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D E C I S I O N
of 9 February 2006

Case Number: T 0784/03 - 3.4.01

Application Number: 92306760.7

Publication Number: 0547734

IPC: A61N 1/365

Language of the proceedings: EN

Title of invention:
Pacemaker using antiarrhythmia pacing and autonomic nerve stimulation therapy

Patentee:
PACESETTER, INC.

Opponent:
Biotronik GmbH & Co

Headword:
Antiarrhythmia pacemaker

Relevant legal provisions:
EPC Art. 54(1)(2), 56

Keyword:
"Novelty (yes; main request)"
"Inventive step (no; main request and auxiliary request)"

Decisions cited:
-

Catchword:
-

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Case Number: T 0784/03 - 3.4.01

D E C I S I O N
of the Technical Board of Appeal 3.4.01
of 9 February 2006

Appellant: (Opponent)
Biotronik GmbH & Co.
Ingenieurbüro Berlin
Woermannkehre 1
D-12359 Berlin (DE)

Representative:
Eisenführ, Speiser & Partner
Patentanwälte Rechtsanwälte
Postfach 31 02 60
D-80102 München (DE)

Respondent: (Proprietor of the patent)
PACESETTER, INC.
15900 Valley View Court
Sylmar
CA 91342 (US)

Representative:
Hackett, Sean James
Marks & Clerk
Patent Attorneys
Alpha Tower
Suffolk Street Queensway
Birmingham B1 1TT (GB)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 5 May 2003 rejecting the opposition filed against European patent No. 0547734 pursuant to Article 102(2) EPC.**

Composition of the Board:

Chairman: B. Schachenmann
Members: H. Wolfrum
R. Bekkering

Summary of Facts and Submissions

I. The appellant (opponent) lodged an appeal against the decision of the opposition division, dispatched on 5 May 2003, rejecting the opposition against European patent No. 0 547 734. The notice of appeal was received on 8 July 2003 and the prescribed fee was paid on the same day. On 5 September 2003 the statement setting out the grounds of appeal was filed.

II. Pursuant to Article 100(a) the opposition had been based on the grounds of lack of novelty and inventive step (Articles 52(1), 54(1) and (2) and 56 EPC). In the appeal, reference was made to the following documents:

E1: G. Zuanetti et al: "Protective Effect of Vagal Stimulation on Reperfusion Arrhythmias in Cats"; Circulation Research, vol. 61, no. 3, 1987, pages 429 - 435;

E2: US-A-4 967 748;

E3: M. B. Waxman et al: "The protective effect of vagus nerve stimulation on catecholamine-halothane-induced ventricular fibrillation in dogs"; Canadian Journal of Physiology and Pharmacology, vol. 67, no. 7, 1989, pages 801 - 809; and

E4: M. Stramba-Badiale et al: "Sympathetic-parasympathetic interaction and accentuated antagonism in conscious dogs"; The American Journal of Physiology, vol. 260, no. 2, part 2, February 1991, pages H335 - H340.

III. The Board summoned the parties to oral proceedings to take place on 9 February 2006 and issued a communication dated 16 November 2005.

IV. In response to the Board's communication, the respondent (patentee) informed the Board by letter of 7 December 2005 that it did no longer wish to be represented at the oral proceedings and, therefore, would not attend the hearing.

V. The appellant announced by letter of 12 January 2006 that it also would not participate at the oral proceedings.

VI. Oral proceedings were held on 9 February 2006 in the absence of both parties.

VII. The appellant requested in writing that the decision under appeal be set aside and the European patent be revoked in its entirety.

VIII. The respondent requested in writing, as a **main request**, that the appeal be dismissed and the patent maintained as granted. By way of an **auxiliary request**, maintenance of the patent in amended form was requested on the basis of an amended claim 2, filed with the letter of 22 March 2004, and the remainder of the claims and the patent specification as granted.

