Fractal Coated Leads: Advanced Surface Technology for Genuine Sensing and Pacing

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Summary

This review article provides a comprehensive summary of facts and clinical findings related to the fractal concept. A succinct introduction covering principle and technology of fractal coating is followed by a review of its physical characteristics and consideration of published data from a variety of single- and multicenter clinical studies. Based on clinical evidence, fractal leads exhibit excellent durability and overall reliability. Their essential feature is 1,000x larger electrochemically active than the geometric electrode surface area, resulting in three major advantages of fractal coated leads. The first advantage is the capability of sensing undistorted intracardiac signals such as the monophasic action potential and the evoked response. A near perfect correlation between the monophasic action potential morphology recorded by fractal coated versus Ag/AgCl electrodes ("gold standard") was demonstrated in numerous studies. While the application of Ag/AgCl electrodes is limited to < 3 hours, fractal leads allow monophasic action potential recording by external or implantable devices over several weeks. This may be utilized for various diagnostic and therapeutic applications, like tailoring drug therapy, detecting impending arrhythmia, etc. It has been demonstrated that fractal leads offer undistorted ventricular evoked response recording over years, which is already utilized for capture control and heart transplant rejection monitoring. The second advantage of fractal leads is freedom from electrode polarization even for small electrode surfaces (e.g., 1.3 mm^2). This allows safe capture control with any fractal lead (also using high-impedance battery-saving electrodes) and in pacemakers without charge-controlled counter-pulse circuitry that costs energy. The third advantage is optimal charge transfer at the electrode surface. Consequently, acute and chronic pacing thresholds in fractal leads are comparable to that in steroid-eluting leads, where a cortisone-like drug is disseminated into the myocardium from a reservoir at the tip. When, however, this reservoir gets depleted, the chronic threshold may rise unexpectedly, jeopardizing the patient safety for manually optimized output settings. As fractal leads contain no consumable component, the chronic threshold is stable and maximum patient safety is maintained at pacing outputs similar to those in steroid leads. An overview of fractal lead designs available for clinical application is given at the end. The paper may also serve as an orientation to what has been studied and published appropriately, and where the future research may be directed to.

Key Words

Fractal electrodes, fractal technology, low polarization, monophasic action potential sensing, evoked response, threshold stability

Introduction

Essential questions addressed in this work in a succinct yet sufficiently documented way are:

- Why was the fractal surface structure introduced to pacing?
- What is fractal surface and how is it approximated in practical realization?
- Which technology is used to generate fractal coating and which materials are considered optimal?
- What are advantages of fractal over conventional rough electrodes?
- How do fractal leads perform in clinical practice with respect to:

- lead reliability,
- pacing threshold,
- stimulation impedance,
- sensing properties?

- Which fractal leads are available for clinical application?
- What could be next steps in development and research?

Fractal Coating Principle and Technology

The fractal coated pacemaker electrode was invented nearly 10 years ago, to enhance charge transfer between the metal surface of the electrode and the electrolyte (Figure 1). The inspiration was found in nature, where the fractal principle is applied whenever transfer process has to be optimized, e.g., in the ramified structure of the blood vessels in the liver and in the bronchia-alveoli system of the lungs. Figure 1 visualizes a model description, where the fractal surface is constructed by repeated application of a mathematical operation which doubles the electrochemically active surface area.

In the practical realization, the number of doubling steps approximates 10, giving rise to the ratio between electrochemically active and geometric electrode surface area of about 1,000 [1-6]. Under "electrochemically active surface area" is considered a total electrode surface in contact with the surrounding electrolyte, while the "geometric surface area" represents calculated surface area using the mathematical equation for a hemisphere (also called "envelope area"). The technology of fractal coating is described in Figure 2.

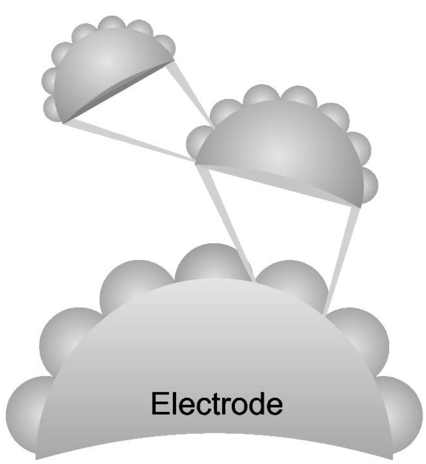

Figure 1. Principle of the fractal surface structure. Each hemisphere is covered by smaller hemispheres, with endless decrease in the size of the covering hemispheres. Each new layer of hemispheres ("doubling step") increases the electrochemically active surface area by a factor of 2, yielding a total enlargement of the active surface of 2^n, where n is the number of doubling steps.

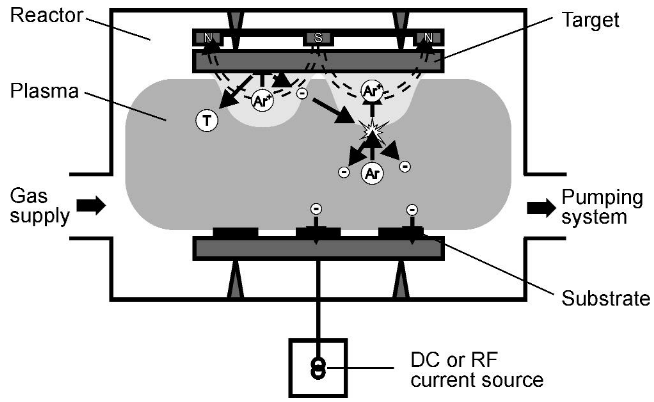

Figure 2. Schematic view of the physical vapor deposition reactor for production of fractal coated electrodes. The argon (Ar) ions are generated by ignition of the plasma and subsequently accelerated towards the target (iridium) by high voltages. Very small particles of iridium, struck off by the kinetic energy of the bombarding Ar ions, will diffuse through the reactor and be deposited onto the electrode substrate, forming a thin layer featuring fractal surface structure.

