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Penumbra: Jet7 Catheter Susceptible to Malfunction, Risking Injury or Patient Death

In certain cases, the use of the new XTRA FLEX variant of Penumbra's (PEN) Jet 7 catheter, used to clear blood clots in stroke victims, is resulting in an increase in malfunctions leading to death and injuries, according to a review of an FDA database of device malfunctions and interviews with doctors.

In some cases, the catheter is expanding in the arteries of patients when doctors inject a contrast agent into the catheter. This process, according to doctors interviewed by *The Capitol Forum* as well as Stryker, a competing manufacturer of catheters, is a routine use of catheters like the Jet 7 XTRA FLEX.

Despite the potential problems with the catheter, Penumbra has not issued a recall of the device, to the consternation of some doctors.

Instead, Penumbra sent a letter to members of The Society of NeuroInterventional Surgery (SNIS) warning them that the product was never intended to inject contrast agent. Most, but not all, malfunctions that resulted in death involved the injection of contrast agent.

Doctors interviewed by *The Capitol Forum* have expressed frustration with how Penumbra has handled the issue, particularly the company's contention that the catheter is being used improperly.

"I think that this catheter should absolutely be taken off the market and improved, and I don't have any trust for it based on reports I have heard," one practicing neurointerventionalist told *The Capitol Forum*.

A spokesperson for the FDA told *The Capitol Forum* that "we are aware of the reports and are looking into this matter," but noted that recalls are generally voluntary and initiated by the manufacturer, rather than the FDA.

Neurointervention. Most strokes are caused when a blood clot or fatty deposit blocks an artery supplying blood to the brain, according to the World Health Federation.

In order to remove the clot, neurointerventional doctors insert thin catheters into the arteries of a stroke patient and navigate them to the clot in the brain. Once at the clot, doctors can use either a stent or suction to remove the clot, a procedure known as aspiration.

To help visualize the blood vessels in the brain and identify the precise location of the clot, doctors often inject a contrast agent that is visible to X-rays, a procedure known as an angiogram.

The use of the Jet 7 XTRA FLEX to inject the contrast agent appears to have caused the catheter to rupture, resulting in several deaths as well as well as disagreement between Penumbra and neurointerventional doctors about the proper use of the catheter.

In a statement to *The Capitol Forum*, Penumbra said that "reperfusion catheters are not for contrast injection, as any injection pushed through the catheter may re-introduce clot to the brain arteries. The Penumbra System labeling has always stated contrast injections should be made through a different catheter."

Doctors, however, disagree with this explanation, noting that the procedure is typical in thrombectomies and that there had been relatively few issues prior to the introduction of the XTRA FLEX, a claim supported by FDA data.

A spokesperson for Stryker Corporation said they designed its catheter to allow for this "procedurally common practice."

XTRA FLEX. Penumbra dominates the market for catheters and other neurointerventional devices, with the company estimating that its products are used in 60-65% of all stroke procedures, according to a February earnings call.

In July of 2019, Penumbra introduced the XTRA FLEX variant of its Jet 7 catheter, and by September of that year, about half of all Penumbra customers had the EXTRA FLEX variant of the Jet 7, according to a November earnings call. Penumbra also labelled the new XTRA FLEX variant as a "near term growth driver" in a December presentation to investors.

"Physician experience with JET 7 with XTRA FLEX technology has been very positive," Penumbra CEO Adam Elsesser told investors in February of 2020, "we have not had a product in our history with this level of trackability," referring to the XTRA FLEX's ability to maneuver through the tortuous arteries of the body.

Data for FDA approval not independently verified. In June of 2019, a month prior to the introduction of the XTRA FLEX, Penumbra received 510(k) approval from the FDA to market a "Modified Jet 7."

While the approval does not include any reference to "XTRA FLEX" technology, Penumbra confirmed to *The Capitol Forum* that the June 510(k) approval was for the XTRA FLEX.

A 510(k) like the one Penumbra received for the XTRA FLEX variant is based off of self-reported data from the manufacturer.

Penumbra submitted documentation showing that the modified Jet 7 catheter had the same characteristics of the standard Jet 7, except for a polyurethane extrusion and a hydrophilic coating that Penumbra labelled as "equivalent" to the preceding device.