IX. Independent **claim 1** of the **main request** reads as follows:

"1. An antiarrhythmia pacemaker (10) for detecting and treating arrhythmia episodes in a patient's heart, comprising:
means (17) for detecting an occurrence of an abnormal condition of the heart,
heart stimulating means (16) for generating and delivering electrical stimulation to the heart (11),
at least one nerve stimulation electrode adapted to be placed in electrical contract [sic] *with preselected nerve fibers (9) within the patient's nervous system,*
nerve fiber pulse stimulating means (20) electrically coupled to said nerve stimulation electrode for generating and delivering stimulating pulses to the preselected nerve fibers, and
arrhythmia therapy control means (19) responsive to said detecting means for controlling said heart stimulating means and said nerve fiber pulse stimulating means to direct performance of a combined heart and nerve stimulation therapy;
wherein the therapy control means is operative for detecting and treating arrhythmia episodes in the patient's heart and said detecting means (17) detects tachycardia and fibrillation episodes and said arrhythmia therapy control means (19) selects and directs an appropriate parasympathetic autonomic nervous system stimulation therapy in the form of repetitive brief bursts of electrical pulses in combination with an appropriate heart therapy selected from the group of antitachycardia pacing, cardioversion and defibrillation."

Independent **claim 2** of the **main request** differs from claim 1 in that

the detecting means detects "*precursors to malignant cardiac arrhythmias*" instead of the "*occurrence of an abnormal condition of the heart*",
the parasympathetic autonomic nervous system stimulation therapy is "*in the form of single electrical pulses*" instead of "*repetitive brief bursts of electrical pulses*", and
the appropriate heart therapy is selected from the group of "*bradycardia pacing support, overdrive pacing and antitachycardia pacing.*"

Claims 3 to 6 are dependent claims.

In amended **claim 2** according to the **auxiliary request** it is additionally specified that the detecting means detects precursors to malignant cardiac arrhythmias "*primarily by abnormalities in the IEGM waveform*".

X. In the written procedure the appellant argued *inter alia* that the subject-matter of claim 1 of the patent as granted lacked novelty with respect to the prior art according to document E1 or was at least rendered obvious by the teaching of this document when applied to a conventional antiarrhythmia pacemaker. The skilled person would gather from E1 that a combined stimulation of the heart and the vagal nerve system at least avoided the occurrence of a ventricular tachycardia. Similar teachings were given by documents E3 and E4. Moreover, the nerve stimulation discussed in E1 operated with pulses of a frequency of 10 to 15 Hz. E1 thus at least implicitly disclosed the repeated application of bursts of pulses, which measure was at any rate explicitly known from E4.

XI. The respondent submitted in writing that E1, relating to an academic research paper, merely presented the results of a narrowly focussed experiment on cats as to a protective effect of vagal stimulation against a specific type of arrhythmia. Vagal stimulation was started well before any arrhythmia was induced. Thus the teaching of E1 was not directed to an antiarrhythmia pacemaker and, in particular, did not disclose arrhythmia therapy control means responsive to a detected arrhythmia within the terms of the patented invention. Pacing was employed in the experiment for a subgroup of cats only to compensate for the effect of vagal stimulation on the heart rate. Furthermore, a vagal stimulation therapy in the form of repetitive brief bursts of electrical pulses did not follow unambiguously from the disclosure of E1.

As a matter of fact, none of the cited prior art documents hinted at a pacemaker having means for a combined antiarrhythmia stimulation therapy of the heart and the vagal system, so that a skilled person could have devised the claimed subject-matter only with the benefit of hindsight knowledge. E1, in particular, taught away from the invention in that the experimental results presented clearly showed that only vagal stimulation alone could prevent a reperfusion induced fibrillation from occurring, whereas no such protective effect was observed for vagal stimulation combined with a simultaneous ventricular pacing.

The teaching of document E3 relating to an experiment on dogs to study the protective effect of vagal stimulation on drug-induced arrhythmias was no more relevant than that of E1. In fact, vagal stimulation

was not combined with a stimulation of the heart and acute fibrillations were conventionally treated by delivering electrical shocks to the heart.

Reasons for the Decision

1. The appeal complies with the requirements of Articles 106 to 108 and Rule 64 EPC and is, therefore, admissible.

Main request

2. *Novelty (Articles 52(1) and 54(1) and (2) EPC)*

2.1 Document E1 (see in particular Figures 1 to 3 and pages 429, 430 and 433) refers to an experimental study as to the effect of vagal stimulation on the prevention of heart arrhythmias in cats. Restoration of blood flow to the heart following an artificially generated acute myocardial ischemia gives rise to ventricular arrhythmias, so-called "reperfusion arrhythmias". In one group of animals (group 3), vagal stimulation by a train of electrical pulses (pulse width 4 ms; frequency 10-15 Hz; amplitude 4 -10V) was started 30 seconds before the start of reperfusion and continued for 2 minutes after reperfusion (see the paragraph bridging the left-hand and the right-hand column on page 430). For another group (group 4), right ventricular pacing at a rate of about 235 beats/min (corresponding to the pre-stimulation value of the heart rate; Table 1) was additionally started 15 seconds before reperfusion and was maintained throughout reperfusion. Compared with control groups (groups 1 and 2) getting no stimulation