The fractal surface structure is achieved by carefully controlling the process parameters in order to obtain a diffusion limited growth of the deposited material. It is not influenced - or is influenced to a lesser degree - by characteristics of the used electrode materials [6-8]. This opened the space in the early 1990s for clinical studies comparing long-term performance of fractal coated electrodes using different materials featuring high biocompatibility and biostability, mostly titanium alloys (e.g., titanium nitride) and the noble metal iridium [1,7-11]. The inert iridium coating exhibited the most stable and lowest threshold values in the long term, and is exclusively used for fractal coating ever since [5,7,8]. The electrode substrate in hemispherical electrodes is composed of titanium and in screw-in and ring electrodes of a platinum-iridium alloy [12].

Physical Characteristics of Fractal Coated Electrodes with Respect to Detection and Stimulation

Rough electrodes are generally preferred over smooth electrodes due to: (1) increased Helmholtz capacitance

(capacitance of a double layer of adsorbed water molecules at the electrode-tissue interface), improving sensing performance and charge transfer and (2) a lower peak and chronic pacing threshold resulting from tissue ingrowth into electrode pores, fixating the electrode and minimizing tissue irritation caused by electrode movements [2,7,8,10,13-16]. Conventional rough electrodes use metal mashes, porous surface textures, sandblasting, sputtering grooves, or slots/pores drilled onto the electrode surface to enlarge active surface area by a factor of 2-10 [6,13,17]. And this is clearly inferior to the 1,000x increase in electrochemically active area in the cauliflower-like fractal electrode surface (Figure 3). The huge electrochemically active area is linked to three unique features of fractal

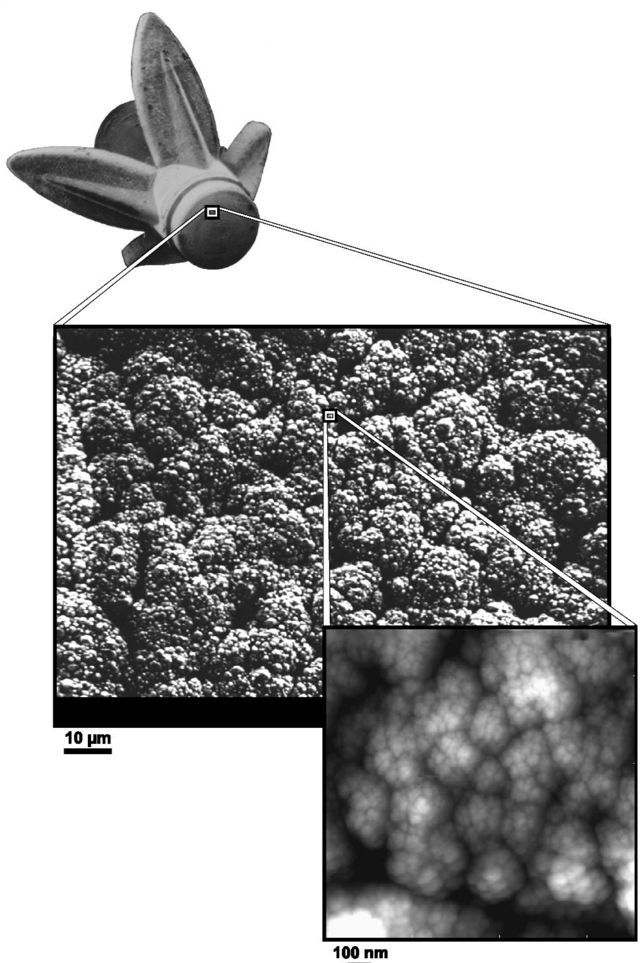

Figure 3. A microscopic view of the fractal electrode surface using different magnification factors indicated at the bottom of images.

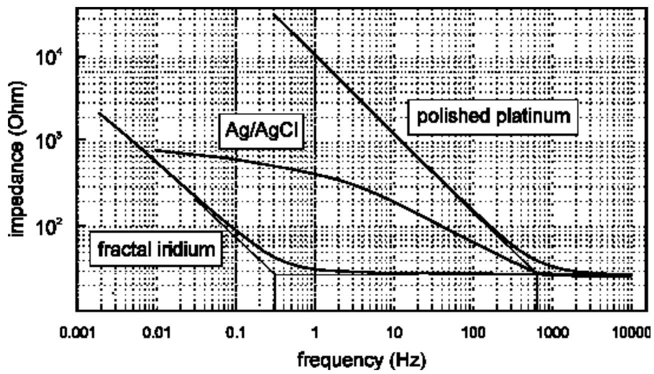

Figure 4. Electrode impedance as the function of signal frequency. The "cut-off" frequency (knee on the curve) is about 0.3 Hz for fractal iridium and 700 Hz for polished platinum.

leads unparalleled by any other electrode surface design:

- Sensing of undistorted intracardiac signals,
- Diminished electrode polarization even for very small, high-impedance electrodes,
- Optimal charge transfer during stimulation.

Sensing of Undistorted Intracardiac Signals

The background for sensing of undistorted intracardiac signals is shown in Figure 4. Fractal iridium electrodes feature very low and nearly constant impedance in the range from 0.1 Hz to 200 Hz, where all important spectral components of intracardiac signals are situated. This is a consequence of a very high Helmholtz capacity at the electrode surface (25 mF/cm^2), which is nearly 1,000x larger than in polished platinum [4,6-8].

