

Health Technology TRENDS

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Experts say device problems unlikely from most CT scans

The U.S. Food and Drug Administration (FDA) recently alerted healthcare providers that computed tomography (CT) scans may trigger malfunctions in some implanted and external electronic medical devices. *Health Technology Trends* asked imaging experts about this likelihood, and what providers could do to minimize risk.

The potential problems affect only a small fraction of the total number of CT exams. "The risk to device performance is only a problem when the CT table remains in a fixed position and the same area is scanned over and over again, with the x-rays hitting a device contained in the area of that scan," says Ella A. Kazerooni, M.D., M.S., professor of radiology and director of cardiothoracic radiology, University of Michigan Health System (Ann Arbor, MI, USA). "Examples . . . include CT perfusion scans of a tumor or lung nodule that are used to evaluate the vascular supply and vascularity of lesions," Kazerooni told *Health Technology Trends*.

Other CT experts generally concur. "For the majority of CT exams, including cardiac CT, the table moves through the scan plane during the scan; thus, the direct beam will not dwell over a device for more than a few seconds," says John M. Knudsen, M.D., assistant professor of radiology, Mayo Clinic (Rochester, MN, USA). "Based on these routine diagnostic imaging protocols, devices will rarely be significantly affected," he notes.

"The devices are not malfunctioning, but rather, the ionizing radiation is interacting with the device's electronic circuitry," notes Cynthia H. McCollough, Ph.D., associate professor of radiologic physics, Mayo Clinic. "It is an interference issue more than a malfunction issue," she says.

Background

On July 14, 2008, FDA issued a Preliminary Public Health Notification titled "Possible malfunction of electronic medical devices caused by CT scanning." The agency stated that possible adverse events likely caused by x-rays during CT scans included unintended shocks from neurostimulators, malfunctions of insulin infusion pumps, and transient changes in cardiac pacemaker output pulse rate. FDA cited adverse event reports from ECRI Institute and others, as well as experimental studies.

"There are very few reports of x-rays interfering with electronic devices during CT studies," according to Jason Launders, M.Sc., senior project officer and medical physicist, ECRI Institute. "All the reports have been of transient effects without any lasting consequences."

Nonetheless, potential problems include generation of spurious signals, including cardiac defibrillation pulses, misinterpretation of x-ray-produced signals as actual biological signals, missed detection of actual biological signals, and resetting or reprogramming of device settings. The list of implanted or externally worn electronic medical devices that are theoretically susceptible to x-rays includes, cardiac pacemakers, implantable cardioverter defibrillators (ICD), neurostimulators, drug infusion pumps, cochlear implants, and retinal implants.

According to Launders, "the effect appears to be related to the x-ray dose rate. As the scanners have become faster, the dose rate for some exams has increased."

CT scans and device interference
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FDA's recommended steps to reduce risk during CT scans include the following:

- Check for implanted devices using a low-dose scout view before a CT exam.
- Move external devices out of scan range.
- Ask patients with neurostimulators to shut off the device.
- Use the lowest possible x-ray settings.
- Make sure that the x-ray beam does not dwell over the device.

Practice impact

The safety recommendations should add little extra work, says Kazerooni, who wrote a new protocol for the University of Michigan Health System.

McCullough believes that different practices will develop different workflow solutions. "Clinical staff can screen for devices at the point of the CT scan by examining the scout images that are routinely acquired; therefore, prescanning workflow is unaffected," says McCullough.

When a device is identified on the scout image, "workflow will slow as additional interrogation will be required to identify the type of device and determine appropriate management," Knudsen says. "However, most of these situations can be managed effectively by technologists or nursing personnel through physician-directed practice protocols and policies," Knudsen says. "Nonetheless, as the use of implantable and external electronic medical devices is increasing, we can expect some slowdown in throughput for a busy CT practice," he states.

"Alternatively, a practice might wish to screen for these devices before the patient is placed on the scanner," Knudsen suggests. "While this will require more time and effort during the patient preparation phase, it may prevent unnecessary delays on the scanner," he notes.

Additional measures are warranted with life-sustaining devices such as an ICD. Kazerooni explains that as soon as the imaging technologist recognizes that a device may be in the x-ray path for more than a few seconds, arrangements should be made for a cardiologist to check the device function before the patient leaves the healthcare facility. "If an imaging facility does not have

an onsite cardiologist available to check implantable cardiac devices, these specialized CT exams should probably not be done."