treatment, animals from groups 3 and 4 did not develop ventricular tachycardia. Moreover, group 3 animals developed significantly less incidences of ventricular fibrillation when the heart rate was allowed to decrease from 230 to 100 beats/min, whereas such a "protective" effect was only slightly and not significantly pronounced for group 4 animals, the hearts of which were paced at about 235 beats/min. A further reference group of animals was treated by ventricular pacing alone. No protective effect on the occurrence of reperfusion arrhythmias was observed for this group.

2.2 Thus the experimental setup used in the experiments disclosed by E1 comprises, in the terms of independent claims 1 and 2 of the patent in suit, the following features:

- means for detecting an occurrence of an abnormal condition of the heart;

- heart stimulating means for generating and delivering electrical stimulation to the heart;

- at least one nerve stimulation electrode adapted to be placed in electrical contact with preselected nerve fibers within the patient's nervous system;

- nerve fiber pulse stimulating means electrically coupled to said nerve stimulation electrode for generating and delivering stimulating pulses to the preselected nerve fibers; and

– arrhythmia therapy control means (in the broadest meaning of this term; presupposing some kind of automated control of the arrhythmia-suppressing experiment).

2.3 However, although the setup of E1 certainly implies means for monitoring the heart rate and recording an intracavitary electrocardiogram, there is nothing to suggest that the heart stimulation applied to group 4 animals is anything else than a ventricular pacing at a predetermined, fixed rate corresponding to the normal heart rhythm. The pacing as such is not intended to form part of a therapy, such as antitachycardia pacing, cardioversion and defibrillation, of an **existing** arrhythmia. Moreover, as a matter of fact, there is nothing in the setup of E1 which would resemble an arrhythmia therapy control means which is operative, **in response to** the detection of an arrhythmia, so as to select and direct an appropriate parasympathetic autonomic nervous system stimulation therapy in combination with an appropriate heart stimulation therapy.

Finally, a continuous train of pulses applied at a fixed rate, as known from E1, is not identical to repetitive brief bursts of electrical pulses, *ie* groups of pulses separated by intervals without pulses.

Therefore, contrary to the appellant's submission, the experimental setup according to E1 does not constitute an antiarrhythmia pacemaker having arrhythmia therapy control means falling under the terms of claim 1 of the patent as granted.

2.4 For these reasons, the subject-matter of patent claim 1 is novel with respect to the teaching of document E1.

The Board is also satisfied that none of the other prior art documents cited in the appeal discloses an antiarrhythmia pacemaker having arrhythmia therapy control means for a combined stimulation therapy of the heart and the parasympathetic autonomic nervous system as defined in claim 1 under consideration. Moreover, none of the cited documents discloses an antiarrhythmia pacemaker having therapy control means operative in response to the detection of precursors to malignant cardiac arrhythmias to select and direct a combined stimulation therapy of the heart and the parasympathetic autonomic nervous system as defined in claim 2 of the patent as granted.

3. *Inventive step (Articles 52(1) and 56 EPC)*

3.1 Conventional antiarrhythmia pacemakers as known for instance from document E2 (see in particular the chapters "background of the invention" and "summary of the invention; and Figures 1 and 3) comprise:

- means for detecting an occurrence of an abnormal condition of the heart such as tachycardia and fibrillation episodes;

- heart stimulating means for generating and delivering electrical stimulation to the heart; and

- arrhythmia therapy control means responsive to said detecting means for controlling said heart

stimulating means; wherein the therapy control means is operative for treating arrhythmia episodes in the patient's heart by an appropriate heart therapy selected from the group of antitachycardia pacing, cardioversion and defibrillation.

The subject-matter of patent claim 1 differs from such a conventional antiarrhythmia pacemaker in the provision of:

- at least one nerve stimulation electrode adapted to be placed in electrical contact with preselected nerve fibers within the patient's nervous system,

- nerve fiber pulse stimulating means electrically coupled to said nerve stimulation electrode for generating and delivering stimulating pulses to the preselected nerve fibers, and

- arrhythmia therapy control means selecting and directing, in combination with the appropriate heart therapy, an appropriate parasympathetic autonomic nervous system stimulation therapy in the form of repetitive brief bursts of electrical pulses.

