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Review

# Leadless pacemakers: A new era in cardiac pacing

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ABSTRACT

Cardiac pacemakers are a critical management option for patients with rhythm disorders. Current efforts to develop leadless pacemakers have two primary goals: to reduce lead-associated post-procedural morbidity and to avoid the surgical scar associated with placement. After extensive studies on animal models and technological advancements, these devices are currently under investigation for human use. Herein, we review the evidence from animal studies and the technological advancements that have ushered in the era of use in humans. We also discuss different leadless pacemakers currently under investigation, along with limitations and future developments of this innovative concept.



**Contents**



## Introduction

It is estimated that more than 700,000 pacemakers are inserted annually worldwide [1]. The number of permanent pacemaker implants is rising due to an increase in mean age of populations and other medical co-morbidities [2]. Despite the fact that conventional lead pacemakers improve patients' clinical status, the pacing leads have long been considered their Achilles' heel [3]. It has been reported that up to 10% of the patients suffer from acute and chronic lead-associated complications [4]. Similarly, pacemaker pocket infection continues to be a problem [4] despite strict adherence to sterile techniques in electrophysiology laboratories and improved device design. This usually results in complete removal of entire hardware including battery and leads and can be a source of significant morbidity for the patient. The incidence of pacemaker lead fracture is about 1–4% [4]. Usually

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lead fracture occurs as a result of lead compression between clavicle and first rib just lateral to subclavian vein entry site due to mechanical trauma. Most patients need immediate medical attention when lead fracture is suspected especially if they are pacemaker-dependent. Another significant issue is lead insulation failure [4]. Insulation failure can result in abnormal pacing/sensing and delivery of inappropriate shock therapy all leading to significant short battery longevity. Leadless pacemakers (LCP) can overcome these issues due to absence of leads and no requirement for a surgical pocket. Spickler et al. in 1970 were the first to introduce the concept of LCP [5]. The leadless cardiac pacemaker (LCP) is an innovative concept involving placement of a completely self-contained intra-cardiac device. Usage of LCPs in humans became a realistic target when they were successfully studied in animal models [6]. In this article we review the progress that has been made in the field of LCPs and also analyze the potential use of LCPs as a first choice in various rhythm disorders.

## Animal studies and technological advancements

Several studies have been conducted in which the feasibility, efficacy, and safety of LCPs have been evaluated [6–10]. Spickler and colleagues were the first to successfully implant the LCP in dogs, but the nuclear-powered device could not be practically used due to safety concerns and short battery life. In 1991, Vardas et al. [7] tested their own miniature pacemaker device in 8 dogs. The pacemaker used was constructed by the research team and powered by three 1.5 V batteries. The pacemaker did not have any inherent sensing capability so pacing mode used in the study was VOO. VOO mode has limited implications in practice and is usually employed in surgical procedures to avoid sensing of electrical current generated by electro-cautery. Therefore, this pacemaker was not deemed suitable for clinical application, even though pacing was found to be successful in certain dogs [7].

Spickler et al. and Vardas et al.'s research was ahead of its time, and it was not until 1999 that Goto et al. explored the concept of using an automatic power-generating system (AGS) to power the LCP. The AGS converts kinetic energy to electric energy similar to what is seen in quartz watches. The AGS system is implanted in the right ventricle, and it transfers kinetic energy to the rest of the device. It was found that the AGS could generate 13 micro-Joules per heartbeat, suggesting that it supplied sufficient energy to power an LCP. The investigators successfully paced a mongrel dog's heart at 140 beats/min for 60 min with a fully charged AGS system [11]. Later, in 2006, Echt et al. would go on to use ultrasound as a power source. Ultrasound energy, which was emitted from a receiver on the chest wall, would reach an electrode placed in contact with the myocardium. The electrode would then convert ultrasound energy to electrical energy and thus cause pacing. Pacing was achieved in more than 30 different sites in right atrium and ventricle with ultrasound energy [12]. The same ultrasound system was used in several other studies and most concluded ultrasound to be a viable power source. Lee and co-investigators showed that at 80 different sites within the heart, ultrasound could be used as a power source [13]. They further studied ultrasound systems and assessed various acoustic windows, which can be used to deliver ultrasound energy from transmitters on chest wall to receiver electrodes in the heart [14]. Wieneke et al. brought yet another power source based on induction using a subcutaneous transmitter unit and an endocardial receiver unit at the apex of the right ventricle. Two trials concluded that induction systems were a feasible option as a power source and could be used at a distance of up to 10 cm between the transmitter and receiver units, which is more than the required 6 cm. This particular source has not been widely used as of yet, and thus, it remains to be seen if it can be applied in clinical settings [9,10]. Currently, in most LCPs, these power sources are not being used as they need to be further investigated. LCPs available now are mainly powered by lithium batteries, and it will continue to be that way until a better source of power can be established [15].

Recently, Koruth et al. [8] carried out a study to evaluate the usage of LCP implanted in the right ventricle of sheep. Pacing was seen to be successful in 10 out of 11 cases for a period of 90 days. They concluded that LCP was well suited for use in their sheep models [8]. Sperzel et al. also used a right ventricle LCP in sheep models, but their study was focused on retrieval, as well as re-implantation of the device. It was successfully shown that the LCP could be easily retrieved and replaced as needed [6]. Although these studies show acceptable recordings in animals, the efficiency of LCPs in humans had yet to be evaluated.

## Current LCPs

Currently, there are three major LCPs being made and tested. The first is the Nanostim™ device made by St. Jude Medical (St Paul, MN, USA). It is smaller than an AAA battery and can be completely placed within the heart (Fig. 1). Most of the LCP consists of a battery. This 4-cm long, 6-mm wide, and just 2 g in weight LCP is delivered by an 18F catheter attached to a docking button on the end of the device, which introduces it into the body via the femoral vein and subsequently into the right ventricle. A tether mode is used to tug on the device after implantation to ensure that it is fixed to the heart wall. The LCP can be unscrewed during the operation if positioning needs to be changed or if it has not been completely fixed. Since it uses electrical impulses to communicate rather than the standard antenna and coil system it has a long battery life of 9–10 years, which is particularly useful as fewer replacements will be needed [15]. After the LEADLESS trial, this particular LCP was given the CE mark.

Another device is the Micra Transcatheter Pacing System (TPS), made by Medtronic Inc. (Dublin, Ireland), which is claimed to be the 'world's smallest pacemaker' with dimensions of just 7 mm in width, 26 mm long, and weighing 2 g (Fig. 2). Currently, TPS is undergoing a study in which 780 patients will be enrolled and followed to evaluate clinical usefulness in terms of major complications and pacing parameters. Like the Nanostim™ device, the TPS is delivered to the right ventricle via a catheter through femoral vein, can be repositioned as necessary, and has an estimated battery life of 7–15 years. Whereas Nanostim™ LCP is fixed mainly by the helix, the TPS is attached by small self-expanding nitinol tines. The TPS is delivered by a 23F catheter. In addition, TPS is not intended to be removed when its battery is


**Fig. 1.** St. Jude Medical Nanostim Pacemaker.
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