These changes helped to improve the Jet 7's flexibility as well as aspiration power, according to marketing documents from Penumbra's Japanese distributor.

Based on Penumbra's statements, the agency "determined the device is substantially equivalent" to the standard Jet 7.

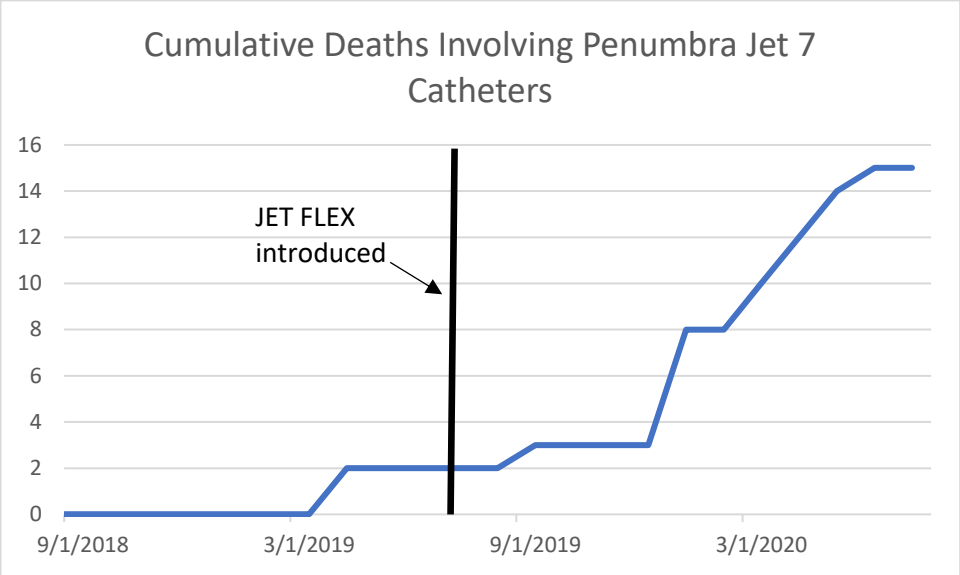
Asked whether the FDA had conducted an independent assessment of Penumbra's application, a spokesperson for the agency said that "the FDA generally does not conduct independent laboratory analysis of medical products."

The spokesperson directed *The Capitol Forum* to the FDA's manual for 510(k) approval, noting that "all 510(k)s must include a statement certifying that all information submitted in the 510(k) is truthful and accurate and that no material fact has been omitted."

Increased incidents, not all relating to contrast injection. According to a review of the FDA's Manufacturer and User Facility Device Experience Database (MAUDE), incidents involving the use of the Jet 7 catheter began to increase when the XTRA FLEX variant was introduced in July of 2019.

The original Jet 7 was introduced in September of 2018. Between then and the introduction of the XTRA FLEX variant, two deaths involving a Jet 7 device were recorded in the MAUDE database. However, both of these incidents included no indication of device failure and were labelled as an "Adverse Event Without Identified Device or Use Problem."

After the introduction of the XTRA FLEX variant in July of 2019, 13 deaths involving a Jet 7 device were logged in the MAUDE database, with many of these reports detailing problems such as material deformations, stretching, expansions of the catheter within patient, and the tip of the catheter breaking off:



Source: FDA's MAUDE Database

Two neurointerventionalist doctors spoke with *The Capitol Forum* about concerns they had with the Penumbra catheters, though one declined to be quoted in this article given the small nature of the field.

According to the neurointerventionalists, one of the most common problems with the Jet 7 XTRA FLEX is the ability for it to unintentionally expand like a balloon during the injection of the contrast agent used to map arteries. That expansion can cause arteries to rupture, seriously injuring or killing patients.

For example, a March 15, 2020 incident logged in the MAUDE database reported that "while injecting contrast through the Jet7, the physician experienced a 'spongy' feeling and the distal tip of Jet7 expanded. Subsequently, the M1 [artery] ruptured. The procedure was then ended. There was no report of any action was taken to treat the M1 rupture. Shortly after the procedure ended, the patient passed away due to M1 damage."