The corresponding objective problem to be solved which is associated with these measures could be seen in a further improvement of the therapeutic capabilities of existing antiarrhythmia pacemakers.

3.2 As already discussed in paragraph 2.1 above, there is experimental evidence, such as provided by document E1, for the fact that electrical stimulation of the parasympathetic autonomic nervous system has a prophylactic effect on the occurrence of arrhythmias in that it prevents development of a ventricular tachycardia and significantly reduces incidences of ventricular fibrillation. The protective effect caused by vagal stimulation is considered to be due to a lowering of the heart rate.

A similar teaching is given by document E3 (see the chapters "Introduction" and "Discussion"; Tables 1 and 2 and Figures 1 and 2 with the corresponding description), which refers to an experimental study as to the protective effect of vagal stimulation against the occurrence of heart arrhythmias and in particular ventricular fibrillations. The experiments were conducted on dogs, with the fibrillations being induced by administration of certain chemicals. For one group of dogs vagal stimulation with electrical pulses of a pulse length of 2 ms and a frequency of 20 Hz was effected during administration of the chemicals, whereas no vagal stimulation was done for a control group. Vagal stimulation was continued either until ventricular fibrillation occurred or for 30 s in cases where fibrillation did not develop. During all experiments, the heart rate was simultaneously stabilised by atrioventricular sequential pacing at a constant rate. When ventricular fibrillation occurred, immediate cardioversion was achieved by a 100 J transthoracic shock. It was found that vagal stimulation significantly raised the dose of the chemicals required to induce ventricular fibrillation

and prolonged the time to onset of the arrhythmia. On the basis of the experimental findings, it was supposed that vagal stimulation could protect against evocation of ventricular arrhythmias by sympathetic neural activation and thus inhibited the arrhythmogenic effects of sympathetic stimulation (page 808, first paragraph).

The fact that vagal stimulation lowers the heart rate by acting as an antagonist to sympathetic nerve activity is further confirmed by document E4 (see *eg* Figures 2 and 3), which reports on experiments conducted on dogs. The vagal stimulation was performed by bursts of pulses of varying frequency (Figure 1; page H336, left-hand column, first paragraph). As regards the pathophysiological implications of the experimental findings, it was supposed that an antidefibrillatory effect of vagal activation was partly dependent on direct electrophysiological effects and even present under conditions of elevated sympathetic activity.

3.3 The respondent correctly observes that in none of the experimental setups known from E1, E3 or E4 vagal stimulation was used for therapeutic treatment of an existing arrhythmia.

Nevertheless, the documents contain a number of indications on the basis of which the skilled person working in the technical field at issue of antiarrhythmia pacemakers would have reason to believe that vagal stimulation does not only possess a prophylactic effect on arrhythmias of the heart but

would as well constitute a therapeutic means for treating an existing arrhythmia.

In fact, the presumption in document E1 (see page 433, left-hand column, last paragraph) that the observed protective effect may be due to an interruption of the self-sustaining automatic mechanism responsible for the perpetuation of the ventricular tachycardia implies an allusion to circumstances which are normally associated with an existing arrhythmia. As regards E3, the document (see the first paragraph of chapter "Introduction" on page 801; page 807, left-hand column, third paragraph) refers to a number of earlier studies reporting that vagal stimulation can terminate certain forms of ventricular arrhythmias.

Moreover, given the fact that the experimental setup of document E3 already encompasses means for vagal stimulation as well as means for cardioversion, no inventive merit can be attributed to the idea to join together in a single device an antiarrhythmia pacemaker and a vagal nerve stimulator, the latter comprising nerve fiber stimulating means and a nerve stimulating electrode.

3.4 The question arises, however, whether the prior art would have incited the skilled person not just to devise an apparatus capable of applying antiarrhythmia pacing or vagal stimulation as alternative measures of treating an arrhythmia of the heart but to equip such an apparatus with means allowing for a combined application of both measures of therapeutic treatment and thus, more specifically, to provide for a control means which is operative in response to a detected

arrhythmia for selecting and directing a parasympathetic autonomic nervous system stimulation therapy **in combination with** an appropriate heart therapy.