Greater risk or better reporting?

"There is only scant evidence that an adverse event may occur, but it is nevertheless prudent to minimize the risk," says Kazerooni. She believes that one possible contributing factor is the increase in CT-perfusion scans. "The newer, faster scanners allow us to routinely perform tests like CT perfusion scans, which were not even possible as little as five years ago," says Kazerooni.

McCullough notes that "the reporting of even very few events runs counter to accepted dogma that CT systems do not affect such devices." Hence, FDA notification is meant to increase awareness. "This will allow a more thorough understanding of the rate of clinically significant interactions, the types of affected devices, and what risk reduction steps are most appropriate," says McCullough. "CT systems capable of producing the dose rate that we observed to cause interactions (in a limited number of device models from only one manufacturer) have been in use for almost a decade, so I do not think that changes in CT technology, utilization, or patient demographics account for the recent observation of interactions," says McCullough. "I think it is more the case that these incidents are extremely rare and were believed to be nonexistent, hence were not looked for or reported," she states.

"We will not be able to appreciate the importance of this issue unless incidents are reported to a centralized database," noted Lauenders. "Therefore, it is important that when a life-supporting medical device (e.g., a cardiac pacemaker) is scanned with CT and checked after the scan, that any anomalous findings are reported to FDA (via MedWatch) and to ECRI Institute." FDA's MedWatch can be accessed at: <http://www.fda.gov/medwatch/how.htm>. To access ECRI Institute's Problem Reporting Network, visit: <https://www.ecri.org/PatientSafety/ReportAProblem/Pages/default.aspx>. ►

Will more facilities take the full-field digital mammography plunge?

Summary

Health Technology Trends considers the impact of lighter regulatory hurdles on manufacturers of full-field digital mammography (FFDM) systems. Could this costly technology come down in price and, if so, what does this mean for facilities that take the FFDM implementation plunge?

"Images can be checked by the technologist within seconds of an exposure, rather than waiting a few minutes for film to be processed."

In May 2006, the U.S. Food and Drug Administration's (FDA) Radiological Devices Panel voted unanimously to reclassify full-field digital mammography (FFDM) systems from class III to class II status. As class II medical devices, new FFDM systems would be subject to FDA review for marketing under the less-rigorous 510(k) premarket notification process. On May 30, 2008, FDA published a draft guidance document that was open for comment through August 28, 2008. Needless to say, manufacturers eagerly await a move to ease the regulatory burden. But FFDM remains costly from an acquisition standpoint. However, with fewer regulatory hurdles, manufacturers could pass savings on to facilities, resulting in wider diffusion of this technology and market growth. The question then becomes how workflow and patient throughput could impact staff and patients alike.

Why take the FFDM plunge?

The appeal of FFDM is the ability for radiologists to view images on high-resolution computer screens (soft-copy display), which allows them to enlarge and manipulate images to review specific regions more closely. The idea is to accurately identify cancers. Images can also be manipulated to digitally correct for over- or underexposure, with a wider dynamic range than screen-film mammography (SFM), reducing the need for retakes.

Digital image storage may also be an advantage. "Archiving and storage of film is cumbersome and has to be separated from other data sources," says Jason Launders, M.Sc., senior project officer and medical physicist, ECRI Institute.

There is also the promise of increased patient throughput. "Images can be checked by the technologist within seconds of an exposure, rather than waiting a few minutes for film to be processed," Launders noted. Computer-aided detection (CAD) is also facilitated. "FFDM can be easily integrated with CAD, without hindering workflow,

which is the case with SFM," he adds. Telemammography, tomosynthesis, and contrast-enhanced mammography are also considered part of FFDM's future potential as a cancer screening tool.

However, these advantages remain to be conclusively proved. "Digital mammography has never been shown to offer an advantage over regular mammography," says Wendy Bruening, Ph.D., senior research analyst at ECRI Institute. "These so-called advantages may not exist."

The ACIN Digital Mammographic Imaging Screening Trial (DMIST) indicated no difference between digital and film mammography in detecting breast cancer for the general population of women. The study did demonstrate that FFDM is superior to SFM for certain subpopulations of patients, including women age 50 years and younger, premenopausal and perimenopausal women, and women with dense breasts (*N Engl J Med* 2005 Oct 27;353[17]:1773-1783). Further study is necessary, however, to confirm any benefit for younger women.