To link Figures 4 and 5, it is necessary to understand that the attenuation of any spectral component of the sensed signal is calculated according to the equation:

$$U_{Sensed}/U_{Original} = 1 - Z_{Interface}/Z_{Total},$$

where U_{Sensed} is the detected amplitude of the signal, $U_{Original}$ is the true amplitude, $Z_{Interface}$ is the lead impedance at the observed frequency value (the electrode impedance is the most prominent component of $Z_{Interface}$), and Z_{Total} is the sum of the pacemaker input impedance and $Z_{Interface}$. For ideal sensing (no attenuation, no distortion), $Z_{Interface}$ should be 0 at all frequencies, resulting in $U_{Sensed}/U_{Original}$ = 1 irrespective of the frequency. Although this is not feasible in practice, it is best approximated by the fractal iridium curve in Figure 4, with the lowest cut-off frequency of about 0.3 Hz. Conversely,

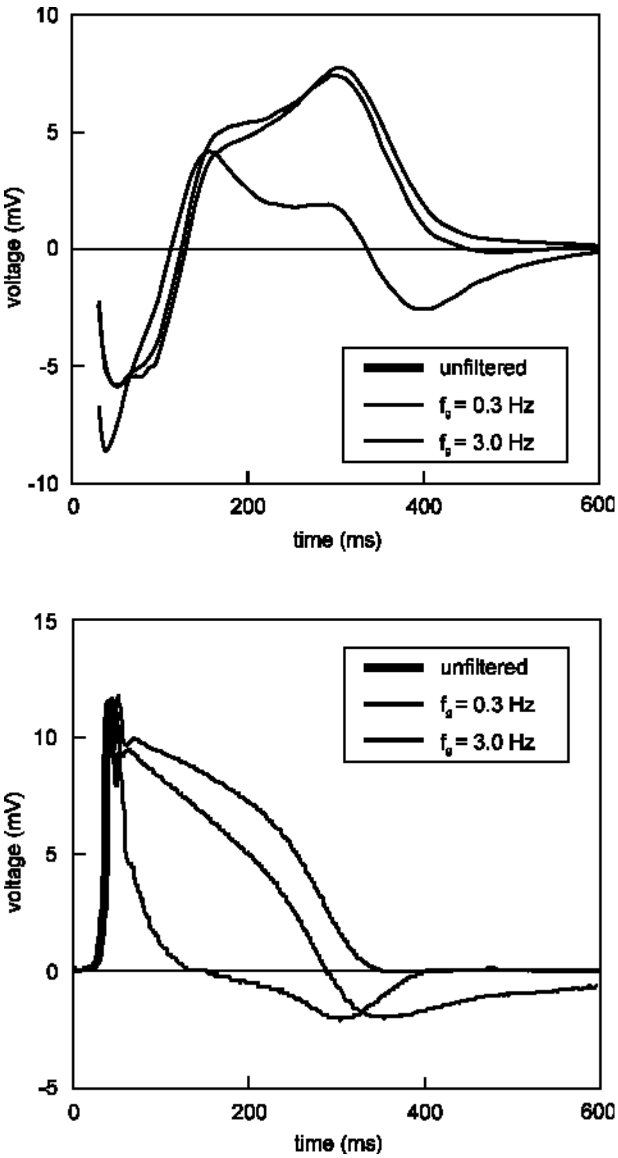

Figure 5. Ventricular evoked response (upper panel) and monophasic action potential (lower panel) recorded by detection systems characterized by different cut-off frequencies: 0 Hz (unfiltered), 0.3 Hz, and 3 Hz. The morphology of the signals is greatly distorted for cut-off frequencies > 0.5 Hz.

polished platinum electrode shows a steady increase in electrode impedance for frequencies below 700 Hz, resulting in a greater attenuation and fading away of low-frequency components from the signal. Consequence of the filtering out low frequency components is illustrated in Figure 5.
Figures 4 and 5 suggest that fractal coating technology permits detection of undistorted, or minimally distorted, signals containing important low-frequency components (e.g., plateau), such as the monophasic action potential (MAP) and the evoked response [2,5,6,18-21].

Diminished Electrode Polarization
After the application of a single pacing pulse to a metal electrode in contact with an electrolyte, the interface is charged like a capacitor (electrode polarization). The charge causes a slowly decaying after-potential, that lasts for about 300 ms following the spike. The magnitude of the after-potential is inversely proportional to the Helmholtz capacity [2,5,7,8]. As fractal coated electrode surface features uniquely high Helmholtz capacity, the after-potential is eliminated [2,5,7,8]. The vast majority of conventional leads are polarizible (Figure 6), producing after-potentials that may be confused with the evoked response signal and misled capture control (autocapture) function for self-adjustment of pacing output [3,22,23].

Optimized Charge Transfer
In addition to the improved sensing, a large electrochemically active fractal surface favorably influences the charge transfer during pacing. The larger the electrochemically active area, the lesser the current is obstructed. In fractal coating, the so-called "outer" electrode surface area is enlarged through the presence of oblique particles surrounded with a lot of open space for undisturbed ion flow (Figure 3). Conversely, the vast majority of other electrode designs have augmented the "inner" electrode surface area, containing valleys and pores, in which the ion flow is slowed down and obstructed. The current will thus face more obstacles than in the "open" fractal coated structure, requiring more energy expenditure to convey the current to the excitable tissue (Figure 7)[2,6,9].

Clinical Evidence

Lead Reliability
Fractal coated leads always featured silicone-rubber insulation and multifilar MP35N conductor wires, the solutions known for their very good quality and long-term reliability [13,17,24,25]. All other components, such as J-shape, tines, screw-in devices, have been designed utilizing the most reliable and highest quality materials and designs. Consequently, fractal leads exhibited extremely low failure rates and have never been subjected to a device recall or intensive surveil-

