Internal distribution code:

(A) [-] Publication in OJ
(B) [-] To Chairmen and Members
(C) [-] To Chairmen
(D) [X] No distribution

Datasheet for the decision of 17 March 2021

Case Number: T 1516/16 - 3.2.02

Application Number: 09773783.7

Publication Number: 2334229

IPC: A61B5/021, A61B5/022

Language of the proceedings: EN

Title of invention:
EVALUATE AORTIC BLOOD PRESSURE WAVEFORM USING AN ADAPTIVE PERIPHERAL PRESSURE TRANSFER FUNCTION.

Patent Proprietor:
Bmeye B.V.

Opponent:
Pulsion Medical Systems SE

Headword:

Relevant legal provisions:
RPBA Art. 12(4)
EPC Art. 56

Keyword:
Admittance of late-filed evidence submited with the statement of grounds of appeal - (yes)
Inventive step - main request (no); auxiliary request 1 (yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

Boards of Appeal

Chambres de recours

Boards of Appeal of the
European Patent Office
Richard-Reitzner-Allee 8
85540 Haar
GERMANY
Tel. +49 (0)89 2399-0
Fax +49 (0)89 2399-4465

Case Number: T 1516/16 - 3.2.02

D E C I S I O N
of Technical Board of Appeal 3.2.02
of 17 March 2021

Respondent: (Patent Proprietor)	Bmeye B.V. Centerpoint 1, 4th Floor Hoogoorddreef 60 1101 BE Amsterdam (NL)
Representative:	Eisenführ Speiser Patentanwälte Rechtsanwälte PartGmbB Postfach 31 02 60 80102 München (DE)
Appellant: (Opponent)	Pulsion Medical Systems SE Hans-Riedl-Str. 21 85622 Feldkirchen (DE)
Representative:	Kehl, Ascherl, Liebhoff & Ettmayr Patentanwälte Partnerschaft mbB Emil-Riedel-Straße 18 80538 München (DE)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 20 April 2016 concerning maintenance of the European Patent No. 2334229 in amended form.**

Composition of the Board:

Chairman	M. Alvazzi Delfrate
Members:	M. Stern
	Y. Podbielski

Summary of Facts and Submissions

I. Both parties filed appeals against the interlocutory decision of the opposition division finding that, on the basis of auxiliary request 2 then on file, the patent in suit met the requirements of the EPC.

II. By letter dated 30 August 2016, the patent proprietor withdrew their appeal.

III. Oral proceedings before the Board were held on 17 March 2021.

The appellant (opponent) requested that the decision under appeal be set aside and that the patent be revoked.

The respondent (patent proprietor) requested that the appeal be dismissed and the patent be maintained in the form held allowable by the Opposition Division; alternatively that the patent be maintained on the basis of one of auxiliary requests 1-3 filed with the reply dated 17 January 2017. They further requested that documents D7 to D13 not be admitted into the proceedings.

IV. The following documents are relevant for the present decision:

D1: M. Sugimachi et al.: "A new Model-Based Method of Reconstructing Central Aortic Pressure from Peripheral Arterial Pressure", Japanese Journal of Physiology, Vol. 51, 2001, pages 217-222

D6: W.J. Stok et al.: "Changes in finger-aorta pressure transfer function during and after

exercise", Journal of Applied Physiology, Vol. 101, 2006, pages 1207-1214

D7: B.E. Westerhof: "Blood Pressure Analysis on Time Scales from Seconds to Days" (Dissertation), Amsterdam, University of Amsterdam, 2005, Chapter 9, pages 141-148

D8: L. Costanzo: "Physiology", 3rd Edition, 2006, Chapter 4: "Integrative Functions of the Cardiovascular System", pages 171-173

D9: S.A. Plowman et al.: "Exercise Physiology for Health, Fitness, and Performance", 2nd Edition, 2003, Chapter 13: "Cardiovascular Responses to Exercise", pages 354-356

V. Independent claim 1 of the main request (which corresponds to the request held allowable by the Opposition Division) reads as follows:

"1. A method for reconstructing an aortic blood pressure waveform of a person from a peripheral blood pressure waveform of the person comprising the steps of:
- determining at least one pre-selected parameter of the peripheral blood pressure waveform from analysis of the peripheral blood pressure waveform;
- reconstructing the aortic blood pressure waveform from the peripheral blood pressure waveform using a pressure transfer function having at least one adjustable characteristic, wherein said adjustable characteristic is determined using the at least one pre-selected parameter of the peripheral blood pressure waveform, wherein the at least one pre-selected parameter of the blood pressure waveform is selected from a group consisting of: cardiac output (CO), heart rate (HR), stroke volume (SV), total peripheral

resistance {TPR), peripheral mean arterial pressure (MAP), diastolic arterial pressure (DBP)."

VI. Independent claims 1 and 8 of auxiliary request 1 read as follows (amendments to claims 1 and 9 of the main request highlighted by the Board):

"1. A method for reconstructing an aortic blood pressure waveform of a person from a peripheral blood pressure waveform of the person comprising the steps of:
- determining at least one pre-selected parameter of the peripheral blood pressure waveform from analysis of the peripheral blood pressure waveform;
- reconstructing the aortic blood pressure waveform from the peripheral blood pressure waveform using a pressure transfer function having at least one adjustable characteristic, wherein said adjustable characteristic is determined using the at least one pre-selected parameter of the peripheral blood pressure waveform, wherein the at least one pre-selected parameter of the blood pressure waveform is ~~selected from a group consisting of:~~ cardiac output (CO)~~, heart rate (HR), stroke volume (SV), total peripheral resistance (TPR), peripheral mean arterial pressure (MAP), diastolic arterial pressure (DBP)~~."

"8. A device for reconstructing an aortic blood pressure waveform from a peripheral blood pressure waveform comprising:
- a memory unit for storing a pressure transfer function having at least one adjustable characteristic and at least the peripheral blood pressure waveform;
- a processor arranged for determining at least one pre-selected parameter of the peripheral blood pressure

waveform from analysis of the peripheral blood pressure waveform;
- determining the adjustable parameter of the pressure transfer function from the at least one pre-selected parameter of the peripheral blood pressure waveform;
- reconstructing of aortic blood pressure waveform from a peripheral blood pressure using the pressure transfer function with the adjusted characteristic,
wherein the processor is further adapted to select cardiac output (CO) for the at least one preselected parameter of the blood pressure waveform ~~an item from a group consisting of: cardiac output (CO), heart rate (HR), stroke volume (SV), total peripheral resistance (TPR), peripheral mean arterial pressure (MAP), diastolic arterial pressure (DBP)~~."

Claims 2 to 7, 9 and 10 are dependent claims. Claim 11 is addressed at a computer program product comprising instructions for causing a processor to carry out the steps of the method according to any one of the preceding claims 1 to 7.

VII. The arguments of the appellant (opponent) relevant for the present decision are summarised as follows:

Admissibility of D7, D8 and D9

Document D7, cited for the first time in the statement of grounds of appeal, should be admitted. D7 supplemented the disclosure of the closest prior art D6, which refers several times to D7 in the context of investigating the influence of various cardiovascular parameters on transfer functions TF. Moreover, D7 was prima facie highly relevant, as it disclosed on page 143 the same formula for the characteristic Fmin of the transfer function as the formula of the peak

frequency of the transfer function in paragraph [0038] of the contested patent. D7 was therefore of high prima facie relevance to the maintenance of the patent in suit.

D8 and D9 should be admitted since they served to evidence what was common general knowledge. According to the case law of the boards of appeal, late filing of such evidence was admissible to prove common general knowledge if challenged.