FFDM's big price tag

In addition, cost remains prohibitive, and could keep FFDM relegated to academic centers and high-volume radiology practices. FFDM systems range in price from \$200,000 to \$400,000, depending on features and system configuration, and annual service costs to maintain FFDM units range from \$40,000 to \$60,000. In addition, Launders, adds, "You must also add the cost of radiologists' workstations and digital storage, which are not trivial."

In comparison, SFM systems cost between \$65,000 and \$95,000, with annual service costs between \$6,000 and \$10,000. Many in the industry argue that reimbursement does not offset the investment and upkeep expenses. Currently, Medicare reimburses screening FFDM at a slightly

*Full-field digital mammography diffusion
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Full-field digital mammography diffusion.
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“It is well known that a number of manufacturers are waiting for the regulatory change to be made. When it does occur, the number of manufacturers will increase, and the cost of the units will decrease, particularly for CR-based systems.”

higher rate than SFM, but some third-party payers have eliminated the premium rate for FFDM. Could all of this change if the regulatory process changes?

ECRI Institute perspective

“At the moment, [class III] premarket approval (PMA) requires extensive multireader, multicase [MRMC] clinical trials, with patients being studied on both FFDM and SFM,” explains Launders. “FDA’s [Class II Special Controls Guidance Document] puts more emphasis on phantom measurements, but still requires some patient images. The draft guidelines are not very clear and leave a lot to discretion/interpretation. Perhaps the final guidance will be more prescriptive; however, the aim is to make it less arduous for the manufacturers.”

“I suspect some original equipment manufacturers with approval in other countries for their digital mammography systems—direct radiography (DR) or computed radiography (CR)—have been waiting for this change from a [class III] premarket approval process to a [class II] 510(k) [premarket notification] process,” stated Bonnie Rush, RT(R)(M)(QM), president, BIS - Breast Imaging Specialists (San Diego, CA, USA), and author of *MQSA Made Easy*. “It is usual for this to take place once the Office of Device Evaluation is comfortable with a technology,” she says.

But Rush isn’t sure if costs will be dropping anytime soon. “I spoke with vendor representatives at the [Association for Medical Imaging Management] conference” held July 27-31, 2008, in Denver, CO, USA, “who felt the only advantage is that it might expedite approval.” But some vendors are speculating that the reclassification reduces, if not eliminates, the need for large-scale MRMC clinical trials, prior to FDA submission. If that’s the case, Rush considered, “equipment manufacturers that have not begun the PMA process, but have been approved in other countries, may find this streamlining a benefit monetarily, due to the reduction in the submission requirements and a streamlined acceptance to establish a timeline to market units with a more specific date of availability.”

Manufacturers such as the Finnish company Planmed (Helsinki) that submitted a premarket application in June 2006 for its Nuance FFDM system, or Kodak, also in line to enter the FFDM market, “may now see the light at the end of the tunnel,” and a drop in pricing, “thus expanding the use of digital mammography systems into facilities that cannot afford the current ticket price,” says Rush.

Launders agrees. “A number of manufacturers are waiting for the regulatory change to be made. When it does occur, the number of manufacturers will increase, and the cost of the units will decrease, particularly for CR-based systems.”

In fact, FFDM’s market share is growing in spite of its price tag. FDA’s updated Mammography Quality Standards Act (MQSA) scorecard data from August 1, 2008 shows that 39.7% (3,515/8,837) of certified mammography facilities have FFDM units, a growth rate of 16.1% within 12 months (in August 2007 there were 2,090 FFDM units out of 8,832 certified facilities, or 23.7%).

Digital reality check: workload impact

“As costs continue to come down, that’s going to be the number one factor in adoption,” says Michael Linver, M.D., F.A.C.R., vice president of the National Consortium of Breast Centers, and codirector of mammography at X-Ray Associates of New Mexico (Albuquerque, NM, USA). “I think sales of digital equipment will continue fairly briskly until all the market of high-volume users is completely saturated,” he predicts. At that point, it’s going to hit a wall, because it’s very expensive technology if you’re going to be doing five to six mammograms a day in your practice.” Market forces could continue to drive costs down, something the FDA ruling could help, says Linver, but reimbursement still doesn’t quite compensate for the additional expenses. But cost is only part of it.

