Trends-in-Medicine

October 2003
By Lynne Peterson

SUMMARY

The first retrievable filter in the U.S., Bard's Recovery, has been approved by the FDA, and doctors are very excited about this device, which is likely to take market share from Johnson & Johnson's OptEase/TrapEase, Boston Scientific's Greenfield, and Cook's Tulip. The IVC filter market is small, but retreivable filters should help the makret grow about 16% in each of the next two years. The key problems with retrievable filters are: medical-legal issues, lack of a code for Medicare reimbursement, lack of data, length of implant time, and cost.

Trends-in-Medicine
Stephen Snyder, Publisher
1879 Avenida Dracaena
Jensen Beach, FL 34957
772-334-7409 Fax 772-334-0856
www.trends-in-medicine.com

INFERIOR VENA CAVA FILTERS

The first retrievable filter – Bard's Recovery – was approved by the FDA on July 28, 2003. Several sources said they are very excited about the retrievable Recovery.

- An expert said, "I was the first person to put it in humans. I've placed 60 so far, and retrieved 50. Four patients died, one was removed during surgery, and three had changed situations that made removal inappropriate." (*NOTE: He didn't explain what happened with the other two.*)
- A Florida doctor said, "I'm currently using Greenfields, but I will change to Recovery when it is available, depending on the price."
- A New England expert said, "Recovery has a good design and good characteristics."
- Another expert said, "The Bard Recovery will shoot for three months, and that begins to approach a better time for explantation."
- A doctor in South Africa commented, "Recovery uses 0.013 nitinol wires, as opposed to Tulip or OptEase which have tons of wall contact and are more like a chain link fence design. With Recovery, the endothelium is just growing around a tube, making it easier to retrieve."
- A doctor in Italy said, "This can be done jugular, femoral or brachial, and the company claims you can retrieve it after a long time but doesn't say how long."
- A North Carolina doctor said, "Recovery seems to get around the idea of having to grab the hook because you can grab the entire umbrella head. So Recovery may have real benefits."

There are actually three approaches to filters:

- **Permanent**, where nothing is removed.
- **Partially retrievable**, where some portion stays and some portion is removed. A Massachusetts doctor, who has designed this type of system, said, "My filter technology fits into that. The goal with this is to extend the theoretical boundaries for removal to the lifetime of a patient. But the limitation to that is that FDA approval will be hard to obtain for the lifetime of a patient, and it may be prohibitively costly. But a company might slowly extend FDA approval on explanting."
- **Fully retrievable**, which means everything can come out, though it doesn't necessarily have to be removed. A source said, "The limitation with that is eventually there will be some tissue incorporation which will prevent or inhibit removal, and when you try to remove it, you may tear the vena cava, and the patient may die."

The vast majority of IVC filters – sources estimated about 70% nationally – are implanted by interventional radiologists. Most of the others are implanted by vascular surgeons, but orthopedic surgeons, cardiologists and trauma surgeons also occasionally use them. There is a wide variation from hospital to hospital in who uses IVC filters and how many are used. Most sources said their hospitals use only 15-20 a year, but a few use as many as 150 a year. A Florida doctor said, "IVC filter use is hospital-dependent. Some do a lot, and others do only a few." A California doctor said, "At our hospital, 100% are implanted by interventional radiologists. We use them only for patients who have failed anticoagulation or patients with documented venous thromboembolism who can't be treated with an anticoagulant." A Colorado doctor said, "Our interventional radiologists put the bulk of them in for us, but more and more people are starting to think about doing filters themselves." An Ohio doctor said, "Here, interventional radiologists tend to do them more than vascular surgeons, and that won't change with the arrival of retrievables."

USAGE GUIDELINES

The American College of Chest Physicians issues guidelines periodically on filter use, and several sources said they follow those guidelines. In 2001, the SCVIR (Society of Cardio Vascular Interventional Radiology) Standards of Practice Committee published guidelines on percutaneous IVC filter placement. The Eastern Association for the Surgery of Trauma (EAST) also has guidelines on filter use. A trauma surgeon said, "We go outside the indications in trauma, in patients where they had a clinical PE (pulmonary embolism) and are very sick. We use the Eastern Association for the Surgery of Trauma. They have guidelines for prophylaxis in high risk patients. And we wrote up some guidelines ourselves that were published in the ***Journal of Trauma*** in 1999 on bedside IVC filters, so we are using them outside the classic indications."

Sources said the key indications for filter use are:

1. Patients with DVT or PE and contraindications to anticoagulation (e.g., recent surgery, stroke, childbirth, etc.).
2. Patients with PE despite therapeutic anticoagulation (failed anticoagulation).
3. Patients with failed previously placed IVC filter.
4. Patients with significant complications of anticoagulation (intracranial/CNS hemorrhage, GI or retroperitoneal hemorrhage, heparin-induced thrombocytopenia).
5. Patients with serious lung disease who absolutely cannot afford to have any further compromise of their respiratory status (e.g., a patient with very bad COPD or a patient who has already had a massive PE). In these patients a filter may be indicated even if anticoagulation has not been tried and is not contraindicated.
6. Patients with massive PE with hemodynamic compromise, who would not be able to tolerate another, even a small, episode of PE.