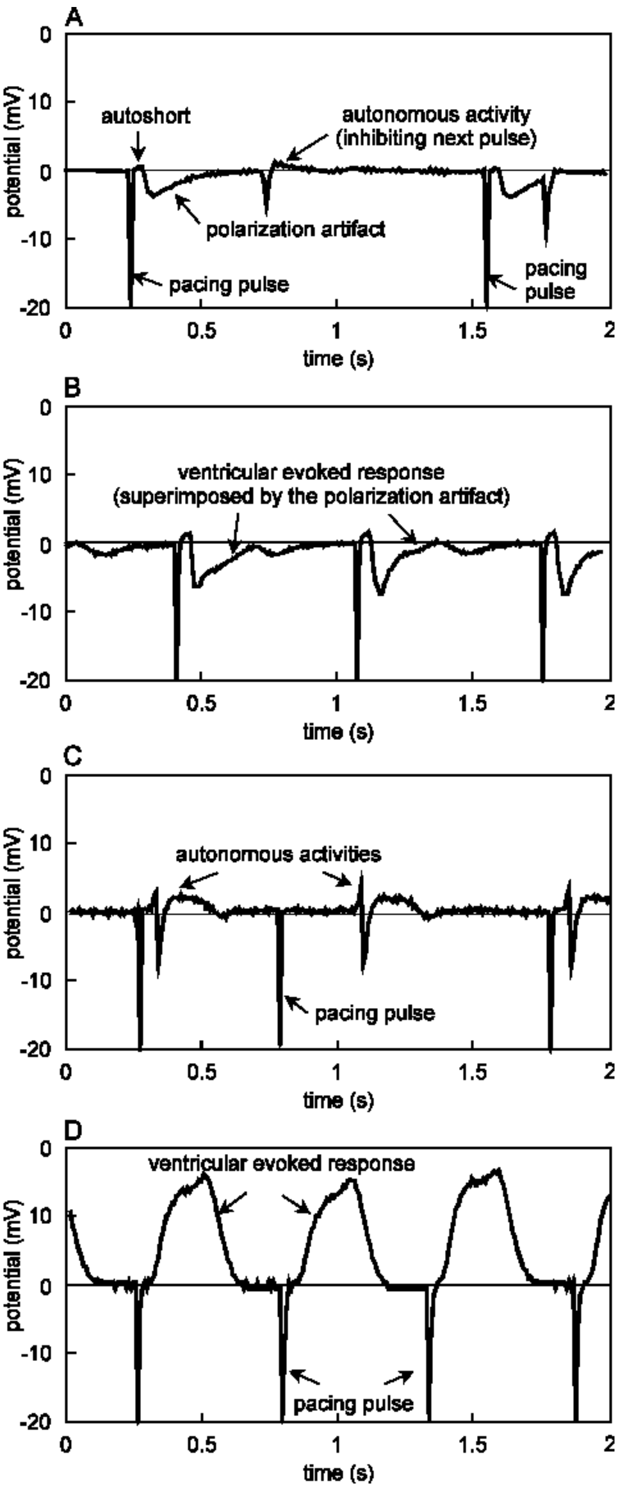

Figure 6. Polarization artifact and the evoked response signal in 9 mm² uncoated Elgiloy electrode (panels A and B), and 6 mm² fractal coated electrode (C and D). Panels A and C show sub-threshold stimulation (no capture), and panels B and D effective stimulation (capture). Signal morphologies after pacing spike on panels A and B are similar and it is difficult to distinguish capture from no capture. Panels C and D show a clear difference between capture and no capture due to a lack of polarization artifacts. Besides, morphology of the evoked response is undistorted, allowing scientific analysis.

lance, that were traditionally linked to polyurethane insulation, a sub-optimal co-axial design, use of retention wire in atrial J-lead, etc. [24,26-31].

Recently, Lazarus et al. (Saint Cloud, France) reported on no component failure in 957 atrial and ventricular screw-in fractal coated leads followed for up to 6 years [32]. The cumulative survival, defined as functional lead without need for re-operation, was 100 % for ventricular and 98.19 % for atrial leads (a few atrial leads required repositioning). Independently, Kreutzer et al. (Cottbus, Germany) observed a component failure in 1.7 % of 917 tined atrial J-leads followed for up to 7 years [33]. The dislocation rate leading to re-operation was 4.6 %. No problems were linked to the J shape. Other centers had similar experiences, resulting in their preference of fractal leads in clinical practice over many years.

Tined fractal electrodes with small surface area featuring high pacing impedance (Synox, 1.3 mm²) appear equally reliable as alternative small electrode designs (e.g., 1.2-mm² CapSure Z electrode, Medtronic, USA). While some clinics report on an increased re-operation rate (> 10 %) with small electrodes caused by lead dislocation or high pacing threshold, many other centers are very pleased with the re-intervention rate (≤ 6 %,

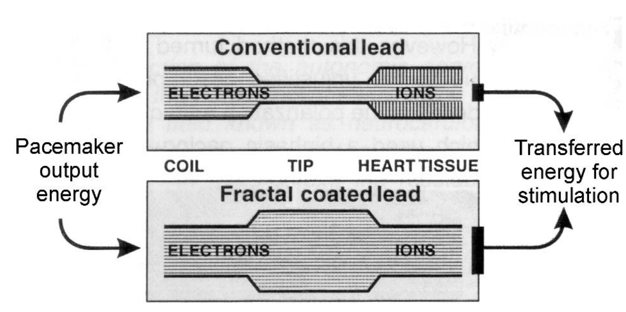

Figure 7. Fractal coating improves the energy transfer at the electrode surface through the increased "outer" surface area. The "inner" surface area in conventional leads (see text) results in greater obstruction to ion flow and increased energy losses at the electrode surface.

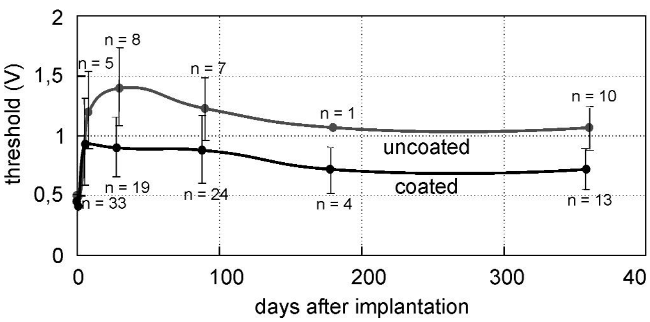

Figure 8. Unipolar threshold trend in a 10 mm² iridium electrode with and without fractal coating (humans, ventricular position).

comparable to that in standard-surface electrodes), overall performance, and advantages of small surface electrodes [17,34-43]. There is a belief that the implantation technique and care during lead positioning may lead to different follow-up results, which is yet to be substantiated by systematic data [17,37].

Stimulation-Related Advantages

The question how fractal coating influences threshold behavior of an iridium electrode is answered by Figure 8 [7]. Due to the optimized charge transfer at the electrode surface, the acute, peak, and chronic pacing threshold values are substantially reduced in the fractal coated lead. Figure 8 also illustrates a "normal pattern" of threshold trends in fractal leads, with a peak values occurring within the first several weeks after lead implantation and a chronic value being established 2 - 6 months later.

