patients.
2. Who will have access to that information and why.
3. Who will use or disclose that information.
4. The rights of a research patient to revoke their authorization for use of their PHI.

In the event that a patient revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of patient authorization. For patients that have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the patient is alive) at the end of their time in the study.

In order to ensure patient confidentiality, all case report forms and patient information (CT / MRI, if reviewed, 3Dmapping study DVDs, fluoroscopic and endoscopic images) will be coded with a unique three-digit patient identifier. Information will be stored in the office of the local study coordinator, which will be locked when he/she is not in the office. The research study coordinators, principal investigator and co-investigators will be the only people with access to this data. All data will be stored coded with the unique three-digit patient identifier. There will be a code sheet that will link the coded data back to the subjects. This will be encrypted and password-protected. One copy will be stored in the primary investigator's computer, and another in the research coordinator's computer.

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Appendix 1:

Swallowing Impairment Score			**COMMENT**	
SYMPTOMS	**Min/ None**	**Mild**	**Mod**	**Severe**
Throat pain/discomfort	☐	☐	☐	☐
Effort required to swallow	☐	☐	☐	☐
Pain during swallowing	☐	☐	☐	☐
SYMPTOMS	**Never**	**Some-times**	**Often**	**Always**
Coughing while swallowing	☐	☐	☐	☐
Sensation of foreign-body in my throat	☐	☐	☐	☐
I notice a change in my voice	☐	☐	☐	☐
Bleeding	☐	☐	☐	☐
Vomiting	☐	☐	☐	☐
Nausea	☐	☐	☐	☐
Abdominal Pain	☐	☐	☐	☐
Other, specify:_____				

Appendix 2: Summary Flow Sheet

Esophageal Deviation in Atrial Fibrillation Ablation

A single-arm study

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INCLUSION CRITERIA

A maximum of up to 64 patients will be enrolled in this prospective single-center single-arm study. Patients undergoing AF ablation (including paroxysmal and persistent AF) will be included in this study. Consistent with the current definitions, paroxysmal AF are episodes that will self-terminate in less than 24 hours. Persistent AF, is defined as ≥1 documented AF lasting >1week in duration or lasting less than 7 days but requiring electrical or pharmacological cardioversion to sinus rhythm.

- Age >18 - Age < 80 yr
- Documentation of atrial fibrillation (AF)
- General anesthesia
- All patients must understand and adhere to the requirements of the study and be willing to comply with the post study follow-up requirements.

EXCLUSION CRITERIA

- Any reversible cause of AF (post-surgery, thyroid disorder, etc.)
- INR > 4.0 at the time of the procedure
- H/o of severe esophageal ulcers, strictures, varices, bleeding, laceration or perforation, esophagitis
- Severe GERD
- H/o esophageal surgery or any esophageal banding or cautery

- H/o chest radiation
- Significant abnormality on Swallowing Impairment Score
- Mental impairment precluding signing consent or completing follow up
- Patients with any other significant uncontrolled or unstable medical condition
- Women who are known to be pregnant or have had a positive β-HCG test within 7 days prior to procedure
- Presence of left atrial thrombus

PRIMARY CLINICAL ENDPOINT

The following primary endpoint will be assessed:

1) The extent of esophageal deviation as measured by the incidence of successfully moving the esophagus to achieve a minimum distance of 1 cm between the ablation line for the ipsilateral PV pairs and the trailing edge of the esophagus.

SECONDARY CLINICAL ENDPOINTS

The following secondary endpoints will be assessed:

1) The extent of esophageal deviation as measured by the incidence of successfully moving the esophagus by an average of 2 cm from the ablation line for the ipsilateral PV pairs.
2) The incidence of esophageal laceration as assessed by a Barium swallow study performed within 1-3 days of the procedure.
3) Incidence of PV reconnection at 30 min post-ablation
4) Fluoroscopy time
5) Procedure duration
6) Time from start of ablation to last ablation lesion for pulmonary vein isolation