“Workflow is one of the biggest challenges,” Linver told *Health Technology Trends*. “Things change dramatically once an FFDM system is implemented.” Assuming a facility maintains the same patient volume, “workload immediately goes up by as much as 50%,” he says, adding that at his practice, “we’re putting in an

extra two to three hours a day.” Part of the workload increase has to do with increased interpretation times associated with the digital exams. Linver referred to the study conducted by Eric A. Berns, M.D., and colleagues, in which researchers compared SFM to FFDM processing times. Berns concluded that FFDM significantly shortened acquisition time, but significantly increased interpretation time. The total interpretation time averaged 1.4 minutes for SFM and 2.3 minutes for FFDM, a highly significant 57% ($p < 10^{-11}$). Berns and colleagues also noted more technical problems encountered with FFDM that delayed the interpretation of digital cases (*AJR AM J Roentgenol.* 2006 Jul;187[1]38-41).

Linver agrees the shortened acquisition time benefits workflow. “[The digital system] allows the technologists and those involved in obtaining the mammograms to perform their work more efficiently,” he says. “They don’t have to stand around waiting for the films to drop out of the processor.” However, efficiency has its downside. “The danger is, it’s almost too efficient. There’s a tendency to push more patients through, because we can, but this can create a factory-like environment. We don’t ever want that to be the case, because that’s probably the biggest detractor in being able to keep these women in the system, so they get their mammograms when they’re supposed to,” he adds.

Linver also says the promise of fewer callbacks isn’t realized, at least upfront. “I think most centers have the opposite experience initially, because all of the sudden everything looks like cancer.” With digital enhancement, “you see things you never saw before; especially little clusters, powdery calcifications, things that have a low likelihood of being malignant.” The instinct of the radiologist, of course, is to “act as they would if they saw this on film screen,” recommending a recall and a possible biopsy, notes Linver. “I think it takes a while to get used to the fact that you’re going to see more initially, and there’s definitely a learning curve in terms of what you’re going to accept as your new threshold of abnormal.”

As a consultant to the mammography community, Rush agrees that initial implementation of FFDM systems can be rough.

In the first year, radiologists must often make hard copy comparisons with digital studies. But beyond the curve, “facilities that go digital are able to decrease their scheduling wait times to next-day in most cases, from a timeframe of a two- to three-month wait.” Rush observed that “most of the facilities found not only that their patients were happier, but so were the technologists, the radiologists, and the referring physicians.”

Telemammography and subspecialization

However, Linver sees the benefits further down the road. “I think [FFDM] will eventually transform the way we do breast imaging in this country.” This is where telemammography comes in. “Given the continuing shortage of qualified breast imagers, and the trend toward subspecialization throughout medicine, we’re going to be seeing a need for centralization of mammography services, which will allow people with a dedicated commitment to high quality mammography to do it.” To Linver, telemammography can centralize the practice and free up radiologists who don’t otherwise want to read mammograms.

“I’ve been a long-time proponent of subspecialization in mammography,” says Linver. “It makes a huge difference if you’re seeing lots of cases and lots of cancers. You’re going to have a much better chance of finding early cancers than someone who doesn’t have that opportunity.” From centralized FFDM centers to mobile telemammography, he speculates, “these are all possibilities which may allow digital to penetrate that more difficult market that I see right now.” But given the existing political, economic, and clinical climate, Linver is not sure how long it will take to get there.

In the interim, “I think there’s some slight diagnostic advantage to digital. I think it does a slightly better job for women with dense breasts,” notes Linver. “But that has to be offset against the extra time it takes to perform a good digital interpretation. There’s no question it’s coming, and it’s a good technology, but the biggest challenge right now is the workflow issue.”

“The danger is, it’s almost too efficient. There’s a tendency to push more patients through, because we can, but this can create a factory-like environment.”

Is ultrasound the answer to catheter-directed thrombolysis?

Summary

Thrombolysis catheter systems have been around for a few years, but one company is claiming to have perfected the device by utilizing ultrasound to assist in the delivery of thrombolytic drugs to dissolve blood clots related to arterial occlusions, deep vein thrombosis, and pulmonary embolism. Yet with little evidence that this surpasses traditional anticoagulation therapy, is it worth the leap of faith?

► Ultrasound: a new wave in stroke treatment?