Table 1 compares acute, peak, and chronic threshold values in modern tined leads, including 1.3 - 6.0 mm² fractal coated iridium electrodes, platinized steroid-eluting electrodes (Medtronic), membrane-covered and titanium-nitride electrodes (St. Jude, USA), iridium oxide electrodes (Intermedics, USA), etc. [4,11,17,34-40,44-49]. Despite similar chronic thresholds, fractal leads offer several advantages over alternative solutions. The first advantage is maximum patient safety for manually optimized output settings, due to extraordinary stability of chronic thresholds in fractal iridium electrodes [4,7,36,50]. Alternatively, steroid leads may exhibit chronic threshold rise following depletion of steroid reservoirs, thus jeopardizing patient safety for manually optimized pacing outputs [17,38,51,52]. Unlikely to inflammation-suppression devices in other leads, fractal coating has no consumable component, rendering unexpected threshold rise in the chronic phase the least likely.

Electrode	Acute (at 0.5 ms)	Peak (mean @ 0.5 ms)	Chronic* (mean @ 0.5 ms)	Overall advantage
Fractal iridium	Depends mostly on the electrode surface area and to a lesser degree on the electrode technology: - the lowest in < 1.5-mm² electrodes (0.1-0.3 V in 80% of the leads), - the highest in 6-mm² electrodes (typically in the 0.3-0.7 V range)	around 1 V	0.6 - 0.8 V	For manual output optimization, the highest patient safety due to best chronic threshold stability For automatic output adjustment: - the safest capture control due to absence of electrode polarization, - minimal energy consumption due to compatibility of a small electrode surface (< 4 mm²) with the capture control
Steroid-eluting		around 0.8 V	0.5 - 0.8 V	The lowest peak threshold
Other**		≥ 1 V	0.6 - 1.2 V	-

* One year after implantation. ** Membrane-coated, iridium oxide, titanium nitride, activated carbon, etc.

Table 1. Comparison of stimulation thresholds in modern tined leads.

If automatic capture control is used for continuous self-adjustment of pacing outputs, the absence of electrode polarization in fractal leads will preclude any incorrect capture evaluation. A sufficiently low polarization artifact (< 2 mV) in nearly all patients is achievable with conventional rough electrodes only if their geometric surface area is increased to about 9 mm^2 [15,45]. The large geometric surface area will in turn lower pacing impedance, increase pacing threshold, and thus augment battery energy consumption [15,17,34,39,53-55]. With fractal coating, even small, high-impedance, 1.3 - 4.0 mm^2 (battery-saving) electrodes are virtually polarization-free [5,37,56,57]. Some pacemakers employ charge-controlled counter pulses (i.e., tri-phasic stimuli) to eliminate polarization artifact in every lead [23,58]. But modified pacing pulses consume more battery energy than standard biphasic pacing pulses, and this method is not as efficient and safe for capture control as simply implantation of a fractal coated lead [5,21].

A slightly lower peak threshold in steroid-eluting than in fractal coated leads (Table 1) is of little clinical relevance, since nominal pacemaker output settings (2.5 - 3.5 V at 0.3 - 0.5 ms) used during several months after implantation should maintain patient safety equally with either lead design. In case of self-adjustment of pacing outputs, the peaking period is too short and the differences in peak thresholds too small to translate into enhanced battery longevity in steroid leads.

Similarly to other lead designs, pacing impedance trends in fractal leads exhibit an initial post-operative drop, followed by a rise toward a chronic impedance value established 2 - 6 months after implantation [34,36,48,59-61]. Tined fractal leads offer approximately 550 Ω mean chronic impedance for 6 mm^2 electrodes, 650 Ω impedance for 3.5-mm^2 electrodes, and about 1000 Ω mean values for 1.3-mm^2 electrodes [4,34,35,37,59-63]. This is in line with other lead designs, with the note that small-surface electrodes (< 2 mm^2) are available only for fractal coated and steroid technology [8,34,44,64]. The small electrodes conserve battery energy by means of high pacing impedance and of slightly reduced chronic pacing threshold owing to the increased current density at the electrode surface [4,17,34,35,38,39,54,55].

Favorable threshold and impedance values have been demonstrated also in screw-in and epicardial fractal leads [65-67]. Satisfactory values were obtained in floating and coronary sinus pacing [68-71].

Unique Sensing Performance of the Fractal Surface

Fractal coated leads exhibit larger R- and P-wave amplitudes than alternative lead designs [4,7], which may improve the signal to noise ratio for enhanced sensing. In the ventricle, this may bring little additional merits, as all modern leads supply a sufficiently large (> 7 mV) mean R-wave amplitude. The atrial signal is generally threefold smaller than the ventricular, and increased P-wave amplitudes owing to fractal coating may lead to better distinction by pacemaker circuitry between atrial depolarization and far-field electromagnetic fields [4,7,17].

The remaining of this section is dedicated to the sensing of evoked response and MAP by fractal leads. Both signals are extracellulary recorded waveforms reflecting the time course of transmembrane action potentials, containing a wealth of information about the status of the heart. While the evoked response is a unipolar signal recorded from within the atrium (atrial evoked response) or the ventricle (ventricular evoked response), the MAP is the bipolar potential difference between the lead tip pressed against the myocardium and a ring electrode located behind the tip [21,72]. The unipolar nature of the evoked response takes into account the electrical activity of many myocytes and contains the information on the global myocardial state, while the MAP reflects more local cellular effects near the electrode tip.

The two signals have a different morphology, and the evoked response lasts longer due to the global signal propagation time added to the duration of the individual transmembrane action potentials (Figure 5). The analysis of the MAP morphology is valuable in studying the characteristics of local myocardial repolarization in beating hearts, in different clinical settings such as long QT syndrome, triggered or impending ventricular arrhythmias, arrhythmia characterization, myocardial ischemia, or drug evaluation [18,73-75]. The evoked response always represents triggered activity, while the MAP may be measured during spontaneous or triggered heart beats, with negligible differences in signal morphology [5,21].