Main request - inventive step

Document D6 was the closest prior art. It disclosed a method comprising the steps to determine at least one parameter of the peripheral blood pressure waveform and to reconstruct the aortic blood pressure waveform using a transfer function having at least one adjustable characteristic, Fmin, which was determined using said at least one parameter of the peripheral blood pressure waveform. The parameters recited in claim 1 of the main request differed from those disclosed in D6, in particular, on page 1210, first sentence. However, this sentence pointed to publication (45), i.e. D7. Hence, following this pointer when attempting to improve the TF, the skilled person would take into account D7, in particular, the formula for Fmin on page 143, presenting a linear combination of, inter alia, the peripheral mean arterial pressure (MAP) and the diastolic blood pressure (DBP). These parameters were recited in claim 1. This formula was the same as that disclosed in the patent (paragraph [0038]) for the corresponding characteristic Fpeak. Hence, if Fpeak in the patent was considered to be an adjustable characteristic, the same had to be concluded for Fmin in D7. Starting from D6, which provided the skilled

person with linear relationships between cardiovascular parameters and the Fmin of individual transfer functions during rest and exercise, the skilled person would certainly consider using Fmin of D7 as an adjustable characteristic of the TF. Therefore, the subject-matter of claim 1 was not inventive.

Auxiliary request 1 - inventive step

The subject-matter of independent claims 1 and 8 was limited to cardiac output as the pre-selected parameter of the peripheral blood pressure waveform. The skilled person would, by means of his common general knowledge as represented by basic textbooks (D8, page 172, table 4-8; D9, page 354 et seq., Figure 13.4), be incited, starting from D6, to improve the reconstructed systolic and diastolic pressure as well as wave shape by predicting even further the transfer function parameters disclosed in D7. Thus, he would consider the prediction of Fmin using further parameters derivable from the peripheral blood pressure waveform, namely CO, SV and TPR. Therefore, the subject-mater of independent claims 1 and 8 was not inventive.

VIII. The arguments of the respondent (patent proprietor) relevant for the present decision are summarised as follows:

Admissibility of D7, D8 and D9

The appellant introduced document D7 for a new objection of lack of inventive step starting from D6. D7 was filed for the first time in appeal proceedings, although it could have been filed in opposition proceedings, particularly since it was explicitly cited

in D6. Furthermore, it was not prima facie relevant, as it led away from the claimed subject-matter.

The appellant referred to D8 and D9 as evidence of the common general knowledge regarding the response of cardiovascular parameters, such as heart rate or cardiac output, with exercise. However, D8 and D9 did not contain any hint at a transfer function used to reconstruct aortic blood pressure waveforms. Thus, D8 and D9 were not prima facie relevant.

As a consequence, D7, D8 and D9 were late filed and were thus not to be admitted for lack of prima facie relevance.

Main request - inventive step

The method of claim 1 was inventive over D6 in combination with D7. Document D6 did not disclose or suggest that Fmin could be an adjustable characteristic of the transfer function TF for adapting the transfer function by means of a pre-selected parameter of the peripheral blood pressure waveform. D6 merely disclosed that Fmin varied depending on certain blood parameters, but did not disclose that a generic transfer function TF could be individualised and adjusted using its characteristic Fmin as an adjustable characteristic. Also D7 failed to disclose or suggest reconstructing the aortic blood pressure waveform from the peripheral blood pressure waveform using a pressure transfer function having at least an adjustable characteristic. Moreover, D7 did not disclose to use the peripheral blood pressure waveform in order to maintain the parameters appearing in the formula on page 143. Instead, D7 used a catheter tip manometer to obtain aortic pressure waveforms at a central site for an ARX

model method (regression calculations) to obtain individualised transfer functions. The appellant's allegation that a skilled person would clearly consider Fmin as a suitable adjustable characteristic of the transfer function TF was unfounded and only based on hindsight. In contrast, a skilled person learnt from D6 that the measured transfer function TF changed in different ways when comparing different subjects (cf. Figure 5). Thus D6 led away from the subject-matter of claim 1 as maintained, so that a skilled person reading D6 would not contemplate that an adaptation of a transfer function to a state of exercise could be fixed to Fmin.

Moreover, D6 and D7 disclosed that generic and even individualised transfer functions obtained during rest were unreliable under exercise, so that aortic blood pressures (such as diastolic pressure DBP) determined by analysis of the peripheral blood pressure waveform were unreliable. Hence, D6 and D7 taught away from the approach of the patent in suit which adjusted an adjustable characteristic (e.g. Fmin = Fpeak) of a generic transfer function by means of a parameter determined by analysis of a peripheral blood pressure waveform to obtain an individualised transfer function.