According to a recent article in the journal Ultrasonics, in vitro and animal studies have shown that thrombolysis with intravenous (IV) tissue plasminogen activator (tPA) can be enhanced with ultrasound, which could benefit patients suffering an acute ischemic stroke. Ultrasound delivers mechanical pressure waves to the clot, exposing more thrombus surface to the circulating drug. Small early-phase trials have shown promising results concerning the potential applications of ultrasound-enhanced thrombolysis in treating acute ischemic stroke. Potential enhancement of intra-arterial tPA delivery is being clinically tested with 1.7 to 2.1 MHz pulsed wave ultrasound (EKOS Corp., Bothell, WA, USA) in ongoing phase II and III trials (2008 Aug;48[4]:303-11).

Robert Hubert, president and CEO of EKOS, confirms that his company's small vessel ultrasound device was used to treat patients in the phase II Interventional Management of Stroke (IMS-II) study, sponsored

Venous thromboembolic disease (VTD) is common among populations in the United States, according to the American College of Physicians (ACP). It affects 7.1 people per 10,000 in the general population, with males and African Americans suffering at higher rates. Medical societies such as ACP and the American College of Chest Physicians (ACCP) agree that early anticoagulation treatment of deep venous thrombosis (DVT)—when clots form in leg veins—is optimal. Symptoms of DVT include pain, edema, skin changes, and/or ulceration. If untreated, DVT can result in pulmonary embolism—when clots in the legs break free and travel to the lungs. It also increases a patient's risk of stroke and heart attack. But these medical societies have not reached consensus on catheter-directed thrombolysis.

Traditional VTD treatments

Traditional inpatient treatment of VTD is directed at stopping further growth of the clot, and involves monitored doses of anticoagulation therapy. Depending on the patient's condition, clinicians may administer appropriate doses of heparin. Fractionated heparin is delivered with an intravenous catheter and must be closely monitored on an inpatient basis. Low-molecular weight heparins are injected without the need for patient monitoring, allowing for outpatient treatment, provided that the patient has appropriate home support. Warfarin (Coumadin), taken orally, requires daily or weekly adjustments based on blood testing, and can also be administered on an outpatient basis.

Shortfalls in traditional treatments include lengthy bouts in the intensive care unit (ICU), and the inherent risk of bleeding on anticoagulation therapy. Depending on the severity of VTD, patients can be on anticoagulation medications for more than 12 months. This is where the case is made for catheter-directed thrombolysis devices. Acute removal of the clot is thought to reduce the risk of post-thrombotic

syndrome, and reduce the amount of subsequent anticoagulation therapy.

Catheter-based technologies

Catheter-based treatments have been around for several years. Catheter-directed thrombolysis involves reliquifying the clot by putting catheters through the clot and administering blood clot-dissolving medications such as recombinant tissue plasminogen activator (tPA). Other devices use purely mechanical means (e.g., suction or mechanical maceration to fragment or aspirate the clot). Combination devices use mechanical action, along with the thrombolytics, to reduce overall time to treatment. Next generation devices promise to further reduce treatment time and overall amount of anticoagulation medications needed to reduce bleeding risk, as well as length of hospital stay.

Delivery systems can vary. For example, Bacchus Vascular, Inc. (Santa Clara, CA, USA) makes the Trellis Peripheral Infusion System, featuring two occluding balloons with drug infusion holes and mechanical drug dispersion capabilities. Arrow International Inc.'s (Reading, PA, USA) Arrow PTD features an expandable fragmentation basket designed to remove residual thrombus. Ev3 Inc.'s (Plymouth, MN, USA) Rinspirator Thrombus Removal System aspirates the debris and prevents it from moving downstream, putting patients at risk for distal embolization or future occlusions. Ev3's X-SIZER Catheter System employs a helical cutter and vacuum system to excise thrombotic debris.

Ultrasound: the new wave

The most recent device to receive 510(k) clearance is EKOS Corp.'s. (Bothell, WA, USA) EkoSonic Endovascular System with Rapid Pulse Modulation Technology, an advanced version of its earlier Lysis Infusion System available since 2005. The company has developed a catheter-directed device that uses ultrasound waves to

by the National Institute of Neurological Disorders and Stroke (NINDS). The nonrandomized, multicenter trial's purpose was to refine thrombolytic therapy for patients with acute ischemic stroke treated within three hours. "The IMS-II study shows that EKOS-delivered tPA is 40% more effective in reestablishing cerebral blood flow than standard, (non-ultrasound) catheter-directed thrombolytic drug treatment alone," says Hubert.