Before the advent of fractal coated leads, MAP waveforms could only be recorded during electrophysiological investigations, with the aid of Ag/AgCl electrodes [5,75,76]. The Ag/AgCl electrodes have been regarded as "gold standard" for non-traumatic sensing of cellular activity using the contact electrode technique [18,73-75]. Their excellent sensing characteristics

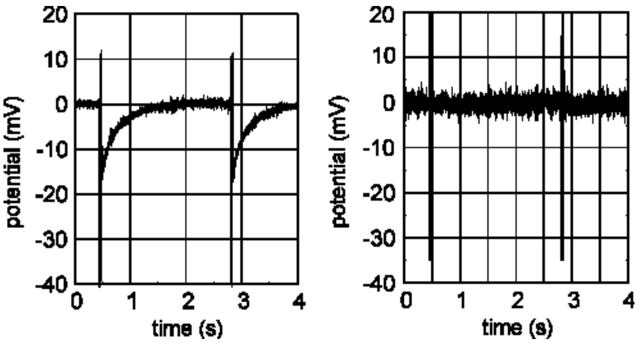

Figure 9. Polarization artifact of Ag/AgCl (left) and fractal coated electrode (right) after stimulation at 4.8 V/ 0.5 ms.

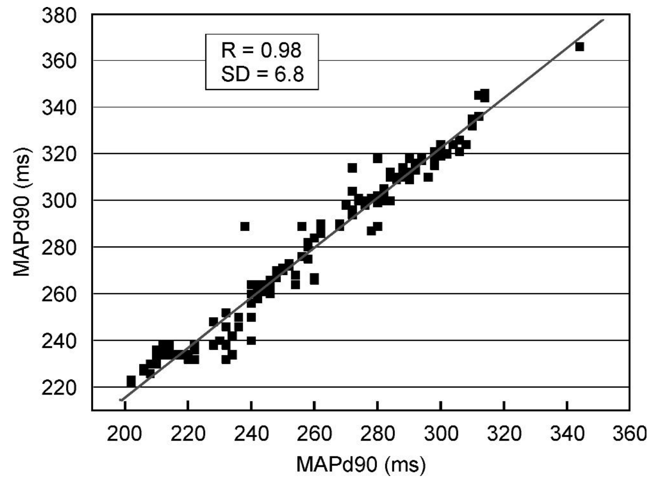

Figure 11. Correlation between the MAP duration recorded with Ag/AgCl electrodes (x-axis) and fractal coated electrodes (y-axis) before, during, and after sotalol bolus. MAPd90: MAP duration until 90 % of repolarization are completed (Merkely et al. [72]).

originate in the reversible reactions between the chloride ions in the electrolyte and the silver chloride layer at the electrode surface [5]. The redox pair at the surface of the electrode results in a substantially lower interface impedance in Ag/AgCl than in the polished metal electrode surfaces (Figure 4). However, the toxicity, insufficient biostability, and polarizibility of Ag/AgCl electrodes (Figure 9) make them unsuitable for applications longer than 3 hours [5,21,76,77].

The knowledge behind Figure 4 suggested that fractal coated leads might successfully substitute Ag/AgCl electrodes in the recording of MAP and evoked response signals, and add necessary biocompatibilty for long-term applications. Experimental results during routine electrophysiological investigations and from animal laboratories confirmed that fractal leads faithfully reproduce MAP and atrial/ventricular evoked response signal morphologies [5,21,72,75,76,78-86]. In these experiments, standard screw-in and tined pacemaker leads, defibrillator leads, and specially design catheters were tested. Figures 10 and 11 illustrate the strong correlation of MAP duration for fractal coated versus Ag/AgCl electrodes. Simultaneously, the MAP duration correlated well with the evoked response interval (Figure 12).

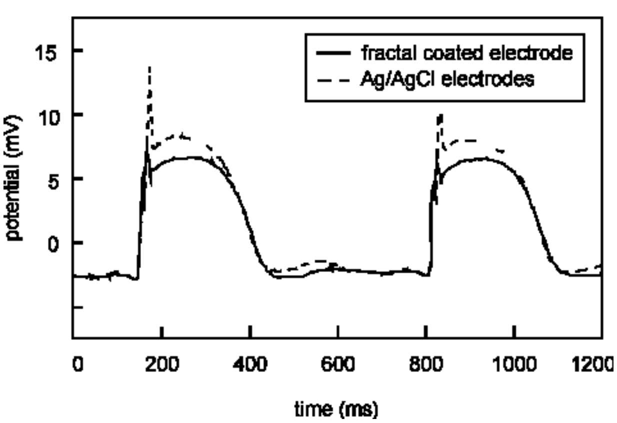

Figure 10. Comparison of monophasic action potential morphology in "gold standard" Ag/AgCl electrodes and fractal coated electrodes, measured simultaneously from approximately the same site (Fröhlich et al. [5]).

In addition to a near perfect correlation between MAP morphology in fractal coated and Ag/AgCl electrodes ($r = 0.99$), Zrenner et al. found that even small negative deflections, notches, or broken-shaped upstrokes of the MAP signal, or spike over/undershootings were recorded as often with fractal coated electrodes as with Ag/AgCl electrodes [75]. In the 1.3-mm^2 fractal electrodes, MAP amplitudes were equal to that in Ag/AgCl electrodes, while 30 % (50 %) lower amplitudes were recorded using 6-mm^2 ($> 10\text{-mm}^2$) fractal tips [5,75,78]. Unlikely to the polarizible Ag/AgCl electrodes, the same fractal iridium electrode could be utilized for pacing and sensing, reducing the number of leads used in the procedure and "would be necessary" in chronic applications.

Three further issues had to be addressed by investigation and development, in order to pave the way to long-term evoked response and MAP applications:

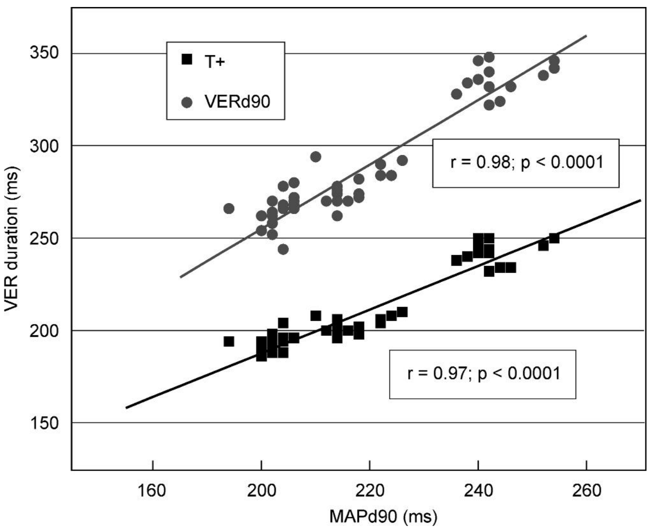

Figure 12. Correlation between the MAP duration and the ventricular evoked response (VER) duration before, during, and after sotalol bolus. T+: duration of the VER until T-wave maximum, VERd90: VER duration until 90 % of repolarization, MAPd90: MAP duration until 90 % of repolarization. Fractal coated leads were used in the measurements (Merkely et al. [72]).