Most sources said the first two of these indications are the main reasons for permanent filter use. A South African doctor said, "Indications for a permanent filter are very limited and very specific. We don't like to put things in patients that stay forever. With anticoagulation what it is now, the new low molecular weight heparin (LMWH), etc., the indications for prophylactic filters are generally pretty small, and the number of patients we find with IVC thrombus, etc., is limited." A Pennsylvania doctor said, "We pretty much follow the FDA indications. We are not retrieving permanent filters. If you are careful on indications, generally a filter is something a patient needs for a lifetime. If you choose the correct patient, there is no reason to retrieve the filter. They are very safe." An Ohio doctor said, "I tell fellows that there are only three absolute indications for filter use, and PE is in each of those…All other uses are relative, like DVT in a patient who can't have anticoagulation; I'd probably put a filter in that patient, but a lot of people wouldn't."

THE IDEAL FILTER

Sources described the ideal filter as one which is:

- **Easy to put in**, with a small lumen, small introducer catheter, a flexible system, low profile, and good visibility (easy to see fluoroscopically). An expert said, "The main thing is to have minimal trauma, ease of deployment and ease of retrieval."
- **Safe and durable**. A source said, "You want to look at the integrity of the device – fatigue testing, ability to endure a lifetime."
- **Effective at catching debris** (clots). An expert said, "It has to stop clots as the bottom line. At the same time, it has to maintain blood flow. The earliest devices trapped well but clogged and obstructed flow, causing venous disease."
- **Good at maintaining caval patency** (good blood flow).
- **Stable**, so it never moves or migrates.
- **Able to be used in a large diameter IVC**. A Florida doctor said, "You don't see a lot of mega cavas but every once in a while you have one too big for standard filters."
- **MRI-safe**.
- **Low rate of thrombogenicity**.
- **Access from multiple site**s – femoral, brachial and jugular.
- **Retrievable**. A New England doctor said, "It needs to be easy to retrieve, when necessary." A Michigan source

said, "Retrievability comes way down my list. If you select the right filter initially, then you don't have to worry about retrieving it. If you put in something with a higher occlusion rate, then you have to be concerned with retrievability." A Texas doctor said, "We use filters outside of just patients with contraindications to anticoagulants, but there is always the dilemma of weighing the advantages and disadvantages of leaving a filter in long-term, which is particularly an issue with young patients."

Doctors said the ideal retrievable filter also could be:

- Left in place at least three months or even longer. A Texas doctor said, "It is nice to be able to leave the filter in longer than two weeks. Ideally, two or three months would be nice because that's usually the duration of treatment, and we are looking for coverage for that time."
- Removed either superiorally or inferiorally.

FDA-APPROVED FILTERS

In the U.S., there are at least 10 FDA-approved IVC ***permanent*** filters, and one FDA-approved ***retrievable*** filter. Doctors described them all as fairly similar, with each having some advocates. However, it appears that the Boston Scientific Greenfield, Johnson & Johnson OptEase and Cook Tulip are the most popular right now.

JOHNSON & JOHNSON/CORDIS:

- **TrapEase.** A doctor said, "The TrapEase has a low profile and good trapping capability." Another expert said, "Personally, I like the TrapEase. I've used more of it than anything else. I just like the fact that it is easy to deploy and stable. There is not much of a learning curve on training, and it works pretty well. Some say it over-works."
- **OptEase.** A source said, "The OptEase is the same as the TrapEase plus it has retrievable potential."

COOK:

- **Gunther Tulip**. This cone-shaped filter has an 8.5 Fr profile. It was designed to be retrievable, and some doctors are retrieving it off-label, but it is not yet FDA-approved for retrieval.
- **Bird's Nest**. A Massachusetts doctor said, "The most effective is Cook's Bird's Nest, which is a jumble of wires. It is highly effective, but the thrombosis rate is too high. Bird's Nest also fits into any size vena cava (including mega size)."

BRAUN:

- **Venatech LGN**, which is the older model.
- **Venatech LP,** a newer, low profile model. A source said, "The Venatech LP has a unique design, with a very thin wire." A Missouri doctor said, "We tend to use a lot of Venatechs because they work well, are easy to use, and, for us, are the least expensive filters."

BARD:

- **Simon nitinol.** This filter was obtained from NMT Medical. It has a narrow introducer sheath (9 Fr), can be placed via the brachial or left CFV approach, and has only minimal MRI artifacts. However, it is reported to have higher symptomatic occlusion rates than the Greenfield or Bird's Nest filters, and exact filter location can be difficult to predict.
- **Recovery.** This nitinol filter, which Bard also obtained from NMT Medical, was approved as a permanent filter in November 2002. On July 28, 2003, it became the first FDA-approved retrievable filter.

