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Reports of Air Embolic Events
Medtronic 4FC12 FlexCath Advance™ Sheath
Important Medical Device Information

September 2018

Dear Physician, Risk Manager:

This notification is to provide you with important information regarding ablation procedures involving the Medtronic 4FC12 FlexCath Advance™ Sheath. Medtronic has received a higher-than-expected number of reports of air embolism in Japan which have led to death or coma.

Air embolism to the systemic circulation is a known risk for patients undergoing percutaneous interventions requiring access to the left atrium, such as ablation procedures. According to the 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation, "the most common cause of air embolism is introduction of air via the transseptal sheath." [1]

Reports of air embolism during use of the FlexCath Advance Sheath leading to death or coma have occurred in Japan at a rate of 0.011%. Between July 1, 2014-August 31, 2018, 4 serious events were reported in Japan (3 resulting in death and 1 patient with reported persistent coma). The rate of air embolism leading to death or coma in the rest of the world, excluding Japan remains stable at below 0.001%, and consistent within design predictions.

In November 2017, following two air embolism events in Japan, Medtronic distributed a customer communication in Japan, that provided specific instructions outlining recommendations on best practices to minimize the risk of air embolism as well as notification for a Japan Package Insert update reflecting this additional information. In June 2018, following regulatory agency approvals, the Japan Package Insert (labeling) was updated to reflect these recommendations.

Following two additional embolism events resulting in death since the November 2017 communication, Medtronic has continued to investigate potential causes for these events. Our investigation has determined that a combination of procedural and patient factors may have increased the risk of life-threatening air embolism in these cases. Medtronic's investigation has not resulted in identification of any product non-conformance contributing to the increased rate of air embolism leading to death or coma.

Based on this information, Medtronic is providing additional clarification regarding precautions that may be taken to reduce the risk of air embolism that is consistent with published literature and a statement issued by JHRS on this topic in August 2018.

Please see **Appendix A** for Important Information, which is briefly summarized below. The Japan Package Insert for FlexCath Advance will be updated to align with these additional clarifications:

As always during any ablation procedure, exercise caution when preparing sheaths and monitor closely for air ingress. Signs of air ingress may include visible bubbles appearing in the side port tubing or audible sucking sounds coming from the hemostatic valve. Air bubbles may also be visible on fluoroscopy or intracardiac echo (ICE), if used. Air embolism may present clinically with signs of cerebral, coronary, and peripheral vascular compromise. If

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air embolism is suspected, begin appropriate therapy immediately per treatment guidelines or consensus statements.[1]

In consultation with JHRS, Medtronic is making the following recommendations:

- Monitor the patient for conditions that may induce negative left atrial pressure such as airway collapse, deep breathing, snoring or apnea. Use particular caution when administering drugs with respiratory depressive effects. Negative left atrial pressure may increase the risk of air ingress through the hemostasis valve particularly during insertion and removal of catheters.[2]

- Avoid any unnecessary catheter exchanges during any left atrium ablation procedure. Medtronic has only confirmed the compatibility of the Medtronic dedicated concurrent devices, Freezor MAX and Arctic Front Advance Cryoablation catheters, with the FlexCath Advance sheath. The use of other catheters has not been fully evaluated; therefore, Medtronic does not recommend their use with FlexCath Advance.

- Avoid placing catheter introducers or sleeves into the valve. These devices could create an air pathway into the sheath or may damage the valve.

Medtronic will continue to commercialize the FlexCath Advance Sheath. There are no changes recommended to the management of Patients who have been previously ablated with a system using a FlexCath Advance Sheath.

Customers please complete the following actions:

1. Review this Important Information on the Medtronic 4FC12 FlexCath Advance Sheath regarding air ingress and air embolism as provided in this letter.
2. Please share this Important Information with those who should be aware of this information and with clinicians in your hospital that use the FlexCath Advance Sheath.
3. After review of this information, complete the Customer Confirmation Certificate and hand it to your Medtronic sales rep. Please retain a copy of this information for your records.