- Adjustment of pacemaker input circuitry and telemetry functions for optimal recording by chronically implanted devices,
- Optimization of lead design for stable long-term measurements,
- Development of novel pacemaker algorithms that will be able to extract useful information from the signal morphology and thereby increase diagnostic and therapeutic value of the pacemaker.

The necessary adjustments of pacemaker input circuitry and telemetric functions have been described in sufficient detail [21]. Conventional pacemakers mostly use a lower cut-off frequency about 3 Hz, matching the "reduced" sensing potential of standard electrodes and leading to great distortion of signal morphology even with fractal leads (Figure 5). The dual-chamber Physios CTM 01 pacemaker (Biotronik, Germany) was designed with cut-off frequencies of 0.33 Hz (lower) and 200 Hz (upper), to utilize sensing potential of fractal leads. Similarly, the circuitry in the Logos dual-chamber pacemaker (Biotronik) was adjusted for evoked response monitoring [21].

With the aid of Physios and Logos pacemakers, or external devices connected to implanted fractal leads, the impact of various factors, such as drugs, ischemia, adrenergic and cholinergic stimulation, triggered and impending arrhythmia, early depolarization, etc., on the MAP and evoked response morphology has been investigated extensively [21,72,77,83,87-97].

An optimal lead design for long-term applications was sought for in parallel [5,75,78-81,98,99]. Both endocardial and epicardial screw-in fixation devices provided an adequate electrode-tissue contact pressure for a stable MAP recording over extended period of time. Tined leads often exhibited drop in MAP amplitude within a few hours, possibly due to a decrease in the electrode-tissue contact pressure caused by continuous heart beating. Although the genuine MAP morphology was usually preserved, the signal was not as stable as in screw-in leads. It is likely that the chronic fibrotic capsule growth around the electrode is responsible for the loss of the typical MAP morphology at 10 - 30 days after implantation in many patients [77,98,99]. It was found that the most faithful reproduction of MAP morphology is achievable with the tip electrode surface area < 2 mm^2, the tip-ring distance < 5 mm, and the ring surface area < 2 mm^2 [78]. In order to facilitate the MAP recording, several fractal leads from Table 2, which normally have 15 - 30 mm tip-ring distance, have been made available also with a shorter, 5 - 10 mm tip-ring distance.

While the MAP recording is presently feasible only in the medium-term (over several weeks), excellent stability of the ventricular evoked response signal was observed during many years even with standard fractal leads [21,72]. There is less experience on the long-term stability and utility of the atrial evoked response. Thus, the first two practical applications of undistorted sensing by fractal leads both utilize ventricular evoked response sensing - for automatic capture control and heart transplant rejection monitoring [56,57,89-91,97,100-102]. A large body of accumulated data on behavior of MAP and evoked response signals under different conditions will probably result in new diagnostic and therapeutic algorithms in future pacemakers. Definitively, fractal coated leads offer more information of potential clinical value than present-day pacemakers are able to utilize.

Available Fractal Coated Lead Models

All fractal coated pacemaker leads, their purpose, and main features are indicated in Table 2.

Lead name	Fixation device, tip electrode surface area	Main features of the lead
Synox	3 tines, 1.3 mm^2	Conventional tined leads: straight (ventricular) and J-shaped (atrial). Bipolar and unipolar models. Lead lengths: 45 cm, 53 cm, 60 cm, and 85 cm (only TIR).
Polyrox	4 tines, 3.5 mm^2	
TIR (ventr.) TIJ (atrial)	4 tines, 6 mm^2	
Solox	3 tines, 3.5 mm^2	Single-pass tined leads for VDD/DDD pacing. Two rings float in the atrium 1 cm apart, 11-17 cm distant from the lead tip. The Solox lead features thicker and stiffer distal portion, for enhanced lead tip stability. Lead lengths: 65 cm (Solox) and 60 cm (SL).
SL	3 tines, 5 mm^2	
Elox	endocardial screw, 9.2 mm^2	Straight bipolar lead with an 1.8-mm retractable, electrically active screw.
Retrox	endocardial screw, 5.3 mm^2	Straight or J-shaped bipolar lead with a 1.8-mm retractable, electrically inactive screw.
YP	endocardial screw, 7 mm^2	Straight unipolar or bipolar lead with a 1.6-mm extendible, electrically inactive screw.
DY Y	endocardial screw, 10 mm^2	Straight unipolar (DY) and bipolar (Y) lead with an 1.5-mm electrically active screw.
ELC	epicardial screw, 10 mm^2	Unipolar epicardial lead with 2-mm and 3-mm screw lengths and 35-cm and 54-cm lead lengths, suitable for pediatric and adult use.
Mapox	epicardial suture, 5 mm^2	Bipolar epicardial lead primarily designed for measurements of monophasic action potentials.
Corox	silicone thread or soft tines. distal ring area: 11.3 mm^2	Coronary sinus lead equipped with two ring electrodes for bipolar left atrial pacing/sensing. The lead tip incorporates either "silicone thread" or "soft tines" fixation device, supposed to be located in the distal coronary sinus or a tributary vein. The tined lead is pre-shaped for enhanced stability within the coronary sinus.

Table 2. Fractal Coated Pacemaker Leads (Biotronik, Germany).