D6 mentioned that a strong improvement in estimation of central pressure by use of transmission delay to individualise the TF was confirmed by D7 (page 1212, right column, lines 24 to 27). From this passage of D6, a skilled person learnt that transmission delay should be used to individualise the TF for improving pressure estimations, but transmission delay was not contained in the parameters of claim 1. In particular, D6 referred to D1 which concluded that the delay could be

used to individualise the TF, and referred to D7 as confirmation of that.

Auxiliary request 1 - inventive step

None of the prior art documents disclosed or suggested using cardiac output (CO) as a pre-selected parameter for determining an adjustable characteristic of a pressure transfer function. Without hindsight, the knowledge that cardiac output changed with exercise would not have led to the conclusion that cardiac output was a suitable pre-selected parameter for determining a technical characteristic of the transfer function.

Reasons for the Decision

1. The invention

Ideally, blood pressure should be measured centrally in the aorta. In practice this is however seldom done, because the aorta lies deep within the human body and can be reached from the outside only by means of a long tubing which is inserted from a peripheral point where the arteries lie closer to the skin. One therefore has to be satisfied with peripheral pressure waveforms, measured, for example, on a finger (paragraphs [0002] and [0003] of the patent in suit).

The invention relates to a method (and the corresponding device and computer program product) for reconstructing the aortic blood pressure waveform of a person from a measured peripheral blood pressure waveform. This is achieved by means of a function, the "transfer function", which reconstructs, or estimates,

the aortic blood pressure waveform from suitable haemodynamic parameters derived from the peripheral blood pressure waveform (paragraph [0008] of the patent).

As succinctly indicated in paragraph [0009], the method of claim 1 comprises, in essence, the steps to determine at least one parameter of the peripheral blood pressure waveform and to reconstruct the aortic blood pressure waveform using a transfer function having at least one adjustable characteristic which is determined using said at least one parameter of the peripheral blood pressure waveform. Claim 1 of the granted patent (and of the main request) defines a list of such parameters.

2. Admissibility of documents D7, D8 and D9

2.1 With the statement of grounds of appeal, that is, from the onset of the appeal proceedings, the appellant objected lack of inventive step on the basis of D6 in combination with D7. D7 had not been introduced into the first-instance proceedings. However, D6 explicitly refers to it in the relevant context of investigating the influence of various cardiovascular parameters on transfer functions (page 1210, first sentence; page 1207, right column lines 7 and 8; page 1212, right column, lines 24 to 27). This already speaks in favour of needing to consider it when properly analysing the broader context of the scientific findings of D6. Moreover, since D7 actually discloses the same formula for the first minimum Fmin of the transfer function (page 143) as the (corresponding) peak frequency of the transfer function in the contested patent (paragraph [0038]), D7 appears to be, prima facie, of

high relevance for the maintenance of the patent in the version allowed by the Opposition Division.

In view of these considerations, the Board admits D7 into the proceedings in exercise of its discretion under Article 12(4) RPBA 2007.

2.2 D8 and D9 were introduced for the first time with the statement of grounds of appeal as evidence of what the appellant considered to be common general knowledge. According to the case law of the boards of appeal, the filing of such evidence, particularly as early as with the statement of grounds of appeal, is generally admissible.

Hence, the Board admits D8 and D9 into the appeal proceedings.

3. Main request - inventive step

3.1 Document D6, a scientific publication co-authored by the inventor, is considered as the closest prior art. It relates to the reconstruction of the aortic blood pressure waveform of a person from a peripheral blood pressure waveform measured on a finger using a transfer function (TF) (see title and first two sentences of the abstract).

D6 explains on page 1210, first sentence, that various parameters of the peripheral blood pressure waveform, such as the blood pressure level or the wave-front delay, were investigated as to their influence on the TF, in particular on the frequency of its first minimum (Fmin). The modulus of transfer functions TF as a function of frequency for different patients at rest and during exercise is shown in Figure 5.

