Datasheet for the decision of 27 September 2006

Case Number: T 1171/01 - 3.5.01
Application Number: 97919229.1
Publication Number: 0901665
IPC: G06K 9/00, G01N 15/14
Language of the proceedings: EN

Title of invention:
Method and apparatus for automatically detecting malignancy-associated changes

Applicant:
MonoGen, Inc.

Opponent:
-

Headword:
Detecting malignancy-associated changes/MONOGEN

Relevant legal provisions:
EPC Art. 54, 56, 123(2)

Keyword:
"Inventive step (no)"

Decisions cited:
T 1173/97

Catchword:
-
Case Number: T 1171/01 - 3.5.01

DECISION
of the Technical Board of Appeal 3.5.01
of 27 September 2006

Appellant: MonoGen, Inc.
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Representative: Spall, Christopher John
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Decision under appeal: Decision of the Examining Division of the European Patent Office posted 30 March 2001 refusing European application No. 97919229.1 pursuant to Article 97(1) EPC.

Composition of the Board:
Chairman: S. Steinbrener
Members: R. Wibergh
          P. Schmitz
Summary of Facts and Submissions

I. This appeal is against the decision of the examining division to refuse European patent application No. 97 919 229.1.

II. The following documents will be referred to in the present decision:


III. According to the decision appealed document D1, regarded as disclosing the closest prior art, anticipated the invention as defined in claim 1 in the version of 21 February 2001 or at least rendered it obvious in combination with D2.

IV. Claim 1 read (including two corrections requested by the appellant by letter dated 25 August 2006):

"A method of detecting malignancy-associated changes in a cell sample, comprising the steps of:
obtaining a cell sample;
staining the sample to identify cell nuclei within the sample;
obtaining an image of the cell sample with a digital microscope of the type that includes a digital CCD camera and a programmable slide stage;
recording the image in a computer system;
focusing the image;
identifying objects in the image;
calculating a set of feature values for each object; and
analyzing the feature values to determine whether each object is a cell nucleus; and computing a set of feature values for each nucleus found in the sample and from the feature values determining whether the nucleus exhibits malignancy-associated change, and characterised in that the determination is made by a classifier constructed from a first database comprising feature values obtained from apparently normal cells of a healthy patient and a second database comprising feature values obtained from apparently normal cells of an abnormal patient".

V. With the statement of grounds of appeal dated 23 July 2001 the appellant requested that the decision be set aside and a patent be granted based on claim 1 on file or on one of three alternative claims filed together with the grounds of appeal.

VI. Alternative claim 1 differed from the main request in that it was directed to a method of detecting malignancy-associated changes in a cell sample "for further investigation" and that it contained the further steps of

"determining a ratio of nuclei determined to exhibit malignancy-associated changes to the total nuclei in the subsample;
comparing the ratio to a predetermined threshold; and determining the need for further investigation if the ratio exceeds the predetermined threshold".
VII. Alternative claim 2 mainly differed from alternative claim 1 in that there was no mention of first and second databases.

VIII. Alternative claim 3 differed from alternative claim 2 in that it was directed to a "method of detecting malignancy-associated changes in a cell sample of a patient to determine the need for further investigation of changes suggestive of cancer in the patient".

IX. By communication dated 6 August 2004, the Board observed in respect of the alternative claims that there appeared to be no original support for the feature "determining the need for further investigation if the ratio exceeds the predetermined threshold". Reference was made to the different statement at page 13, lines 6 to 9 of the application.

X. By letter dated 25 August 2006 in response to a summons to oral proceedings, the appellant requested two minor corrections to claim 1 of the main request (cf. point IV supra) and filed two further claim versions: "Claim A" and "Claim B".

XI. Claim A differed from claim 1 according to the main request in that "cancer patient" replaced "abnormal patient" (cf. the final feature of the claim).

XII. Claim B read:

"A classifier for detecting the presence of malignancy associated changes (MAC) in a cell nucleus, wherein the classifier is constructed using a first database comprising feature values obtained from apparently normal cells which were known to come from healthy
patients and a second database comprising feature values obtained from apparently normal cells which were known to come from cancer patients, wherein data from said databases is used to develop a discriminant function that can discriminate between MAC-positive nuclei and MAC-negative nuclei".