A total of 81 patients were treated with IV tPA (0.6 mg/kg over 30 minutes) within 3 hours of stroke onset. This IV dose was immediately followed by local infusion at the site of the thrombus, using either a standard microcatheter or the EKOS ultrasound micro-infusion catheter. A total dose of up to 22 mg was administered over 2 hours of infusion, or until thrombolysis. The 3-month mortality in IMS-II subjects (those treated with the EKOS micro-infusion catheter) was 16%, compared to the mortality of placebo (24%) and tPA-treated patients (21%) from an earlier NINDS tPA Stroke Trial. The rate of symptomatic intracerebral hemorrhage in IMS-II patients (9.9%) was not significantly different than for tPA-treated patients in the NINDS tPA Stroke Trial (6.6%). IMS II patients had significantly better outcomes at 3 months than the NINDS placebo-treated patients for all end points (odds ratio > or = 2.7), and better outcomes than NINDS tPA-treated patients as measured by the Barthel Index and Global Test Statistic. Results of the study are published in the journal *Stroke* (2007 Jul;38[7]:2127-35).

"We're also involved in the very large, IMS-III trial with 900 patients," says Hubert. The phase III randomized controlled trial is also cosponsored by NINDS. In this trial, patients suffering moderate to severe ischemic stroke will be randomized to receive either a standard dose of IV tPA, or a partial (2/3) dose of IV tPA, followed by one of three different therapies: infusion of up to 22 mg of tPA via a standard microcatheter, via EKOS Micro-Infusion (NeuroWave Infusion), or via mechanical extraction of the clot using Concentric Medical's (Mountain View, CA, USA) Merci Retriever (X5, X6, and L5). The target completion date is December 2012 (Clinicaltrials.gov ID #NCT00359424).

"We have approval in Europe to treat ischemic stroke," explains Hubert. "In the United States, we are cleared to deliver

rapidly disperse the thrombolytic agent into the center of the blood clot.

The EKOS catheter uses a pulse action, explains Robert Hubert, CEO of EKOS. "The ultrasound opens the pores of the clot, and the pulses actually push the drug into the clot, so that you get more drug into the clot, as opposed to it being whisked away to the rest of the body," he explains. The process "allows the thrombolytic to act much faster, so you have significantly reduced bleeding complications, there's no hemolysis, there's no valve damage, and your risk of embolization is hugely reduced."

EKOS' Mach 4 Endovascular Device is part of the second generation version of the concept. "In the last two years, we've figured out how to improve the system to eliminate the clot faster," says Hubert. The device delivers the drugs in the same manner as conventional thrombolysis catheter systems. "A physician inserts the guide wire, and threads the catheter over, except once the catheter is in place, the physician pulls out the guidewire and replaces it with this other 'guidewire' with the ultrasound elements in it, plugs it in and it's done. The machine does the rest." The catheter has embedded sensors, Hubert explains. "It automatically measures the temperature and adjusts delivered energy accordingly, based on the surrounding environment, and it clears the clot." With five different "therapy zones," the device can accommodate clots from 6 cm to 50 cm (2 ft).

Regulatory status

The EkoSonic Endovascular System has 510(k) clearance from the U.S. Food and Drug Administration (FDA) for "selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature" (veins and arteries in the arms and legs). A subsequent 510(k) clearance was issued for the delivery of fluids into the pulmonary artery, but there are caveats. FDA's SPECIAL 510(k) Notification issued to the company reads: "In particular, the ultrasound energy delivered by the EndoWave system is not intended to be therapeutic, nor has it been cleared with an indication for thrombolysis in pulmonary emboli." FDA stated that the safety and efficacy of the product has not been established

for this indication. Hubert says that "EKOS is not off-label for standard usage—when delivering thrombolitics to the heart or lungs. This is about 95% of all EKOS cases" (see sidebar online for more on off-label medical device usage).

Hubert says the EKOS ultrasound system is being used by hundreds of clinicians and more than 6,000 cases have been performed in major medical centers, such as Cleveland Clinic (Cleveland, OH, USA), Emory University Hospital (Atlanta, GA, USA), and Massachusetts General Hospital (Boston, MA, USA).

Adarsh Verma, M.D., an interventional radiologist at Morton Plant Mease Hospital System (Clearwater, FL, USA), has been using the EKOS ultrasound-based catheter technology to treat VTD for about two years. Recalling older, or what he calls "first generation catheter technology," Verma says, "they were just plain catheters with multiple side-holes in them. They were much faster than traditional anticoagulation therapy, but it would still take a couple of days being monitored in the ICU for signs of internal bleeding."