BOSTON SCIENTIFIC:

- **Stainless Steel Greenfield.**
- **Titanium Greenfield.** A Florida doctor said, "The Greenfield is still the best because of what it is made of (titanium)."

RETRIEVABLE FILTERS

Even before the FDA aproved Bard's retrievable Recovery, some sources already were using permanent filters off-label as a prophylactic, *temporary* treatment for certain bed-ridden patients and trauma patients at high risk of a blood clot based on the injuries, length of time in bed, or the surgical procedure. Some doctors are repositioning permanent filters every couple of weeks to keep them from healing into the vessel wall, with the expectation that they may remove the device in the future once the FDA approves that filter for retrieval. A Colorado doctor said, "We use temporary filters a lot. We are retrieving the permanent filters. (Tulip and OptEase)." Another source said, "I know a doctor who is already taking out 10 to 15 a week." A North Carolina doctor said, We are doing retrievables now, specifically in the trauma population, if we feel there is a high risk, and we are starting to do them more and more, but still not a lot, though that may change with FDA approval…We also are beginning to talk to the total joint replacement folks about them. Hips and knee replacements are a huge PE risk, and here is a way to cover them for 10 days. They are also good for very morbidly obese patients – bariatric surgery patients. And one of the highest risks for DVT or PE is having had one before, and it is a good idea to cover those patients prophylactically around the time of the surgery if they are undergoing a general anesthetic, and then to take the filter out."

A number of other retrievable filters are in development. Most are versions of a current permanent filter. An expert said, "Both J&J and Boston Scientific are working on retrievable filters, but they are not jumping to be first, which I think is interesting." Another source said, "Several companies are working on smaller, more easily deliverable filters. You want as small a hole in the vein as possible, and you want them to be very flexible." An Italian doctor said, "The demand is for a filter than can be left in for a year. No filter currently claims to be able to be left that long." A North Carolina doctor said, "People have told me about filters that open, that are held together at the apex like an umbrella and then can unhook and open up like a stent. A couple of different companies are talking about that – one major company and one smaller one." A fifth expert said, "I tell all the companies that basically what they have to show for their product is a good safety profile, and, importantly, it has to be easy to use. Why that will be important is it will open up a diversity of potential users. If it is really difficult to use, where only an interventional radiologist can get it out, then you miss the entire surgical group. So simplicity of the procedure is important…I wouldn't discount Boston Scientific, Cordis, or Cook being very aggressive. They may have something in development that we haven't heard about."

Among the ***retrievable*** filters in development are:

➢ **JOHNSON & JOHNSON/CORDIS'S OptEase**. FDA approval is expected soon for retrieval of this permanent filter. A source said, "We have been using the Tulip, but now we've started using the OptEase a little more because the introducer is smaller." Another expert said, "I like the TrapEase, and if it is retrievable (as the OptEase), that would be attractive. I quite like the design of the TrapEase/OptEase. But it has a relatively larger lumen compared to some of the newer ones being tested." A third source said, "Cordis' next generation retrievable filters look interesting." A fourth expert said, "OptEase will have a removal limit of three weeks, which is very minimal." A doctor in Italy said, "This one can only be retrieved from the femoral route, so if you have a thrombosis in the femora, you can't go that way. It has a hook, and the direction of the hook comes out from the bottom to the top, so you cannot retrieve it form the jugular. It is interesting, but it has tremendous limitations." A North Carolina doctor said, "I plan to do a few OptEase in the next couple of weeks. One thing I like about it is it's almost always perfectly centered, but conceptually I have a problem going after it from the groin, though that is technically easier. I think there is a higher insertion-site DVT risk with an 11F catheter in the groin, but that is a wait-and-see issue."

➢ **COOK'S Tulip**. A source said he likes this because it is retrievable from the jugular approach. Another source said, "The Tulip has a really small cone, and that means pressures become high when it is full of clot, so there is a tendency to get obstructed early. That's a disadvantage." A third source said, "Cook is making some effort, but the Gunther Tulip falls short, especially on the time frame (it can be left in). It has a 10-day implant time only, which is really spitting in the wind. It's not very long, and therefore not very practical." A Colorado doctor said, "The current recommendation for Tulip is to remove or reposition it at two weeks. That's our standard. We reassess patients at two weeks, and if they are still at risk and there are still barriers to anticoagulation, etc., then we just reposition it, and that gives us another two weeks of protection. Then we reassess it again in another two weeks, and if the patient is now a candidate for mechanical methods or anticoagulation, we remove it. If not, we leave it in as a permanent filter." A North Carolina doctor said, "The Tulip can have tilting issues, and if the hook gets against the side wall, it is almost impossible to get it snared (for removal)."

