URGENT: Field Safety Notice Customer Notification

VARIPULSE Bi-Directional Ablation Catheters

Part #	Part Description	Lot #	UDI	Mfg. SRN
D141201	VARIPULSE Bi-Directional Ablation Catheters	All lots	10846835025460	US-MF-000014219

February 17th, 2025

Dear Valued Customer,

Biosense Webster, Inc. ("BWI") is contacting users of the VARIPULSE™ Platform (including the VARIPULSE™ Bi-Directional Ablation Catheter) to inform that it has initiated a field safety notice and share updates to the Instructions for Use (IFU) for the VARIPULSE Bi-Directional Ablation Catheters. These updates to the existing labeling include important updates on the device's risks. VARIPULSE Bi-Directional Ablation Catheters can continue to be used worldwide following the updates included in this letter.

REASON FOR NOTIFICATION

On January 5th, 2025, BWI recommended a pause in the use of the VARIPULSE™ in the United States to investigate four neurovascular events that were reported in the VARIPULSE™ US External Evaluation (the first commercial US cases after FDA approval of the VARIPULSE™ Platform).

Between December 10, 2024, and January 3, 2025, one hundred and thirty-two (132) atrial fibrillation (AF) patients underwent a left atrial ablation in the Unites States and four (4) developed peri-procedural stroke. This resulted in a rate of 3% peri-procedural stroke in the US External Evaluation, which is:

- greater than the anticipated incidence of peri-procedural stroke or TIA following an AF ablation procedure (<1%),
- greater than the rates seen in the US premarket study (AdmIRE) and the European Union (EU) premarket study (InspIRE) and
- greater than the worldwide rate of Stroke and TIA for the VARIPULSE™ ablation catheter which is 0.5%.

For this reason, out of an abundance of caution BWI paused the use of the VARIPULSE™ in the United States and conducted a comprehensive investigation into potential device, procedure, and patient related factors.

The investigation concluded that VARIPULSE™ devices operate as intended and there is no difference in the performance of the available VARIPULSE™ system configurations globally.

Although the mechanism for an incidence of stroke or TIA can be multi-factorial, procedural and patient factors may also contribute to the risk of stroke and TIA. BWI's investigation concluded that the risk of stroke or TIA may increase if a high number of ablations, the stacking of ablations, and/or ablations outside of the pulmonary veins are delivered. For this reason, BWI is sharing the following summaries from all available information regarding strokes and TIAs.

- Ablations beyond pulmonary vein isolation. The use of the VARIPULSE™ ablation catheter for ablations beyond pulmonary vein isolation may be linked to the higher-than-anticipated incidence

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of peri-procedural stroke or TIA. In 70% of the cases of stroke or TIA reported to BWI world-wide, patients received ablations outside the Pulmonary veins. The safety and effective use of this device outside of the pulmonary veins for the treatment of atrial fibrillation has not been clinically established and may increase the risk of patient injury.

- Number of ablations. An increased number of ablations (energy applications) delivered during the procedure may be linked to the higher-than-anticipated incidence of peri-procedural stroke or TIA. In 90% of the cases of stroke or TIA reported to BWI world-wide, patients received a number of ablations greater than the median number of ablations delivered in the InspIRE study (16 ablations) and 60% received a number of ablations greater than the median number of ablations delivered in the AdmIRE study (23 ablation). Moreover, patients received more than 28 ablations in 50% of the cases of stroke or TIA.
- Ablation stacking. “Stacking” occurs when at least five electrodes are placed within a 3 mm distance of one another during consecutive complete ablations sessions. “Stacking” may be linked to the higher-than-anticipated incidence of peri-procedural stroke or TIA observed in the US External Evaluation. At least 35% of the patients who suffered from peri-procedural stroke received stacked ablations.
- Char. Specific workflows, such as “stacking” or a high number of ablations, or patient conditions such as low blood flow, can contribute to heating that could increase the likelihood of char.
- Persistent vs paroxysmal AF. The safety and efficacy of the VARIPULSE™ Catheter when used with a VARIPULSE™ Generator has been determined in the AdmIRE and InspIRE trials in the treatment of subjects with symptomatic paroxysmal atrial fibrillation (PAF). The safety and efficacy of their use in the treatment of other arrhythmias have not been established.

DEVICE USE

The VARIPULSE™ Catheter is indicated for use in catheter based cardiac electrophysiological mapping (stimulating and recording) and, when used with a TRUPULSE™ Generator, for cardiac ablation. The catheter provides location information when used with the CARTO™ 3 System.