"In my own experience, I was using a Jet catheter and noticed that it expanded and ruptured outside of the body," one of the neurointerventionalists told *The Capitol Forum*, "a colleague of mine had a case where the Jet catheter expanded and ruptured, leading to the patient's death."

While Penumbra maintains that deaths are result of the misuse of the Jet 7 XTRA FLEX to inject contrast agent, three of the deaths reported in the MAUDE database appear to show that the JET 7 had malfunctioned in situations in which doctors were not injecting contrast media through the catheter.

A May 31, 2020, incident logged in the MAUDE database noted that "as the Jet7 was retracted under aspiration, the physician observed blood flow in the aspiration tubing (tubing). A follow-up angiogram of the left distal ICA and MCA [arteries] revealed that the distal tip of the Jet7 had broken off and had lodged in the distal pseudoaneurysm, which was actively hemorrhaging."

Penumbra acknowledges reports of malfunction. In response to the reports of increased device malfunctions, Penumbra sent a letter to members of SNIS on July 27, 2020.

In the letter, Penumbra acknowledged that the company "has received reports of Penumbra Jet 7 Reperfusion Catheter with Xtra Flex technology (Jet 7 Xtra Flex) distal tip expansion or rupture when used during injection of contrast media."

The letter warns doctors to "not inject contrast media through the Penumbra Jet 7 Reperfusion Catheter with Xtra Flex technology" and notes that the device "has not been tested for compatibility with other manufacturer's revascularization devices."

In a statement to *The Capitol Forum*, a company spokesperson said that "Penumbra actively discussed the reported adverse events and deaths with the FDA and published a voluntary Notification to Healthcare Providers with FDA's support to notify physicians of labeling changes, intended to further remind physicians about the use of the catheter and contrast injection."

According to neurointerventionalist doctors interviewed by *The Capitol Forum*, the practices Penumbra is warning against in the letter are commonplace during neurointerventional surgery. Penumbra's response, the doctors said, indicated to them that the company was trying to absolve itself of responsibility for the device failures.

"Penumbra released a statement to users of the product," said one neurointerventionalist, "Which is really peculiar, considering that is the intention of the catheter in the first place, because you inject contrast dye to see the path ahead of you to help you navigate the artery, and using another company's device is part and parcel of stroke therapy."

In the opinion of that neurointerventionalist, "I think the number of reports of this catheter suffering this kind of failure is vastly out of proportion to other catheter failures. I am aware of the other reports and other people in the neurointervention space are aware because of the SNIS letter."

Asked about any input the FDA may have had on the July 27 letter, a spokesperson for the agency said that "although we often work with firms on their public notifications, we generally do not discuss our interactions with companies," but noted that they were monitoring the situation.

Comparing XTRA FLEX issue to other Penumbra and Stryker recalls. According to the FDA, companies generally self-initiate recalls, though the agency can step in when it feels a company is not acting appropriately.

In 2017 Penumbra recalled its 3D revascularization Device due to the possibility of the wire breaking during use. The FDA classified the recall as Class I, its most serious type of recall, which indicates that "Use of these devices may cause serious injuries or death."

A review of the MAUDE database in 2017 finds that, while the 3D revascularization device had several malfunctions and injuries, it resulted in no deaths.

In April of 2019, Penumbra competitor Stryker recalled its AXS Vecta 71 and 74 aspiration catheters after several malfunctions and one injury were reported in the MAUDE database.

A spokesperson for Stryker told *The Capitol Forum* that "Stryker's AXS Vecta Intermediate Catheters (71/74) have been designed and tested to enable the procedurally common practice of manually injecting contrast media through the catheter lumen."

"We initiated a voluntary recall called a correction for these catheters after becoming aware that they may fracture if users improperly removed the product from its packaging," the spokesperson continued, "We chose to proactively issue this correction for our AXS Vecta catheters in an abundance of caution to ensure all users were made aware of proper handling techniques."

Reflecting on the FDA's role in device approval and the Jet 7, one of the neurointerventionalists said that "it's very disappointing because these are catheters that should be vigorously tested and robustly proven. That this is still on the market is a definite flaw in the system."