To: File
From: Medical Affairs
Date: October 10, 2016
Subject: Ablation Index settings

Literature Review

A search of published literature was conducted to gather evidence related to the VISITAG™ Module for the CARTO® 3 System, with and without Ablation Index (“VISITAG”) in catheter ablation of cardiac arrhythmia. In general, systematic review practices were followed to assemble the evidence base, including the use of prospectively determined search strategies and study selection criteria.

Only studies published or presented in English since January 1, 2012, using any ablation catheter and the CARTO® System with the VISITAG™ Module (with or without Ablation Index), were eligible for review. Twenty five (25) primary studies were identified having met the criteria, 10 were full papers and 15 were abstracts presented at scientific meetings.

Studies Directly Evaluating Ablation Index

**Pre clinical**

*Ikeda A, Nakagawa H, Constantine G.* Contact force radiofrequency ablation catheter with low irrigation flow rate - relationship between lesion depth and contact force-power-time index in the canine beating heart. Heart Rhythm Society 2013; PO02-162.

*Nakagawa H, Ikeda A, Govari A.* Prospective study to test the ability to create RF lesions at predicted depths of 3, 5, 7 and 9 mm using a new formula incorporating contact force, radiofrequency power and application time (force-power-time index) in the beating canine heart. Heart Rhythm Society 2013: MP03-4.


**Clinical**

**Multicenter Retrospective Study**
Das M, Wynn GJ, Morgan M, Lodge B, Waktare JE, Todd DM, et al. Recurrence of atrial tachyarrhythmia during the second month of the blanking period is associated with more extensive pulmonary vein reconnection at repeat electrophysiology study. Circ Arrhythm Electrophysiol 2015; 8: 846-52: This study also showed significantly lower median Ablation Index values in reconnected segments than in non-reconnected segments (274 [IQR 256-341] vs. 317 [IQR 286-359], p = 0.003, respectively) (Das 2014a).

Das M, Duytschaever M, Gupta D, Lukac P, Sorrel J, Phlips T, et al. Ablation index predicts sites of acute reconnection after pulmonary vein isolation: a multi-center retrospective analysis. Heart Rhythm Society Scientific Sessions 2015: Abstract PO01-47: The authors found that the median Ablation Index values were significantly lower in reconnected segments than in non-reconnected segments (293 [interquartile range (IQR) 255-344] vs. 342 [IQR 293-397], p < 0.0001, respectively)

Das M, Wynn GJ, Morgan M, Lodge B, Waktare JE, Todd DM, et al. Ablation index predicts sites of reconnection at repeat electrophysiology study following pulmonary vein isolation. Heart Rhythm Society Scientific Sessions 2015: Abstract PO04-114: This study also showed significantly lower median Ablation Index values in reconnected segments than in non-reconnected segments (312 [IQR 266-339] vs. 359 [IQR 312-408], p < 0.0001, respectively).

Prospective Feasibility Study

Nakagawa H, , Yamashiro K, Duytschaever M, Taghji P, Tavernier R, Phlips T, et al. High incidence of ipsilateral pulmonary vein isolation by first encirclement using new force-power-time formula with short radiofrequency time in atrial fibrillation patients. Heart Rhythm Society Scientific Sessions 2015: Abstract PO03-102: Radiofrequency (RF) energy was delivered until a target lesion depth, as calculated by the Ablation Index algorithm, was reached. Target lesion depths of 4 mm on the posterior wall and 6 mm on the anterior wall resulted in PVI on the first encirclement in 90-98% of patients. No complications were noted (e.g., pericardial effusion, phrenic nerve palsy, and atrio-esophageal fistula)

Technical justification for VisiTag™ recommended settings with Ablation Index

The range parameter reflects the system sensitivity to catheter movement. The mathematical representation of the catheter movement is a standard deviation test so that the catheter movement standard deviation is compared with the position stability range parameter. A focal ablation catheter tip diameter is 7.5F (2.5mm). During ablation any tissue which is touching the tip, penetrating to some extent into the tissue, is considered to be an ablated tissue after some time.

To ensure the appearance of a single VISITAG™ Module tag the accuracy of the system needs to be taken into account. The mean magnetic-based location accuracy of the CARTO® 3 System is 1 mm. In a close proximity, the actual inaccuracy is less than 1mm but still might impact the identified catheter location to some extent. Therefore, the maximum range should be larger than 2.5mm. Therefore the position stability filter range recommendation is 2-3mm.

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When the position stability time parameter is higher than 3 seconds, the VISITAG™ Location may be delayed until the stability time parameter is met and preventing the display of the ablation index Indication progression. Thus, when the VISITAG™ Location appears, the ablation index value might already exceed the threshold value (according to user predefined threshold).

Based upon the above findings, the following are recommendations for Ablation Index usage with the CARTO® VISITAG™ module:

**Stability Settings:**
- Range: 2-3 mm
- Time: 3 seconds

**VISITAG™ Tag size:**
- 3mm

**FOT %:**
- 25

**FOT (g):**
- 3

**CF and power:**

The recommendations provided are based on data obtained from animal and clinical studies. Use clinical judgment when using this tool paying careful attention to impedance drop, electrogram reduction, time of RF application, and with consideration of individual subject conditions when selecting settings.

Average results from IDE studies:

SMART-AF\(^2\)
- Avg CF = 17.9 g ± 9.42 g
- Avg power = 31.1 ± 4.06 watts

SMART-SF\(^3\)
- Avg CF = 16.7 g ± 6.14 g
- Avg power = 31.3 ± 3.98 watts

CF ≥ 40g may correlate with higher risk of perforation and cardiac tamponade.

**Posterior wall ablation:**

An appropriate strategy to minimize risk of esophageal injury should be used to ensure the physician has accurate information about the location of the esophagus relative to intended sites of ablation. The following are examples that can be used, esophageal temperature probe, CartoSound/ICE and barium sulfate. Either of the following combinations could be used to reduce the effect on the esophagus during RF delivery: Reduced power, reduced time, and reduced contact.
Start ablation at < 25 W, per the HRS consensus statement<sup>4</sup> for ablations on the posterior wall

Targeting AI values as an end point:

The tool should never be used in the absence of clinical judgment in regards to lesion creation. Pay careful attention to impedance drop and electrogram reduction.

If you have not reached a user defined AI value, due to clinical condition i.e. esophageal temp rise etc., move to a different location allowing the temperature to come back to baseline and retarget in a region away from the area of concern.

Ablation Strategy:

Initial usage of ablation index for draggers should follow the steps outlined below:

1. Start with point by point technique in order to familiarize yourself with the data being displayed on the CARTO<sup>®</sup> 3 system screen.
2. Maintain point by point technique in order to refine the selected target values in order to improve reliability and not compromise safety.
3. Maintain using point by point technique in order to reinforce new workflow.
4. Only after establishing a comfort zone with new parameters should any switch to dragging occur for those users who are draggers.

*Kovoor, P et Al.<sup>5</sup>, reported that tissue temperature decreases with distance as observed in his experiment; 86° C at 4mm vs 93° C at 1mm.

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1 Biosense Webster, Ltd. data on file: REP8605: Technical justification for VisiTag™ recommended settings with Ablation Index
2 Biosense Webster Inc., THERMOCOOL® SMARTTOUCH® Catheter IFU (US), M-5276-693,M-5276-694
3 Biosense Webster Inc., THERMOCOOL® SMARTTOUCH® SF Catheter IFU (US), M-5276-823,M-5276-824
5 KOVOOR, P., ET AL.: Effect of Inter-electrode Distance on Bipolar Intramural Radiofrequency Ablation