Verma says that with the EKOS Mach 4 model, "instead of one to two days, we're now seeing results in six to eight hours." The new Mach 4 model "can transmit ultrasound beams at multiple different intensities, so it can affect the thrombus in a more efficient manner. The previous catheter system transmitted beams at just one intensity." Verma also says patients embrace the technology. "By the time they come to us, the clinicians have already told them what to expect" with regard to the procedure. "Many of these patients have significant pain and swelling of the extremity, some are bed-ridden, and their normal lifestyles are affected," he explains. "When we tell them that, 'most likely, within days you're going to be back on your feet and the swelling will be gone,' most patients are happy."

Verma is not aware of any serious complications from the therapy other than what he calls the obvious ones. "There's a small risk of bleeding and a small risk of infection.

*Ultrasound for blood clots
(continued on page 8)*

Ultrasound for blood clots (continued from page 7)

“In the last two years, we’ve figured out how to improve the system to eliminate the clot faster.”

contrast with the device, and some physicians choose to use it off-label for delivering thrombolytics to patients with ischemic stroke, but it’s their choice.”

Concentric Medical has U.S. Food and Drug Administration (FDA) 510(k) clearance to market the Merci Retriever device to remove blood clots from the brain in patients experiencing an ischemic stroke. The system includes a flexible nickel titanium (nitinol) wire that obtains a helical shape once it is passed through the tip of the guidance catheter. In practice, the catheter/wire is passed distal to the thrombus, the catheter is removed, and the helical configuration is assumed by the wire; the clot is then trapped in the helix and withdrawn from the vasculature. The Merci Retriever is also indicated for use in the retrieval of foreign bodies misplaced during interventional radiologic procedures in the neuro, peripheral, and coronary vasculature.

The Penumbra Stroke System (Penumbra, San Leandro, CA, USA), another device used to treat ischemic stroke, uses suction and catheterization techniques to rapidly restore blood flow in the brain and limit damage caused by stroke. Its 510(k) clearance states that it is indicated for use in the revascularization of patients with acute ischemic stroke secondary to intracranial large-vessel occlusive disease (in the internal carotid and middle cerebral arteries - M1 and M2 segments, basilar arteries, and vertebral arteries) within 8 hours of symptom onset, according to FDA’s summary document.

Other than that, we have not had any major complications with this device.”

Verma says despite the FDA caveat, “there are studies out there in clinical practice that show the efficacy and safety of these catheters, and if there is a standard of care based on medical literature, these catheters certainly pass that.”

The evidence

Many of the ultrasound catheter studies are small, however, such as the Peripheral Arterial Occlusion Resolution Using the EKOS System (PARES) trial, conducted by Christian Wissgott, M.D., and colleagues at the Department of Radiology at DRK Kliniken Mark Brandenburg (Berlin, Germany). A total of 25 patients (15 men with a mean age of 64 years) were treated for acute occlusions of the lower limb arteries with EKOS Lysus Peripheral Catheter System with an ultrasound core using tPA (1.0 mg/h). Wissgott and colleagues reported a technical success rate of 100%. Total clot removal was achieved in 22 patients (88%) after a mean of 16.9 hours (range 5-24) using a mean of 17 mg (range 5-25) tPA. In 1 patient, lysis was stopped after 2.5 hours because of bleeding, and in 2 cases,

total clot removal could not be achieved and patients were successfully treated with thromboaspiration (*J Endovasc Ther.* 2007 Aug;14[4]:438-43).

Some medical societies have taken a conservative approach to catheter-directed thrombolysis devices in general. Clinical practice guidelines on treatment of VTD published by ACP and the American Academy of Family Physicians looked at catheter-directed thrombolysis, involving the administration of thrombolytics directly through the side ports of a catheter traversing the thrombus. With only one small, randomized trial indicating its efficacy (and smaller observational studies), they concluded that the evidence is insufficient to make recommendations (*Ann Intern Med.* 2007 Feb 6;[146]:204-210).

However, ACCP saw things differently, concluding that “select patients with lower extremity and upper extremity may benefit from catheter-based thrombolytic techniques,” referred to as pharmacomechanical thrombolysis. They looked at a single-center randomized trial and data registry to support the recommendation. (See *CHEST online*: 2008; 133:454S-545S) ▶

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