That is, using the terminology of claim 1, Fmin in D6 is a "characteristic" of the transfer function which is "determined using the at least one pre-selected parameter of the peripheral blood pressure waveform". Moreover, the disclosure in D6 that these pre-selected parameters were investigated as to their influence on the characteristic Fmin means that their functional dependence was "adjusted" in order to obtain satisfactory transfer functions for reconstructing the aortic blood pressure waveform. As indicated by the appellant, D6 in fact discloses that transfer functions were calculated using an autoregressive exogenous (ARX) model method (page 1208, left column, last full paragraph). Therefore, Fmin is a characteristic that is "adjustable", as claim 1 defines.

3.2 Claim 1 defines to select at least one parameter of the peripheral blood pressure waveform from a group of parameters which is not explicitly disclosed in D6. Thus, the parameters listed in claim 1 distinguish the method of claim 1 from that of D6.

3.3 However, in that same sentence on page 1210 referred to above, D6 points to further publications related to the same problem of studying the influence of parameters of the peripheral blood pressure waveform on the TF, inter alia, publication (45), that is, document D7. (D6 also points to D7 on page 1207, right column, lines 7 and 8, and on page 1212, right column, lines 24 to 27.)

Hence, the person skilled in the art intent to improve the reconstruction of the aorta pressure transfer function would certainly consider the reference to D7 given in D6 (D7 is the doctoral thesis of one of the authors of D6). D7 discloses Fmin as a linear

combination of parameters according to the formula on page 143, involving, inter alia, the peripheral mean arterial pressure (MAP) and the diastolic blood pressure (DBP). These are parameters listed in claim 1.

Hence, when attempting to improve the reconstruction of the TF in D6 it would be obvious for the skilled person to use the formula for Fmin given on page 143 of D7. It is noted that the formula is essentially the same as that disclosed in paragraph [0038] of the patent (only the number of digits after the comma of the coefficients varies). As a consequence, the skilled person would readily arrive at the method of claim 1.

3.4 The respondent argued that D6 did not disclose or suggest that Fmin could be an adjustable characteristic of the transfer function TF for adapting the transfer function by means of a pre-selected parameter of the peripheral blood pressure waveform. D6 merely disclosed that Fmin varied depending on certain blood parameters, but did not disclose that a generic transfer function TF could be individualised and adjusted using its characteristic Fmin as an adjustable characteristic. Also D7 failed to disclose or suggest reconstructing the aortic blood pressure waveform from the peripheral blood pressure waveform using a pressure transfer function having at least an adjustable characteristic.

The Board considers, however, that claim 1 does not refer to "individualised" transfer functions, or any "individualised" characteristic of the same. Moreover, claim 1 does not recite the step of "adjusting" the characteristic Fmin. It merely specifies that the characteristic of the TF should be determined using the at least one pre-selected parameter and specifies the characteristic as an "adjustable" characteristic. For

the reasons given under point 3.1 above, Fmin in D6 satisfies this specification of claim 1. Also the formula on page 143 of D7 shows that Fmin is an adjustable characteristic. It is a linear combination of peripheral blood pressure waveform parameters, with coefficients obtained using regression calculations (page 142, last full sentence) to provide a satisfactory TF for reconstructing the aortic blood pressure waveform. Incidentally, it is the same linear combination of parameters of the peripheral blood pressure waveform as the one presented in the patent as an example of an adjustable characteristic (paragraph [0038]).

3.5 The respondent also argued that D6 and D7 disclosed that generic and even individualised transfer functions obtained for the patient during rest were unreliable under exercise, so that aortic blood pressures (such as diastolic pressure DBP) determined by analysis of the peripheral blood pressure waveform were unreliable. Hence, D6 and D7 taught away from the approach of the patent in suit which adjusted an adjustable characteristic (e.g. Fmin = Fpeak) of a generic transfer function by means of a parameter determined by analysis of a peripheral blood pressure waveform to obtain an individualised transfer function.