➢ **BRAUN'S Venatech LP.** A source said, "The retrievable version takes the hooks off and relies on radial force to keep it in place. It has a better profile for maintaining flow than either the Bard Recovery or the Tulip." Another expert said, "Braun has some interesting technology, but it is not really removable." A third expert said, "This is interesting, but you cannot put it in through the femoral vein, only the jugular."

➢ **BOSTON SCIENTIFIC.** A source said, "Boston Scientific is working on a new retrievable filter."

➢ **RAFAEL MEDICAL'S SafeFlo.** Rafael, a small Israeli company, has a new nintinol design. Human clinical trials recently began in South Africa and were due to start in Europe in September 2003. A source said, "The biggest advantage of this filter is its reduced size, and it may be able to be removed at a longer interval. It is not transformational, but it has some advantages." Another expert said, "This filter is absolutely interesting because if you are unable to retrieve all of the filter, you can retrieve just the active part, and you can leave the fixing part because it is just a ring. That is a fascinating design. It is very innovative. It is very interesting, very impressive…I am enthusiastic because you can pull it from the jugular, femoral or brachial vein…(but) it requires more skill."

➢ **CLEVELAND CLINIC**. Doctors at the Cleveland Clinic are working on their own design for a small retrievable filter.

➢ **ALN**, a French company. A source said, "The problem with this is the construction. It can tilt and that causes contact between the head of the filter and the wall of the vena cava – and endothelialization of the head – so you can't retrieve it after six months or even less. They claim you can retrieve it when you want, but that is not true. The resistance of the flow is low, and the flow is high. It is hand-made, and sometimes one unit looks different from another. And the deployment kit is not as kind as American or Japanese kits; it is primitive. The envelope also is very bad."

MARKET OUTLOOK

Sources estimated that about 100,000 IVC filters are placed each year in the U.S., and use is slowly increasing. Not every source is happy with this trend. A California doctor said, "Filter use is slowly increasing due to ignorance on the part of doctors who don't know that filters do ***not*** work well."

Usage is much lower in Europe. Sources said this is due to cultural differences, cost, and greater European use of LMWH. A doctor said, "The U.S. is 80% of the market. France and Germany are the majority of the rest of the world, France especially." Another U.S. expert said, "It is a different culture in Europe. In Edinburgh, for example, people over age 70 are not dialyzed. The way we practice is very different in the U.S., so it is not just cost. It is partly cost, but partly a different culture." A third source said, "Europeans treat patients very differently from American doctors. We are a bit more aggressive in this country. We do tests they don't do. And it could be there is better marketing here." A fourth expert said, "Europe had LMWH well before we did, got very comfortable with it for DVT, were willing to use it in situations we still balk at. They used LMWH in orthopedic knee and hip replacements early on, and even today a lot of U.S. orthopedic surgeons are loathe to use heparin pre-operatively. So part of the reason Europeans use fewer filters is that they feel they can prevent disease – and if you don't look for a DVT you might not find it."

With the FDA approval of retrievable filters, most sources predicted that filter use would increase substantially. A South African doctor said, "Retrievables will make a difference, and change the indications. I don't want to put a permanent filter in a 20-year-old patient with DVT because I don't know what that filter will do in 20 years…But we have a long way to go before retrievable filters become routine. There are still indications for permanent filters that are fine, though that will change with the advent of temporary filters. But you can get into a Catch 22 very easily with retrievables." A Canadian doctor said, "If someone tells you there is no reason to remove a filter, ask if he would want an IVC for the rest of his life, and the answer would be clearly, no." A Florida doctor said, "The new retrievables are changing the whole game. In the past, in young patients with multiple traumas, doctors were very reluctant to put in a filter because it would be with them for 40 years, but now you can put in a filter to prevent a PE from a DVT and can take it out 6 to 12 weeks later." A Texas doctor said, "FDA approval of retrievable filters will not increase use because doctors are already using them off-label. But as there is more and more talk about retrieval devices, use will go up. It's not the FDA approval that's key." A Colorado doctor said, "The concept of retrievability is attractive, and as more people become familiar with retrievables, I think people will become more aggressive in using them." A New England doctor said, "There will be a revolution in usage when FDA-approved removable filters that are practical hit the market." A Texas doctor added, "It is the gray areas where retrievables will come into play."