Pre-procedure testing

- Baseline swallowing impairment score
- Collect any pre-procedural imaging of Left atrium (if performed): MRI/CT within 6 months of procedure
- Baseline CBC-Platelets, PTT/PT-INR

AF ablation procedure:

- Patients will be brought to the electrophysiology laboratory in a fasting state.
- General anesthesia will be used for all cases

- Venous ± arterial access, number of transseptal punctures performed, and catheter selection (coronary sinus catheter, right atrial catheter, intra-cardiac echocardiography (ICE), and ablation catheter) will be left to the discretion of the operator.
- Any 3D Mapping system can be used
- Any thermal based ablation system can be used for the procedure.
- Insertion of the DV8 tool will be performed at the beginning of the procedure.
- The esophagus will be then moved with a goal of deviation of 2 cm from the ablation sites.
- Circumferential pulmonary vein (PV) isolation will be performed next. Bidirectional block in and out of the PV must be demonstrated after PV isolation (again, this is usual clinical practice).
- Use of adenosine to assess for dormant conduction.
- Per usual practice of the clinical site, Isoproterenol may be used at the end of the study protocol to assess for PV reconnection
- After performance of PV isolation on both sides additional LA ablation is left to the discretion of the electrophysiologist

POST-PROCEDURE TESTING

- Swallowing impairment score: next morning

- Preferably the next day, but up to 3 days after the procedure: Barium swallow to be performed on all patients.

POST-PROCEDURE FOLLOW UP

- 2 week and 3-month phone follow up: Repeat swallowing impairment score (to be obtained trans-telephonically)

POST-PROCEDURE MEDICATION MANAGEMENT

- All medications are left up to the discretion of the investigator.
- Visualization of any esophageal injury should prompt proton pump inhibitors for 2 weeks (per usual practice of the clinical site), CT scan of the chest, and referral to the gastroenterology service.
- Therapeutic anticoagulation (example warfarin or equivalent agent) is at the discretion of the patient's electrophysiologist.

POST-PROCEDURE DATA COLLECTION

- At the end of the case a copy of the endoscopy (Coded) will be obtained on CD/DVD.
- Coded fluoroscopy/CINE images.
- Coded electroanatomical mapping data.

Work Flow

- Ensure all consents are signed and patient meets inclusion/exclusion criteria
- Baseline Swallowing impairment score
- After induction of general anesthesia, the DV8 tool will be inserted.
- PV isolation will be performed after the deviation of the esophagus.
- Baseline esophageal position (record (cine) straight AP view) to be identified with contrast in the esophagus. Exclude from deviation if esophageal diverticulum is identified.
- After maximum possible deviation is performed, cine fluoroscopic view is to be acquired for both left sided and right-sided ablation.
- Care must be taken to ensure fluoroscopic images are acquired at the same level of magnification. Care must also be taken to ensure that the esophagus has sufficient barium at all times.
- Esophageal LET probe must be manipulated to approximate catheter tip at all times during any posterior wall ablation: Note: All posterior wall lesions are to be recorded:
  - Duration of lesion
  - Power delivered for all lesion

Esophageal deviation and data collection:

- Extent of esophageal deviation measured on the electroanatomic mapping system as the distance between the ablation line and the trailing edge of the esophagus. The trailing edge of the esophagus will be delineated on the EAM system guided by fluoroscopy.
- Time from first ablation to last ablation for PV isolation for all four veins.
- From start of deviation maneuver to last ablation for PV isolation.
- Total procedure duration
- Total Fluoroscopy time
- Confirm PV isolation at 30 minutes, record if vein reconnects.
- All non-PV ablation should be performed after PV isolation only. Above parameters should be recorded if additional deviation is performed for non-PV ablation such as CFE or atrial tachycardia ablation.
- Obtain all Fluoro/cine images and electroanatomic mapping data.

Post-procedural care

- Next morning; Administer SIS symptom scale and record score
- Barium swallow.

Outpatient follow- up

- 2 weeks/ 3 months – Telephonic assessment of Swallowing Impairment Score
- Any further follow up that may be relevant to complications during the procedure