Additional Information
Medtronic will notify all applicable regulatory agencies, as required, about this matter. Please share this notification with others in your organization as appropriate.

Local contact details
Please contact your Medtronic representative if you have and questions/concerns. We are committed to patient safety and welcome any questions you may have regarding this communication.

Sincerely,

[redacted]
Christopher D. Harrold
Vice President, Quality and Regulatory Affairs, CRHF
[redacted]

Cc: Chairman Medical Board and Relevant Head of Departments

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APPENDIX A

Existing warnings and precautions are shown below in bold with additional clarifications in italics:

Note: The updated package insert content may differ from the content of this communication based on regulations and consultation with regulatory authorities. You will be notified when the package insert has been updated.

Prior to introducing the sheath and during the procedure, observe and remove any air. Follow insertion or withdrawal of catheters with appropriate aspiration and flushing.

Use caution when preparing the sheath and dilator. Ensure the full 12cc volume of the sheath is flushed.

During use of the FlexCath Advance sheath, monitor closely for air ingress. Signs of air ingress may include visible bubbles appearing in the side port tubing or audible sucking sounds coming from the hemostatic valve. Air bubbles may also be visible on fluoroscopy or intracardiac echo (ICE), if used.

Introducing a catheter or sheath into the circulatory system entails risk of air embolism. Air embolism can occlude the blood vessel and may result in tissue infarction, leading to serious consequences.

If air embolism is suspected, begin appropriate therapy immediately per treatment guidelines or consensus statements.[1]

Minimize catheter exchanges to limit the possibilities of air ingress during catheter insertion and extraction. Always advance and withdraw components slowly. Pay particular attention when inserting a catheter other than the dedicated concurrent device. The vacuum created by quick movements may increase the risk of air embolism.

Unnecessary catheter exchanges during any left atrium ablation procedure should be avoided. Medtronic has only confirmed the compatibility of the Medtronic dedicated concurrent devices, Freezor Max and Arctic Front Advance Cryoablation catheters, with the FlexCath Advance sheath. The use of other catheters has not been fully evaluated; therefore, Medtronic does not recommend their use with FlexCath Advance.

Avoid placing catheter introducers or sleeves into the valve. These devices could create an air pathway into the sheath or may damage the valve.

Cardiac catheterization procedures should be performed only in a fully equipped facility. When analgesics and/or sedatives are used follow breathing management practices per treatment guidelines. [1, 3-5]

Monitor the patient for conditions that may induce negative left atrial pressure such as airway collapse, deep breathing, snoring or apnea. Use particular caution when administering drugs with respiratory depressive effects. Negative left atrial pressure may increase the risk of air ingress through the hemostasis valve particularly during insertion and removal of catheters.[2]

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References:

[1] Calkins H, et al. 2017 HRS/EHRA/ECAS/APHRS/SOLAECE Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation. Heart Rhythm. 2017 Oct;14(10):e275-e444.

[2] Franzen OW, et al. Mechanisms underlying air aspiration in patients undergoing left atrial catheterization. Catheter Cardiovasc Interv. 2008 Mar 1;71(4):553-8.

[3] Japanese Society of Anesthesiologistsm. JSA airway management guideline 2014: to improve the safety of induction of anesthesia. Journal of Anesthesia & Clinical Research. 2014;28(4):482–493

[4] Japanese Society of Anesthesiologists. (July 2014). Monitoring Guideline for Safe Anesthesia. Retrieved from http://www.anesth.or.jp/guide/pdf/monitor3.pdf

[5] American Association of Nurse Anesthetists. (February 2016). Non-anesthesia Provider Procedural Sedation and Analgesia. Retrieved from https://www.aana.com/docs/default-source/practice-aana-com-web-documents-(all)/non-anesthesia-provider-procedural-sedation-and-analgesia.pdf?sfvrsn=670049b1_