This device is targeted at patients who have been diagnosed with cardiac arrythmias and are undergoing an electrophysiology procedure. The device is intended for adults 18 years old and above.

RECOMMENDATIONS - Review the information above and adhere to the updated Instructions for Use included in *Attachment 1 Instructions for Use (IFU) Modification Details*.

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POTENTIAL PATIENT IMPACT - The investigation into workflows used worldwide concludes that a greater number of ablations, stacking ablations and/or ablation outside of pulmonary veins may increases the risk of neurovascular event.

WHAT TO DO

1. Carefully review the information contained in this letter.
2. Be aware of the known and inherent risk of neurovascular events that may occur during catheter-based ablation procedures for rapid, irregular heartbeats (atrial fibrillation).
3. Review all instructions for use and updates included in *Attachment 1. Instructions For Use Modification Details*.
4. Healthcare providers who have treated patients using this device should continue to follow those patients according to their standard of care as with any ablation procedure.
5. **Product is not being removed.**
6. Ensure that anyone in your facility who needs to be aware of this notification reads this letter carefully.
7. Keep a copy of the notice in your facility records.
8. Complete the mandatory acknowledgement form in *Attachment 2* and return it promptly.

CONTACT INFORMATION - Report all adverse events or quality concerns with use of these devices to Johnson and Johnson. The appropriate regulatory agencies have been notified and are aware that Biosense Webster is voluntarily providing this information. If you have additional questions about this medical device field safety notice, please contact your Biosense Webster Representative.

Sincerely,

Maria Jose Arana
Sr. Director, Quality & Compliance
Biosense Webster, Inc.
31 Technology Drive, Suite 200. Irvine, CA 92618 USA
www.biosensewebster.com

** Joglar JA, et al; Peer Review Committee Members. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024 Jan 2;149(1): e1-e156. doi: 10.1161/CIR.0000000000001193. Epub 2023 Nov 30. Erratum in: Circulation. 2024 Jan 2;149(1): e167. doi: 10.1161/CIR.0000000000001207. Erratum in: Circulation. 2024 Feb 27;149(9): e936. doi: 10.1161/CIR.0000000000001218. Erratum in: Circulation. 2024 Jun 11;149(24): e1413. doi: 10.1161/CIR.0000000000001263. PMID: 38033089; PMCID: PMC11095842.*

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Attachment 1: Instructions for Use (IFU) Modification Details

SECTION: **WARNINGS AND PRECAUTIONS**

New or Modified Warnings:

- The safety and efficacy of the VARIPULSE™ Catheter when used with a VARIPULSE™ Generator has been determined in the AdmIRE trial in the treatment of subjects with symptomatic paroxysmal atrial fibrillation (PAF). The safety and efficacy of their use in the treatment of other arrhythmias have not been established.
- The safety and effective use of this device outside of the pulmonary veins for the treatment of atrial fibrillation has not been clinically established and may increase the risk of patient injury.
- The safety and effectiveness of catheter ablation for the treatment of atrial fibrillation in patients with significant left ventricular dysfunction, advanced heart failure, substantial left atrial enlargement, and structural heart disease has not been established.
- Implantable pacemakers, implantable cardioverter/defibrillators (ICDs), and metal stents can disrupt the electric field produced by PF ablation.
    - Pay close attention when applying Pulse Field (PF) ablation in patients with implantable pacemakers and implantable cardioverter/defibrillator (ICDs). Implantable pacemakers and ICDs may be adversely affected by PF energy. Safety and Effectiveness have not been evaluated for patients with pacemakers and ICDs. It is important to have temporary external sources of pacing and defibrillation available during ablation and to consider temporarily reprograming the pacing system to minimum output or OFF mode to minimize the risk of inappropriate pacing. Exercise extreme caution during ablation when in close proximity to atrial or ventricular permanent leads; program the ICD to the OFF mode during the ablation procedure; perform complete analysis after ablation.
- Carefully follow the catheter directions for use. In clinical studies (AdmiRE and InspiRE), the median number of ablations delivered was 23 (69 applications) and 16 (49 applications), respectively. Safety and effectiveness were established in all treated subjects, 75% of whom had fewer than 28 ablations (84 applications) delivered in the AdmirRE clinical study and 17 ablations (52 applications) in the InspIRE.
- The risk of patient injury may increase if the number of ablations performed exceeds those evaluated in clinical testing and device performance may be impacted.
- Maintain appropriate levels of recommended anticoagulation therapy before and after the procedure. The safety of discontinuing anticoagulation therapy following catheter ablation of atrial fibrillation has not been established. Anticoagulation therapy in such patients should be administered in accordance with the 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation.
- If there is uncertainty regarding the patient's anticoagulation status or rhythm prior to the procedure, evaluate the need to perform a Transesophageal Echocardiogram (TEE) prior to the procedure to confirm absence of mural thrombus and/or thrombus in the left atrial appendage.

