# Off-label use of device to prevent stroke in a-fib patients is prevalent, potentially dangerous

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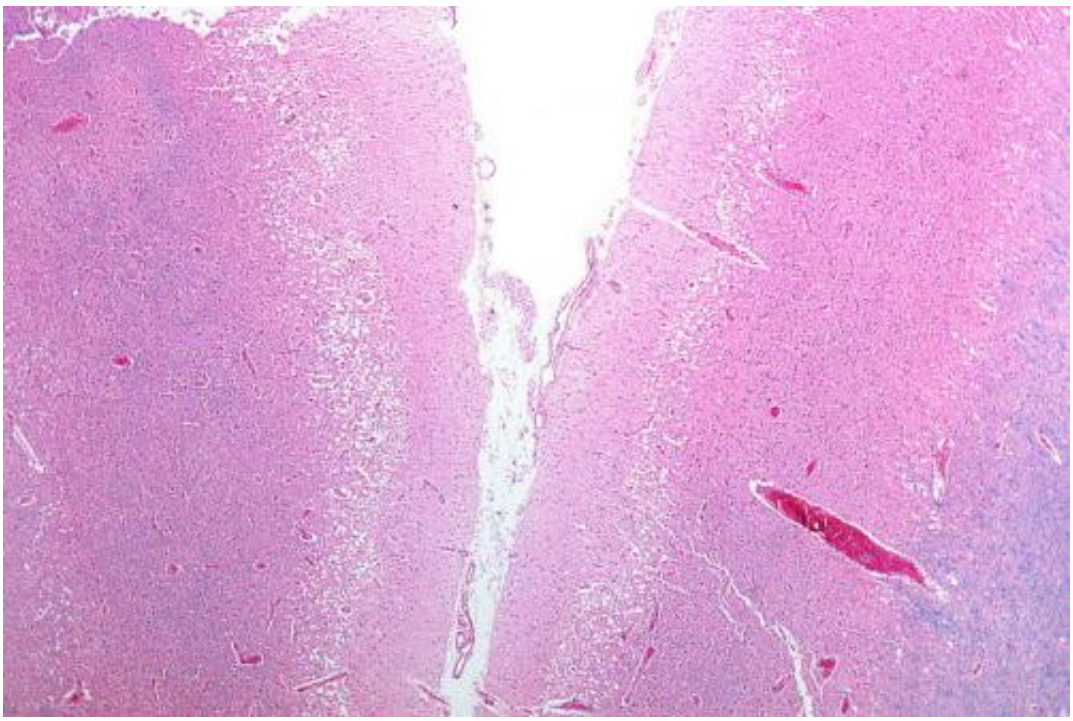

Micrograph showing cortical pseudolaminar necrosis, a finding seen in strokes on medical imaging and at autopsy. H&E-LFB stain. Credit: Nephron/Wikipedia

The Lariat device, which has been cleared by the U.S. Food and Drug Administration (FDA) for soft tissue approximation (placement of a suture) during surgical procedures, is associated with a significant incidence of death and urgent cardiac surgery during its frequent off-

label use to prevent stroke in patients with the irregular heartbeat known as atrial fibrillation. Following a systematic review of case reports and an FDA safety database, researchers at the Perelman School of Medicine at the University of Pennsylvania are calling for formal controlled investigations into the safety and efficacy of off-label use of the Lariat device, which has never been approved for treatment of this condition. Their study results are published this week in *JAMA Internal Medicine*.

"Not only do we believe that high-quality, randomized clinical trials are necessary to determine the safety of the Lariat device for off-label procedures, but our analysis raises broader issues with the FDA 510(k) clearance protocol for medical devices," said study senior author Jay Giri, MD, MPH, assistant professor in the Cardiovascular Medicine Division at Penn. "We believe there needs to be a method for reassessing the safety of a device that has been cleared for one use but is being frequently used for a different purpose in real-world practice."

The Lariat device received FDA 510(k) class II (intermediate risk) clearance for soft tissue approximation in June 2006 based on stated "substantial equivalence" with other devices used to place sutures during laparoscopic surgeries or vein harvesting. The FDA 510(k) clearance pathway does not require the rigorous testing and evaluation that is needed for full FDA pre-market approval of class I (high-risk) devices. However, the researchers say it appears that the Lariat device has never been used for these purposes. Instead, all reported instances of Lariat use have been for off-label left atrial appendage exclusion, a complex and technically demanding cardiac procedure that theoretically may decrease stroke risk in patients with atrial fibrillation who are unable or unwilling to take blood thinning medications.

"The 510(k) clearance protocol is providing a regulatory loophole that allows manufacturers to avoid full safety and efficacy testing of devices cleared for one purpose, but used in practice for another higher-risk

application," said Giri. "In addition to the Lariat, this issue could be important for other devices used in complex procedures that have been cleared through the 510(k) pathway."

The new study consisted of two sources: a systemic review of published reports, and an analytic review of the FDA Manufacturer and User Facility Device Experience (MAUDE) database. For the systematic review, the researchers searched PubMed, EMBASE, CINAHL and the Cochrane Library for any reports of outcomes associated with the use of the Lariat device for left atrial appendage exclusion. They found seven cases of urgent need for cardiac surgery following use of the device (2.3 percent of the 309 procedures reviewed) and one death (0.3 percent of the 309 procedures), with an overall procedural success rate of 90.3 percent. The analytic review of the FDA MAUDE database identified five adverse event reports that noted death and another 23 reports of cases necessitating urgent cardiac surgery.

"The Lariat is an ingenious piece of engineering for closing the left atrial appendage, but ingenuity does not guarantee safety and efficacy," added Giri. "The Lariat must be assessed as a device for left atrial appendage exclusion with randomized, controlled trials before widespread use is adopted by the medical community."

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