PAUL A. FRIEDMAN: Hello, my name is Paul Friedman, Professor of Medicine at Mayo Clinic, and Director of the Implantable Device Lab. I'll be joined today by Dr. Yong-Mei Cha, also Professor of Medicine and Co-director of the Implantable Device Lab. And by Dr. Sam Asirvatham, Professor of Medicine at Mayo Clinic, and Director of Cardiovascular Innovations.

Today, we'll be looking at some of the challenges and innovations to solve those challenges involved with cardiac implantable device therapy. We'll first review what the challenges are. And then we'll talk about the new and emerging therapies designed to overcome those challenges. Specifically, we'll discuss the subcutaneous implantable defibrillator, leadless pacemakers, and then epicardial and intramyocardial technologies-- some technologies that we've been developing here at Mayo Clinic.

When we look at the incidence of cardiac device implantation over the past 20 years or more, we note that in both men and women, there has been an increase in the use of device therapy. This increase is the result of a number of trials showing improved outcomes in terms of morbidity and mortality with use of pacemakers, defibrillators, and more recently cardiac re-synchronization devices in a number of cardiovascular disease states. Despite this growth, we recognize that there are important limitations to device therapy that may ultimately limit their growth if they're not overcome.

When we think about these limitations, we think about what the perfect lead in device would look like to overcome them. So the key challenges in device therapy are first, when we place leads across the tricuspid valve, it can sometimes cause severe tricuspid regurgitation. The lead can impinge on leaflet motion, and at times become so significant that cardiac surgery is required to reposition the lead and replace or repair the valve. Therefore, an ideal device perhaps, would have no leads so that there would be no lead failure rate.

Another issue is that when leads are placed within the vasculature, there is a risk of bloodstream infection. When there is a bloodstream infection, the leads must be extracted. Given that the leads are fibrosed to great vessels and to valves, extraction is associated with the risk of mortality, of damage to the great vessels, of damage to cardiac tissues, valves, myocardium, and the need for surgery.

Additionally, many patients with devices will ultimately require an MRI image. MRI scanning is challenging, and has traditionally been contraindicated in patients with pacemakers and defibrillators. While some newer models permit this form of imaging, it does remain a challenge. Moreover, leads can form thrombus and clot. And in patients with intracardiac shunts, intravascular leads pose a risk of thromboembolism and stroke. So the ideal system would overcome these challenges, yet still be able to deliver pacing, re-synchronization, and defibrillation therapy.

I'll start by reviewing the totally subcutaneous ICD. In contrast to a traditional system with intravascular leads, the system can be placed without fluoroscopy, landmarks are used, and a lateral incision is placed to identify the pulse generator position. The pulse generator will ultimately sit near the midaxillary line. After that incision is made, a xyphoid incision is made, and the lead is tunnelled from the pocket to the subxyphoid position. The subcutaneous system has a lead, but it is not intravascular. The lead sits just outside of the rib cage, is secured in strategic positions by two additional mid-line incisions, and records the signal generated by the heart without actually touching the heart.

The subcutaneous ICD has the advantages of simpler extractability should extraction be required, put a potential advantage of the ability to obtain MRI scans without concerns about cardiac tissue injury or pro arrhythmia. But it doesn't have the depth of experience that transvenous ICD's have. And we don't know as well their long term outcomes in performance with regards to arrhythmia management. The available information however, suggests that it is well tolerated. It is currently approved in the United States by the Food and Drug Administration. This slide on the left demonstrates a kind of incision that's typically seen in a patient following subcutaneous ICD implantation. Here, we see two X-rays of different patients showing the traditional position. The device is in the midaxillary line on the left. And here's a subcutaneous lead up the midline of the sternum. And here's a lateral view.

Now, the totally subcutaneous ICD has several advantages. In the event of infection, extraction is simplified. There is no risk of valve injury. And there is no risk of thrombus caused by the device in patients with the intracardiac shunts In patients with absent vascular access, the system can still be implanted. However, these advantages come with limitations. There's very limited pacing support, briefly aftershocks, transthoracic pacing, which is uncomfortable can be delivered if needed. There's no anti-tachycardia pacing, which has been shown to painlessly terminate rather ventricular tachycardia episodes. And cardiac re-synchronization is not an option.

Detection specificity, that is the risk of inappropriate shocks, is less well-established. Although, it appears to be similar to that with standard devices. Patients do need to undergo a screening surface ECG to see whether they're candidates for the subcutaneous ICD. Although, over 95% of patients will pass that screen. We currently lack randomized trials comparing subcutaneous ICD's to ICD's. Although available data suggests similarity in performance.

In some of the data that are available in this case control trial, note that the age of patients receiving the subcutaneous ICD tends to be younger. Although, in this case, they were matched-- but at 46 years younger than the standard ICD age. And notice also that a much smaller percentage of coronary artery disease reflecting the tendency to favor these devices in younger patients who are more likely to have channel apathy or hypertrophic cardiomyopathy with an expected prolonged longevity and thus concern about lead failure with intravascular systems.

Here, we see two examples of patient shocks. In the left panel, we see an episode of a ventricular tachyarrthymia that was appropriately detected and terminated by a shock. On the right panel on the other hand, we see T-wave oversensing, which in the early iteration of the device was seen more commonly and has since been diminished with software changes. This gives an example of the type of screening performed for the subcutaneous ICD where standard electrodes are placed in the positions that mimic the subcutaneous devices recording sites. And thus, a template can be made to determine whether the T-wave will be excessively large.