In 2004, with at least one retrievable filter available, sources estimated that filter usage in the U.S. will be an average of 16% higher than in 2003, or about 116,000 units. In 2005, sources predicted usage will increase, on average, another 16%, to about 135,000 units. Retrievable filters are likely to become a larger and larger share of the market, but sources do not believe they will totally replace permanent filters, at least over the next few years. A Massachusetts doctors said, "Removable filters will probably double the market in terms of usage. Removable doesn't mean the filter can't be left in; it just gives us more flexibility." A Florida doctor said, "Next year, filter use could go up 20%-40%, and of the 130,000 of so filters, perhaps 50%-70% would be retrievables because we can use them as permanent filters as well. Retrievable filters offer great promise, will get much more widely used, and will bring benefits to a lot more patients." Another Florida doctor said, "When we can remove filters, we'll be more aggressive in where we use them in primary prevention…Next year, use is only likely to increase 5%-10%, but in three to five years, it will be double or triple the use today because the indications for filters aren't that much now." A Texas doctor added, "The increase will occur in removable filters; traditional filter volume will go down as retrievable volume goes up." A North Carolina doctor warned that retrievable filter may take time to catch on, "It is amazing how slow things are to catch on. I've been doing filters in the ICU for seven or eight years, and it is still rocket science for some people. It is actually a pretty easy procedure, and there is no reason you can't do it in the ICU, but that trend has been slow to come along…We need a couple of studies of prophylactic use in particular patient groups to get the kind of patient numbers we need, so it will take a while before they catch on." A Missouri doctor said, "The use of temporary filters is likely to increase the most, and these will be used in younger patients who might benefit from short-term protection, but in whom we don't want to leave a permanent device."

The key factors limiting broader IVC filter use in the U.S. are concerns about:

- **Efficacy**. A California doctor said, "They don't work very well, There is little evidence they prevent death, and no evidence they prevent PE, and they cause DVT in the legs." A Massachusetts doctor was more positive, saying, "They are effective. With the current designs, the failure rate (emboli) is less than 1%-2%. The more effective a filter is, the more chance of thrombosing." Another source said, "Recurrent PE with a filter in place is around 3%-5%."
- **Cost**. A Colorado doctor said, "They are not cheap. In addition to the device, and the kit, there's the radiology cost. Our protocol is to do a venogram when they get a filter, and before when it is removed."
- **Permanency**. A Miami doctor said, "It is a permanent implant, and we want to be absolutely sure when we put in a permanent implant. When patients get healed, they can't be removed."

- **Appropriate patients**. A Pennsylvania doctor said, "The technology doesn't limit use; it is the number of patients in whom filters are appropriate. For this type of problem, anticoagulation therapy is very good and effective. The role of a filter is for people who can't take or who failed anticoagulation therapy."

Experts cited several specific problems with ***retrievable*** filters, including:

- **They could be a fad.** A Michigan expert believes the popularity of retrievable filters will increase sharply and then quickly fade. She said, "There will be a huge jump in use when retrievables are on the market and approved, but I don't think that will be long lasting…I think once we are past the novelty, we will get down to the real need. So I think there will be a blip, with perhaps a 10%-15% increase in 2004, but that will peak in 2004 and no incremental increase after that."

- **The medical-legal implications are poorly defined.** An expert said, "Retrievable filters work fine. The problem is a medico-legal one. No one knows the exact time the risk goes away. If you put a temporary filter in, take it out two weeks later, and the patient has a PE in four weeks, will you get sued? I think a lot of them will be left in for that reason. If the patient is healthy, it is more likely they will be retrieved, but it will be a tough judgment until we get more data on when to take them out." Another doctor said, "Lawsuits are a concern, but patients who have a DVT need to be anticoagulated if at all possible. Even with a filter, they need anticoagulation. So, you use a permanent filter when you can anticoagulate, and a temporary filter when you can't anticoagulate temporarily." A third expert said, "I think a lot of companies will get on the (filter) bandwagon, hoping the fear of lawsuits for not using a filter when it is available will spur greater use in the U.S. than elsewhere. But we may do a lot more harm than good. A lot of these things are very new, and there is not a lot of long-term follow-up. You don't know what these things will do when you put them in young patients. If you find a clot in the filter, is it thrombus or a clot caused by the filter? How do you know the difference?" Another doctor said, "The lawyers are working with us now, and I've spent some time in court because they called me as an expert witness…If the referring physician recommends you take out the filter and prescribes anticoagulant therapy, and then the patient dies, you probably will be in trouble." A North Carolina doctor said, "It will all come down to informed consent."

- **There currently is no Medicare reimbursement code for removal**, which costs about $3,000-$5,000. This means that doctors and hospitals cannot get paid for removing them from Medicare patients. A source said, "Reimbursement on taking them out is still up in the air. If doctors are not reimbursed, they won't take them out."

- **Patient attitude.** Patients may be unwilling to undergo another procedure to have the device removed.

- **Cost.** Retrievable filters are expected to cost more than permanent filters, and there will be a second charge for a retrieval kit. Several sources worried that insurance carriers won't pay for retrieval. A source said, "Finances are an issue. First you pay for the filter, and then you have to pay extra – double – to retrieve it. We need to convince the manufacturers that they should include the retrieval kit with the filter." Another expert said, "My suspicion is that individual hospitals will have stock issues. Why do I need to buy six different filters? A lot of hospitals go with one vendor. If you can leave that filter in or take it out, that is the one I would prefer. Right now retrievables have a permanent indication, and that gives you more flexibility. Having the option of being able to take it out is a great thing. But if it costs more, that will be a problem. Bard tried to convince me I should use Recovery, but when the sales rep said it cost $300 more, I said, 'There is no data to say it is better than the ones I have. So, it comes down to price or I can't use your filter.' Companies won't be able to price themselves out of the market. We know the price of Tulip and OptEase, and we have a lot of experience with them, which is a big advantage over Recovery."