The Board disagrees. D6 is concerned with the problem of how a TF for an individual subject working well under resting conditions could perform under challenging cardiovascular conditions like exercise (page 1207, right column, second paragraph, second sentence). D6 concludes in its last paragraph that during increasing exercise, changes in the aorta-finger TF develop so that the use of rest aorta-finger TFs becomes unreliable, especially at higher heart rates.

Likewise, D7 discloses that during exercise a general transfer function gives an unreliable reconstruction of aortic pressure (page 143, sentence after the formula for Fmin). However, these statements in D6 and D7 do not detract from the fact that under rest conditions of the patient the transfer functions work well. Thus, the teaching of D6 and D7 is certainly applicable and reliable for patients under rest conditions. The method of claim 1 does not specify any of such conditions.

Moreover, the Board considers that, contrary to the respondent's view, it is not relevant that D6 mentions on page 1212, right column, lines 24 to 27 that a different publication, by Sugimachi et al. (D1), found a strong improvement in the estimation of central pressure by use of transmission delay to individualize the TF, which was confirmed by D7. It is thus realistic to formulate the objective technical problem as mentioned under point 3.3 above, to improve the reconstruction of the transfer function of D6, and to consider, for the solution of this problem, further aspects mentioned in D7.

3.6 It therefore follows that the subject-matter of claim 1 of the main request lacks an inventive step in the sense of Article 56 EPC.

4. Auxiliary request 1

4.1 In independent claims 1 and 8 of auxiliary request 1, the list of parameters of the peripheral blood pressure waveform has been restricted to cardiac output (CO).

4.2 The appellant argued that the method of claim 1 (and of the corresponding independent device claim 8) lacked an inventive step in view of D6 in combination with D7 and

the common general knowledge as evidenced by D8 and D9. It was argued that the skilled person, starting from D6, would be incited to improve the reconstructed systolic and diastolic pressure as well as wave shape by predicting even further the transfer function parameters disclosed in D7. Thus, he would consider the prediction of Fmin using further cardiovascular parameters derivable from the peripheral blood pressure waveform, known from common general knowledge, namely cardiac output (CO), stroke volume (SV) and total peripheral resistance (TPR). Regarding the skilled person's common general knowledge, the appellant cited D8, a textbook on cardiovascular physiology, presenting in Table 4-8 on page 172 cardiac output, stroke volume and total peripheral resistance as cardiovascular parameters, and D9, depicting in Figure 13.4 cardiovascular responses to aerobic exercise, such as stroke volume and total peripheral resistance.

4.3 The Board finds this reasoning unconvincing. It requires the skilled person to first combine the teachings of D6 and D7, and then, in a second step, to further improve the result of this combination by applying his alleged common general knowledge. Already this two-step development of the closest prior art D6 is, according to the established problem-solution-approach, an indication of non-obviousness. Moreover, the appellant's assertion that the skilled person would readily choose cardiac output (CO) as a suitable pre-selected parameter for determining a characteristic of the transfer function such as Fmin (for the sole reason that it is allegedly known to be a further parameter derivable from a peripheral blood pressure waveform) is unconvincing. The sole knowledge that cardiac output changes with exercise would not have readily led the person skilled in the art to conclude, without the

benefit of hindsight, that it would be a suitable parameter for determining a technical characteristic of the transfer function.

The Board is therefore not convinced of the alleged obviousness of the subject-matter of independent claims 1 and 8.

4.4 As a consequence, independent claims 1 and 8 of auxiliary request 1 satisfy the requirements of Article 56 EPC. The same holds true, a fortiori, for the preferred embodiments of dependent claims 2 to 7, 9 and 10, as well as for the computer program product of claim 11, comprising instructions for causing a processor to carry out the steps of the method according to claims 1 to 7.

5. There are thus no grounds prejudicing the maintenance of the patent on the basis of auxiliary request 1.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division with the order to maintain the patent in the following version:

   - Claims 1 to 11 of auxiliary request 1 filed with letter dated 17 January 2017

   - Description: pages 2 to 7 filed during the oral proceedings on 17 March 2021

   - Drawings: sheets 1/3 to 3/3 of the patent specification.

The Registrar: The Chairman:

D. Hampe M. Alvazzi Delfrate

Decision electronically authenticated