3.4.1 In this respect, the respondent as well as the opposition division considered the prior art relating to vagal stimulation to even lead the skilled person away from a therapy combining heart stimulation and vagal stimulation as claimed in the present patent. In particular, the experimental findings summarized in Figure 3 of document E1 and the corresponding explanations (cf page 433, right-hand column, third and fifth paragraph), which taught that vagal stimulation in combination with pacing did not prevent the degeneration of ventricular tachycardia into ventricular fibrillation and that ventricular fibrillation was prevented by vagal stimulation only when the heart rate was not controlled by ventricular pacing, would have discouraged the skilled person from providing in one device means for vagal stimulation and pacing for the purpose of a combined antiarrhythmia therapy.

3.4.2 The Board does not share this view for the following reasons :

The argument focuses on comments in document E1 which concern certain observations relating to ventricular fibrillation. What is ignored, however, is firstly the fact that fibrillation is only one (although extreme) form of an arrhythmia. The same Figure 3 of E1 shows that another form of arrhythmia, *ie* ventricular tachycardia, is completely suppressed by vagal

stimulation alone as well as by vagal stimulation in combination with pacing. Secondly, even for the case of ventricular fibrillation the findings of document E1 are not generally valid. Document E3 provides in this respect experimental evidence (see the results listed in Table 1 in combination with the references to the experimental method on page 802, left-hand column, second paragraph) that vagal stimulation performed with simultaneous normal rate pacing of the heart has a substantive protective effect in case of a chemically-induced ventricular fibrillation. Thirdly, constant rate pacing as applied in documents E1 and E3 in combination with vagal stimulation does not constitute and should not be confused with an appropriate antiarrhythmia heart therapy, which, as listed in claim 1, would normally be selected from the group of antitachycardia pacing, cardioversion and defibrillation. Thus, the prior art teaching, which consistently emphasises the sedating effect vagal stimulation exercises on the heart's activity, certainly would not have deterred the skilled person from considering vagal stimulation as a promising therapeutic supplement to a suitable antiarrhythmia heart therapy.

3.4.3 Quite on the contrary, for the skilled person taking up the teachings of documents E1, E3 or E4 it would, for instance, have appeared a promising scheme of therapeutic treatment of arrhythmias of the heart to combine a conventional antiarrhythmia heart therapy applied in response to a detected arrhythmia with an immediately subsequent vagal stimulation, if only to take advantage in such a critical heart condition of the known effect of reducing the risk for recurrence of

the arrhythmia. The implementation of such a function in an antiarrhythmia pacemaker would obviously require the provision of control means which, in response to a detected arrhythmia, does not only select and direct an appropriate heart therapy but, possibly with a certain delay, also selects and directs an appropriate stimulation of the parasympathetic autonomic nervous system.

A device having this readily conceivable functionality would however fall under the terms of patent claim 1, which, in fact, is directed to just any appropriate vagal stimulation therapy in combination with an antiarrhythmic stimulation of the heart, be it preceding, concurrent with or subsequent to the latter.

3.5 Finally, as regards the significance of the requirement for a stimulation of the parasympathetic nervous system by brief bursts of electrical pulses, neither claim 1 nor the patent description offers any evidence or explanation why or in which respect brief bursts of pulses (or a single pulse) would be preferable over a nerve stimulation by a continuous train of pulses. Quite on the contrary, the patent specification notes that "*a vagal stimulation in the form of a single pulse or a short burst of pulses may not be an appropriate therapy in response to the detection of a high rate arrhythmia …*" (column 25, lines 39 to 50).

Since it is not apparent which specific technical or medical effect would be associated with a stimulation by brief bursts of pulses instead of a train of pulses such as known from documents E1 and E3, no inventive merit can be attributed to this claimed measure. At any

rate, protective vagal stimulation by repetitive bursts of pulses is known from document E4 (cf Figure 1 and the corresponding description on page H336).

3.6 For the above reasons, the Board considers claim 1 of the patent as granted to be merely directed to a straightforward implementation in a conventional antiarrhythmia pacemaker, such as known from document E2, of an idea rendered obvious by experimental findings concerning antiarrhythmic effects of vagal stimulation, such as presented in documents E1, E3 and E4. The subject-matter of claim 1 thus does not involve an inventive step within the meaning of Article 56 EPC.

4. Consequently, the respondent's main request is not allowable.

Auxiliary request

5. Since claim 1 of the auxiliary request is identical to claim 1 of the main request its subject-matter does not involve an inventive step either.

Therefore, the auxiliary request is also not allowable.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chairman:

R. Schumacher B. Schachenmann