The list of fractal leads includes tined models with the tip electrode surface area of 1.3 mm^2 (Synox), 3.5 mm^2 (Polyrox), and 6 mm^2 (TIR or TIJ), single-pass leads for VDD/DDD pacing with 3.5-mm^2 and 5-mm^2 tip electrodes (Solox and SL, respectively), several endocardial screw-in lead designs (Elox, Retrox, YP, DY, Y), two epicardial lead models (ELC and Mapox), and the coronary sinus lead (Corox) with either "silicone thread" or "soft tines" fixation [103]. All types of electrode finishes (tip, screw-in, and ring) in all leads are fractal coated.

All leads use silicone-rubber insulation and four-filar MP35N conductor wires - technical solutions known for their long-term reliability. The unipolar Synox lead is the only device incorporating drawn filled tube (DFT) wires instead of MP35N conductors, for extra-small lead diameter of 1.4 mm. The durability of DFT wires remains to be proven [46,104]. Despite the general use of the silicone-rubber insulation, all leads are thin and flexible, with ≤ 1.7-mm lead body diameter in unipolar leads, ≤ 2.2-mm diameter in straight bipolar leads, and 2.5 - 2.7 mm diameter in bipolar J-shaped leads and single-pass leads (Solox, SL).

Two fractal coated single-pass DDD lead prototypes: VECATS and OMEGA are under clinical investigation and may enter routine practice in the near feature. The VECATS lead has three floating atrial rings, one of which is situated in the vena cava superior. The lead offers greater flexibility in the optimization of pacing and sensing parameters and improves pacing threshold stability due to reduced electrode movements within the relatively narrow vena cava [69,105].

The OMEGA lead has two floating rings and is pre-shaped to allow ring positioning in the vicinity of the target pacing and sensing site/area in the atrium.
Tined defibrillator leads are also equipped with fractal coating. Thus, the tripolar SPS lead has a fractal coated tip electrode, a ring electrode, and the defibrillation coil, and is suitable for defibrillators with "active" housing. The quadripolar SL-ICD lead, intended for defibrillators with standard housing, has an additional (proximal) fractal coated coil.
To generate the lead model name/number, the abbreviated names of the leads from Table 2 are, as a rule, combed with the lead length in centimeters (e.g. 53, 60, 65), J-label for J-shaped lead, and the lead configuration (UP = unipolar, BP = bipolar). Thus, the model PX 53-J UP represents atrial unipolar Polyrox lead that is 53 cm long. Abbreviations of lead names are: SX (Synox), SLX (Solox), RX (Retrox), MX (Mapox), CX (Corox). Occasionally, the tip-ring distance is indicated after the lead length, if unusual. For instance, leads designed for MAP recording have 5 mm or 10 mm tip-ring distance instead of > 15 mm, and such models are referred to as: SX 60/5-BP or YP 53/10-BP.

Conclusions and Future Directions

Based on clinical evidence, fractal leads exhibit excellent durability and overall reliability. Their essential feature is 1,000x larger electrochemically active than the geometric electrode surface area, resulting in three major advantages of fractal coated leads. The first advantage is the capability of sensing undistorted intracardiac signals such as the MAP and the evoked response. It has been demonstrated that fractal leads offer an undistorted ventricular evoked response recording over years, which is already utilized for capture control and heart transplant rejection monitoring. A near perfect correlation between the MAP morphology recorded by fractal coated versus "gold standard" Ag/AgCl electrodes was demonstrated in numerous studies. While the application of Ag/AgCl electrodes is limited to < 3 hours, fractal leads allow MAP recording by external or implantable devices over several weeks. This may be utilized for investigating the relationship between local cellular phenomena and clinically relevant events like for example tachyarrhythmia or ischemia.
The second advantage of fractal leads is the freedom from electrode polarization even for small electrode surfaces (e.g., 1.3 mm^2). This allows safe capture control with any fractal lead (also using high-impedance battery-saving electrodes) and in pacemakers without charge-controlled counter-pulse circuitry that costs energy. The third advantage is the optimal charge transfer at the electrode surface. Consequently, acute and chronic pacing thresholds in fractal leads are comparable to those in steroid-eluting leads. When in steroid-eluting leads, however, the steroid reservoir gets depleted, chronic threshold may rise unexpectedly, jeopardizing patient safety for manually optimized output settings. As fractal leads contain no consumable component, the chronic threshold is stable and a maximum patient safety is maintained at low pacing outputs.
A variety of available fractal coated lead designs (Table 2) should suffice in nearly all clinical situations, ranging from a need for single-chamber to single-pass dual-chamber or tri-chamber pacing, for conventional (apex, appendage) and unconventional implant sites (septum, coronary sinus, epicardium), for pediatric or adult use, etc.
What could be directions for future development and research? The addition of the steroid drug to the lead tip was considered but judged as unjustifiable for two reasons. In one hand, only "cosmetic" improvements may be achieved without any impact on clinical practice, since steroids may only slightly reduce already low-peak thresholds in fractal leads. On the other hand, they may alter reactions around the lead tip and give rise to unpredicted threshold behavior at the time of steroid depletion years after implantation. Therefore, it is believed that long-term reliability and patient safety are better maintained with the pure fractal surface without addition of the steroid.
Related to pacing thresholds, it may be systematically investigated whether non-contact stimulation, which is still critical in view of energy consumption (e.g., floating atrial and coronary sinus pacing), is associated with significantly lower pacing thresholds for fractal coated versus non coated leads. Similarly, differences in defibrillation thresholds can be evaluated for fractal versus non-fractal defibrillation springs. Low polarization properties of fractal leads have been demonstrated mostly in laboratory conditions and for smaller clinical series. Larger, randomized trials using full range of electrode surface areas with and without fractal coating may result in interesting publications.
Feasibility and utility of recording ventricular evoked response by using fractal leads have been demonstrated. However, more light should be put into the

feasibility and utility of atrial evoked response recording. The fractal lead presently offers more information of potential clinical value than present-day pacemakers may utilize. A large body of accumulated data on behavior of MAP and evoked response signals under different conditions should result in new diagnostic and therapeutic algorithms in future pacemakers. The goal is to advance physiological aspects of pacemakers. They should increasingly comply with diagnostic tasks and adapt to physiologic circumstances in a more sophisticated, therapy-effective way.

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