- **Need for careful assessment.** A doctor in South Africa said, "You need to be careful of thrombus on the filter. If you are going to retrieve the filter without assessing that carefully, you can actually cause an embolism. You need to do proper venography in at least two places. There is no safety mechanism like a balloon or net to catch any clots you dislodge."

- **Possibility of conversion to permanency.** A doctor may intend a filter to be retrievable but may have to leave it in. A doctor in South Africa said, "I honestly believe we should be conservative in our use of filters, even if we had retrievable filters. If a patient gets a clot with a retrievable filter, or it captures a DVT, then it becomes a permanent filter." However, another source called this an advantage, not a disadvantage: "There is no downside for retrievables because you can leave them in or remove them." A California doctor added, "Retrievable filters sound nice, but they are rarely retrieved."

- **Lack of data.** More data and more experience is needed before retrievable filters will be used more frequently, sources said. A Colorado doctor explained, "Attitudes are starting to change. Most of the experience to date (with retrievables) has been in Canada and Europe, but now we are starting to use them more in the U.S. As more and bigger studies come out, showing that they are safe and more than likely effective, that is what will make people think of using them." A Texas doctor said, "Most referring doctors have no idea you can take them out at this point. And there was bad press in the past that some filters occluded, so use of filters has been tempered by occasional complications related to leaving a filter in a long

time. Many of our referrals are from hematologists, and they are aware that filters thrombose occasionally, so we need to educate doctors, the referring doctors, much more than the doctors who use them." A Missouri doctor said, "Better data (i.e., long-term, prospective, randomized trials) would be needed to increase the use of permanent filters. Marketing would help increase the use of temporary filters. So would letting doctors know that temporary protection is an option for their patients."

➢ **Length of implant time.** An expert said, "Conventional therapy with warfarin and heparin is a minimum of three to six months, so filters with a shorter implant time fall short of optimal therapeutic time."

Retrievable filters are likely to encourage doctors other than interventional radiologists and vascular surgeons to use them, but interventional radiologists are expected to remain the major users. Use was predicted to increase by neurosurgeons, trauma surgeons, interventional cardiologists, and bariatric specialists as well as interventional radiologists. A Colorado doctor said, "In trauma circles, people are very interested in these because standard prophylactic methods don't work very well." A Canadian doctor said, "It has been and will continue to be a turf issue. As an interventional radiologists, I would argue that it should be our domain because of the technical complexities, but clearly some vascular surgeons are competent." A Massachusetts doctor said, "I can see general surgeons and trauma surgeons placing them. And bariatric surgeons may place them. With time, they may be placed by intensivists; that may be the trend in the future." A Florida doctor said, "Retrievables will be widely used by interventional radiologists. Surgeons up to now have not been advocates of retrievables, but that might change, with increased use in ICU patients who don't get them now because of age or because they don't quite meet the indications for a permanent implant. For those patients, there will be more filter use with retrievable filters – any cadre of sick patients in whom we don't want to give high doses of an anticoagulant or who need freedom from emboli."

The types of patient indications also are likely to expand; retrievable filters are expected to have particular appeal for cancer and trauma patients. A Massachusetts doctor said, "When removable filters hit the market, it will create a huge range of cases that weren't there before, such as (a) trauma patients with long bone fractures and multiple injuries who can't be anticoagulated because of internal injuries or bleeding potential, or (b) patients with elective surgery like obesity which has a high risk of clotting problems and can't be immediately anticoagulated for a variety of reasons." A Texas doctor said, "There is huge potential in trauma." A Canadian doctor said, "Patients will be predominately high risk, pre-op, young, trauma, neurosurgical patients with a well-defined risk. Obesity is a specific key population that could benefit...But retrievable filters shouldn't really affect how filters are used. There are fairly accepted indications for filter placement, and having temporary filters available shouldn't change that. The only difference is that now someone might be more inclined to place a filter in prophylactic patients, where before a 23-year-old girl might not have gotten one…In trauma, burn and neurosurgical ICU patients we previously we didn't want to put a filter in a young person. We would just watch and anticoagulate as best we could. Then, if they developed a clot, we would use a filter. Now, we can identify an at-risk population and reduce the number of patients who die from PE." A Texas doctor said, "Filters will be used a lot in trauma and in patients who need situational prophylaxis – patients with a very short window where we need to protect the patient." A Florida doctor said, "Retrievable filters will increase use for really sick patients undergoing a known risk for a short period of time, pregnant women with leg blood clots, and moderate risk ICU patients who will improve in a week or two where we have been reluctant to put in a permanent filter." An Italian doctor said, "Cancer patients are living longer, especially elderly patients. As you treat those patients, you drop in some complications, like DVT for lung cancer…DVT is the enemy of cancer treatment, so a retrievable filter is more attractive (for those patients) than a permanent filter. I put more than 50 retrievable filters in each year."