So in summary, the subcutaneous ICD may be particularly useful in patients with congenital heart disease, in patients awaiting transplant, in younger pediatric patients where transvenous leads are less desirable, in patients with a previously infected transvenous system, and then in selected primary prevention patients. Next, we'll turn to the leadless pacemaker, and Dr. Yong-Mei Cha to tell us about it.

YONG-MEI CHA: I'm Yong-Me Cha, one of the electrophysiologists at the Mayo Clinic. So in the next few minutes, I'm going to discuss leadless pacing-- the future of bradycardia therapy. This is my financial disclosure. In 1958, the first implantable epicardial pacemaker was placed in a patient in Sweden. He went on to receive 26 different pacemakers during his lifetime, and died at age of 86. Actually, he was out living the inventor as well as the implant surgeon.

Four years later, the first transvenous lead was placed in conjunction with a pacemaker. Over five decades, the lead technology has evolved substantially. The passive fixation lead is one of the commonly used leads. As you can see, a few ties at the lead tip that can anchor of the lead into the myocardial trabecular prevent the lead from dislodgment. The slowly released steroid eluting tape reduces the tissue and lead interaction. Active fixation lead has a small screw at the tip of the lead. This is a left of ventricular lead that is placed into the coronary venous branches and for the purpose of bi-ventricular pacing.

Despite advancement and technology in the lead system, the permanent transvenous lead is associated with the morbidity and mortality as Dr. Friedman has before mentioned. The lead placement can cause perforation, dislodgment, in the long term the lead can fracture, malfunction, cause venous abstraction requiring lead extraction. And they can also cause tricuspid valve regurgitation. With all these issues, wouldn't that be nice if we had a pacemaker without a lead?

Actually, the concept of leadless pacemakers was proposed 40 years ago. This was an original article published in 1970. And shows a small tiny leadless pacemaker only about two centimeters long. Now, 40 years later, the leadless pacemaker is becoming a reality. This is a Medtronic designed leadless pacemaker. It's 24 millimeters long and 20 French in size that can be delivered through a long sheath from a femoral beam. And as you can see, there are four barbs functioned to anchor the device to the myocardium. The estimated battery life is about 7 to 10 years. And as a fourth generation device, it only serves as a single chamber pacemaker.

And this is the Nanostim from St. Jude Company. And as you can see, is as small as one cc and only weighs two grams. It's also a single chamber pacemaker with adequate longevity time of more than seven years. That device was designed compatible with the current Merlin programmer and it's retrievable as well.

So the advantages of leadless pacemaker is it does not require surgery, less invasive, fewer complications, the reduce lead traffic, venous obstruction, and the potential of infection, and avoid across native or bioprosthetic tricuspid valve, and avoid potentially lead extraction associated complications. In conclusion, physicians and the industry have envisioned leadless pacing for over 40 years. Technological advances and the convergence have now made the concept of leadless pacing realizable. We anticipate a human study will begin in 2013. And we're looking forward to the outcome of this device's clinical application.

SAM ASIRVATHAM, MD: I'm Sam Asirvatham, one of the cardiac electrophysiologists. You've heard from my colleagues, Paul Friedman and Dr. Yong-Mei Cha, about the challenges for cardiac devices today. I'd like to focus now on where some of the innovations that are unique to Mayo Clinic may fulfill some of these needs.

We know the epicardial space has some advantages for placing implanted leads. We wouldn't be in contact with the vasculature. Infections wouldn't be as much of an issue. But at the same time, innovation is needed in order to prevent damage for example, to the coronary arterial system or stimulation of the phrenic nerve, which runs in the parietal pericardium. One of the technologies developed tries to address these issues. The key is a special steerable sheath that can be placed into the pericardial space and then angled towards the myocardium with electrodes to help us find the best site to actually place the lead.

In addition, other elements like a doppler can be used to be sure we're not near the vasculature. Innovation for lead design once we're in the space is also needed. For example, differentially insulated leads to limit phrenic or extracardiac stimulation. And in addition, enough steer ability that would allow us to actually get to a specific site of interest. Note in this design, there's this bat swing type device with the large surface area electrode to optimize defibrillation of the heart using this innovative vantage point.

Another very interesting method for trying to avoid some of the problems that Dr. Friedman has mentioned, especially avoiding crossing the tricuspid valve, at the same time giving us the chance to stimulate the ventricle involves using an important anatomic landmark called the atrial ventricular septum. If a lead is placed in this site, not only do we avoid crossing the tricuspid valve, but we can stimulate the ventricle and more so we can stimulate the right and left ventricle simultaneously to mimic physiological pacing. This is even more relevant when we consider that this location, the atrial ventricular septum, is the closest neighbor to the left ventricular free wall that we can access anywhere from the right side of the heart.

What this means is, however, that since we are pacing or placing our leads very close to the atrium, we need to have a unique design on the lead tip that will allow sensing and pacing of the ventricle alone despite being so close to the atrial myocardium. Here is an example of what we would see when we pace in the atrium with a lead that has electrodes all within its screw. You would get just atrial electrograms with no far field sensing of the ventricle. Similarly, if this lead is placed on the atrial ventricular septum, we would get only ventricular activation or sensing-- something that would be ideal for this type of technology. Initial experiments including in live beating hearts of canines, have shown that it's possible with guidance through intracardiac ultrasound to access this location without crossing the tricuspid valve. Similarly, we have also shown from our work--