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- Confirm ACT ≥ 350 seconds prior to ablation with the catheter and check every 15-30 minutes while the catheter is in the left atrium. Failure to maintain appropriate anticoagulation levels may increase the risk for thromboembolic events.
- Use both direct imaging guidance (such as fluoroscopy and/or intracardiac echocardiography) and electrogram data to monitor catheter advancement and reduce risk of tissue injury.
  - When using the catheter with conventional systems (such as fluoroscopy or intracardiac echocardiography), with the CARTO™ 3 System, careful catheter manipulation must be performed in order to avoid cardiac damage, perforation, or tamponade. Catheter advancement should be done under direct imaging guidance.
  - Do not use excessive force to advance or withdraw the catheter when resistance is encountered. The firmness of the braided tip dictates that care must be taken to prevent perforation of the heart.
- Unsheathe the catheter from the sheath in the middle of the chamber to prevent entrapment or perforation.
- When using the catheter in or around the atrioventricular valve, take precautions to prevent the catheter from slipping into the ventricles and becoming entangled with the valve. Entanglement may lead to damage to the valve, entrapment of the device, and/or need for surgical intervention.

SECTION: **DIRECTIONS FOR USE**

New or Modified Directions for Use

- **Performing PF Ablation with the Catheter**
  - One ablation sequence consists of three applications. Each application has a ten second interval delay. This ablation sequence is programmed in the TRUPULSE™ Generator.
    - Reposition the catheter between each complete ablation (up to 3 consecutive applications) to avoid stacking of ablations in the same location.

- **Workflow for Pulmonary Vein Isolation**
    - For each pulmonary vein, create a concentric ring of lesion using 4 ablations (2 ostial with the contracted loop and 2 antral with an open loop) (12 applications).
    - The catheter position should be co-axial to the vein.
    - Place an electrode catheter in the right ventricle or a ventricular branch of the coronary sinus to be ready for ventricular pacing in the event of vagal response.
    - Perform 1 ostial ablation (3 applications) with the contracted loop at the same catheter position without moving the catheter.

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- Within the ostial area (with the contracted loop), reposition the catheter and perform an additional ablation (3 applications). The new catheter position should cover any potential gaps from the first ostial catheter position.
- Ensure that all applications are complete (1 complete ablation) (Generator screen reads 100%).
  - If any ablation is not complete (less than 100%), then repeat the incomplete ablation in the same location.
- After completing the 2 ostial ablations (6 applications with the contracted loop), move the catheter into an antral side (with an open loop) and follow a similar workflow completing 1 ablation (3 applications) at the same catheter position and repositioning to complete the final antral ablation (a total of 6 applications with an open loop).
- Deliver 4 ablations (12 applications) per vein.
- In anatomy with a common PV, deliver 8 ablations (24 applications) per common.
- If isolation is not obtained, apply additional applications of PF ablation where needed.
  - It is recommended to check all rotations of the CARTO™ map to ensure full circumferential co-axial lesions were achieved on all map surfaces.
- In clinical studies (admIRE and inspIRE), the median number of ablations delivered was 23 (69 applications) and 16 (49 applications), respectively. Safety and effectiveness were established in all treated subjects, 75% of whom had fewer than 28 ablations (84 applications) delivered in the admIRE clinical study and 17 ablations (52 applications) in the InspIRE clinical study.

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Attachment 2. BUSINESS REPLY FORM

Please complete this Business Reply Form (BRF) and return it to [Enter Local Affiliate Information] within 5 business days upon receipt of this letter.

Biosense Webster, a division of Johnson & Johnson Medical NV/SA
Attn: *[Affiliate to Enter Representative or Recall Coordinator Name here]*
Mailing Address: *[Affiliate to Enter contact information here]*
e-Mail Address: *[Affiliate to Enter contact information here]*
Fax Number (If applicable), affiliate could enter here.

Part 1. Please check and complete the following box to acknowledge receipt of notification:

☐ I have read and understand the notification.

Your Name/Title:	Facility/Business Name:
Sign*:	Date:
Facility/Business or shipping Address, City:	
Biosense Webster Sales Representative (if applicable):	
Date the notification was received:	
Telephone Number:	