In addition, newer filters may allow bedside placement. A Texas doctor said, "We and others want to do it at bedside, using external ultrasound guidance or IVUS (intravascular ultrasound), which is just beginning, particularly in very ill patients where moving them is a problem. But bedside placement is experimental." A Massachusetts doctor said, "There will be different imaging techniques in the future, and accessory devices for deployment, so it can be done, for example, in the ICU – techniques like ultrasound for vascular imaging that allow bedside placement."

Two sources warned against overuse of filters – whether permanent or retrievable. One said, "DVTs are difficult to diagnose in those patients because of other injuries. That's where the increase in filter use has been impressive over the last five to eight years, and where some doctors got overly aggressive in patients without disease yet, and whose risk wasn't clearly defined yet…Retrievables are not a good idea. In this country, there is no approved retrieval system for a filter, even though some can be retrieved. It's off-label use, though that's not stopping people. I run into doctors all the time who say they retrieve filters, and I say, 'You are brave.' The bottom line is the risk of having a second DVT or PE is real, and the timeframe for the event can vary – up to six to eight weeks or more. So, if you take a filter out at two to four weeks, and the patient goes on to have a PE, you have a very weak position legally and morally." Another expert commented, "My own personal opinion is that we don't really need retrievables. I can see the concept that while patients are bedridden in the hospital, in a temporary state of immobility, then the risk of developing clots in the large leg veins is increased, the blood is not moving around as fast, and clots

can form, which can then flip to PE. So, right now we do tremendous prophylactic care to prevent that from happening, with anticoagulation therapy, stockings to compress veins, and devices to intermittently squeeze on the legs to keep blood flowing – and that works pretty well. The argument is that with immobile patients you don't want to use existing devices; you could put one in temporarily. I understand that argument, but I don't see that as a big argument because patients do well, and a retrievable filter would only prevent PE but not prevent clots from forming in the legs, and we want to do both."

Most sources agreed that there is nothing on the near horizon that is likely to make filters obsolete. An expert said, "There will be a lot of new anticoagulants, but unless they diminish the complication rate significantly, they won't have an impact (on filters)."

One source suggested that AstraZeneca's Exanta (ximelagatran) may have an impact on filter use when and if it is FDA-approved. She said, "It is not an anticoagulant but an antithrombotic. You will have less risk of bleeding than you would with an anticoagulant, so I think people will use it in situations where you could or would not use an anticoagulant. It will directly compete with the contraindication for coagulation as an indication for a filter. And where it may have the most impact is on retrievables." However, most other doctors disagreed. However, other souces disagreed. One said, "I don't see Exanta changing things. I would still be loathe to give any anticoagulants to patients who had recent surgery."

The Choice of Filter

Because IVC filters are a low volume item, doctors generally can choose the filter they want, sources agreed. Some companies have been trying to bundle filters in with other products, but sources said most hospitals stock more than one filter – whichever ones the doctors request. An Ohio doctor explained, "Purchasing follows the advice of our doctors." A Michigan source said, "We stock probably three or four different kinds that are used in special situations. The bulk are Greenfields, but we also have others available." A Florida doctor said, "At our hospital, the physicians make the choice, but they have to go through the New Products Committee." A Massachusetts doctor said, "Currently, I'm using Greenfields. We put in fewer than 20 a year at our hospital, so even if the number doubles, it is not a lot. So, there is not a lot of pressure to bundle them, make deals or have pricing as an issue."

Brand name is not as important as quality and data, sources said. A California doctor said, "There is no good data comparing filters." A New England expert said, "The quality of the product and scientific data to support it is what's important." A Florida doctor said, "Brand name is not important if it works. But bundling is a big issue here. If Boston Scientific is selling a lot of stents and gives us a good price on this, then that becomes a selling factor."

With major companies such as J&J, Boston Scientific and Bard offering filters, it would be difficult for a smaller company to sell a retrievable filter. Thus, sources expect any good design to be sold to a larger player. Sources had mixed opinions on the outlook for a new player:

Difficult. A Florida doctor said, "It would be very hard. J&J has an enormous presence." A Michigan source said, "Smaller or newer devices coming through will have a harder time. If it is the widget company with one product, someone will buy it. The small company won't take it to market." An Ohio doctor said, "A small company will develop it, and then they will get bought out by a bigger player. But a mid-size player could do it…Most small companies have trouble beating Boston Scientific, Cordis or Guidant, so small companies are all looking to be purchased." A Massachusetts doctor said, "I have a patent that was published in January 2003 for a removable filter, but unless a minor player is able to develop a platform to bring a filter to the masses, it won't constitute much of anything." A Texas doctor said, "The challenge is to be able to afford to run the clinical trials. A smaller company could sell it, but it would have to create a stand-alone package with sheath, dilator, etc."

Possible. A Canadian doctor said, "Sure, a smaller company could do it, but it takes time to get a retrievable filter approved." A Pennsylvania doctor said, "I think a small player could enter the market if it had something fast, easy, and small. People might pay extra for the retrievable option."

The Regulatory Path for Retrievable Filters

As mentioned above, the first retrievable filter was approved in the U.S. on July 28, 2003. A Canadian doctor said, "Some recent filters have gotten through fairly quickly. I was surprised that the original TrapEase was approved on 64 patients and a short trial period. But retrievables have been more complex and gone slower…It is not a one-year process. I think Bard started in 1994 (with Recovery). J&J's OptEase has been in the works for a couple of years, and now it is in human clinical trials."

The FDA does have **guidelines** as to the route of approval for IVC filters, but at this time, they relate only to permanent IVC filters. The permanent filters are cleared via the 510(k) process. There was a recent decision to allow marketing clearance of the temporary filters via this route, as well. However, an FDA official explained, "The temporary filters (and permanent ones that are not substantially equivalent with respect to design or other features that may introduce new safety and effectiveness issues) require clinical data for clearance."

The **size of a trial** needed for IVC filter approval, depends on the claims to be made or features of the device. An FDA official said, "If the filter is basically the same as others, we may need little or no clinical data. If it is markedly different, or has a unique feature or claim, we may need a statistically valid study, with several hundred patients. We always want good clinical practices and design, such as multiple users, to ensure that removal/retrieval is feasible in the hands of several different physicians, for example. A larger sample size is always better than smaller, and a randomized design is always better than not. We recommend early interaction in this area."

The **length of a pivotal trial** used for FDA approval, depends on what the company wants to show. An FDA official said, "The goal of a study for a temporary IVC filter would be to determine the optimal time for removal. Many designs become embedded in the tissue after some critical period, and removal would be problematic after this period. After that period is established, we would want some additional follow-up to determine if the removal caused any problems, such as late thrombosis due to damage of the vessel. We anticipate that most problems that may occur would be observable soon after removal, and would result in either an adverse event that is correctable, or one that could need further surgical correction, or would correct itself after a healing period. Depending upon whether there are data already existing for the design as a permanent device or not, the period of follow-up may vary, but the minimum should be 12 months."

Some but not all of the FDA **requirements for retrievable filters** will be different from that required for permanent filters. An FDA official said, "The optimum time point for a retrieval endpoint would be different, and there may be adverse events that relate to the removal, but the anticipated adverse events would otherwise be the same for both permanent and retrievable filters, so the study would be similar, and the adverse events to be assessed would be similar after removal. Also, some additional bench and animal testing would be needed to assess removal."

Asked **how much data** (and what type of data) would be needed with a retrievable filter to show that it can be retrieved without losing the clot, an FDA official said, "In all likelihood, if the clot was lost, it would cause a pulmonary embolism, and result in a serious adverse event or death. A warning is recommended against removal when there is a large amount of clot in the filter. As we monitor adverse events for these types of devices, we may recommend more rigorous assessments."

Companies can get **expedited review** of their retrievable filter provided certain criteria are met. An FDA official said, "A submitter of such an application would have to provide FDA with justification for why an expedited approach is warranted, and we would take each case into consideration. Since we have made the decision to clear them under the 510(k) route, this route is shorter/more expeditious than the PMA route."

The criteria for expedited review are:

1. **The device represents a breakthrough technology.** The medical device represents a ***clear, clinically meaningful advantage*** over existing technology. A clear clinically meaningful advantage is defined as having major (not incremental) increased effectiveness or reduced risk compared to existing technology. In order to meet this criterion, the device should have been evaluated utilizing well defined, clinically meaningful outcome measures or acceptable surrogates for such measures.

2. **No approved alternative exists.** That is, no legally marketed diagnostic/therapeutic modality is available for the intended patient population.

   NOTE: Applications in this category that are granted expedited review status will not only be placed at the beginning of the review queue, but will also undergo accelerated evaluation as review staff are available to be assigned.

3. **The device offers significant advantages over existing approved alternatives.** This criteria would apply to a device which provides for clinically important earlier diagnosis or offers important advances in safety and/or effectiveness over existing alternatives.

4. **The availability of the device is in the best interest of the patients.** For a device to meet this criterion, it is expected that the device would provide a specific public health benefit or meet the need of a well-defined patient population. For example, this criterion would apply to a device designed or modified to address an unanticipated serious failure occurring in a critical component of an approved device for which there are no alternatives, or for which alternative treatment would entail substantial risk of morbidity for the patient.

However, the FDA considers a temporary filter to have a different indication than a permanent filter, and therefore, a "Special" 510(k) submission would not be appropriate. ♦