XIII. Grant of a patent was requested in accordance with a main request and ten auxiliary requests. These requests were based on the following independent claims:

Main request:
Claim 1 of 21 February 2001 (including the corrections filed on 25 August 2006) and claim B as claim 11;

Auxiliary request 1:
Claim 1 of 21 February 2001 (including the corrections filed on 25 August 2006);

Auxiliary request 2:
"Alternative claim 1" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 3:
"Alternative claim 2" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 4:
"Alternative claim 3" of 23 July 2001 as claim 1, and claim B as claim 11;

Auxiliary request 5:
"Alternative claim 1" of 23 July 2001 as claim 1;
Auxiliary request 6:
"Alternative claim 2" of 23 July 2001 as claim 1;

Auxiliary request 7:
"Alternative claim 3" of 23 July 2001 as claim 1;

Auxiliary request 8:
Claim A as claim 1 and claim B as claim 11;

Auxiliary request 9:
Claim A as claim 1;

Auxiliary request 10:
Claim B as only claim.

XIV. Oral proceedings, which the appellant did not attend, were held on 27 September 2006. After deliberation the Board announced its decision.

Reasons for the Decision

1. Background of the invention

The invention is a method of detecting malignancy-associated changes (MACs) in a cell sample. As explained in the application, MACs are "subtle changes that are known to take place in the nuclei of apparently normal cells found near cancer tissue. In addition, MACs have been detected in tissue found near pre-cancerous lesions. Because the cells exhibiting MACs are more numerous than the malignant cells, MACs offer an additional way of diagnosing the presence of
cancer, especially in cases where no cancerous cells can be located" (paragraph bridging pages 1 and 2).

2. The prior art

2.1 D1

The appellant accepts that D1 discloses the features contained in the preamble of claim 1. Multivariate analysis is referred to at column 5, line 16 onwards, and is said to comprise "cluster analysis leading to a decision tree made up of thresholds and discriminant functions". There is no mention of classifiers.

2.2 D2

D2 is concerned with the detection of nuclei of abnormal cells, in particular cancerous and precancerous cells (cf. claim 9). It does not explicitly concern MACs. The detection of normal and abnormal cells is performed automatically by means of a classifier (cf. page 8, line 20 to page 10, line 10).

The main request

3. Claim 1

3.1 The invention being a method of detecting malignancy-associated changes in cells, the question whether or not it constitutes a diagnostic method in the sense of Article 52(4) EPC would normally have to be investigated. However, in the present circumstances no answer to this question is required since, as set forth below, the invention does in any case not involve an inventive step.
3.2 The examining division held that D1 anticipated the invention because it suggested using *a posteriori* clinical knowledge of the patients' medical history (decision, point 3). This could be concluded from the definition of MACs in D1 as "changed nuclear features of ostensibly normal cells growing in the vicinity of the cancerous or precancerous lesion compared to those of normal cells from the same type of tissue of a normal, healthy individual" (column 2, lines 19 to 25). The examining division thus considered that knowledge of cells exhibiting MAC as well as cells not exhibiting MAC was necessary in order to identify discriminant features.

3.3 The appellant has argued that since D1 does not mention a classifier constructed from two databases comprising features from healthy and abnormal patients, respectively, the cluster analysis mentioned in D1 would not involve using cells from a healthy patient. If it did it would lead to a diagnosis of "not-normal" rather than "exhibits MAC", which would seem nonsensical (cf. letter dated 25 August 2006).

3.4 The Board finds the argumentation of the examining division convincing. It would indeed appear strange if abnormal changes could be identified without knowledge of the normal state, and the Board cannot see how D1 could possibly be interpreted along the lines suggested by the appellant. A classifier constructed from "normal" and "abnormal" cell databases in accordance with claim 1 is therefore to be regarded as implicitly disclosed in D1. On the basis of this understanding all features of claim 1 are known from this document.
Moreover, as pointed out in the decision under appeal (point 3), a classifier constructed from a training database containing normal and abnormal cells is known from D2 (page 9, line 32 to page 10, line 4).

The appellant has observed that D2 is concerned with the detection of cancer cells rather than MACs, but this is in the Board's view no reason for ignoring the document. Cytologists working with MACs must be assumed to take an interest in any method used for categorization of cells or cell nuclei, and particularly methods for diagnosing cancer.

The appellant has further argued that in D2 there is no consideration of a population of (apparently) normal cells in both healthy and cancerous patients. But this difference merely reflects the fact that D2 is concerned with malignant cells, not with cells exhibiting MACs. It goes without saying that the training databases must be chosen in accordance with the purpose of the detection.

The Board thus concludes, as did the examining division, that if the skilled person found the indications in D1 insufficient he would consult D2. This document would lead him to apply a classifier constructed from a first database comprising feature values of normal cells (obtained from apparently normal cells of a healthy patient) and a second database comprising feature values of abnormal cells (such obtained from apparently normal cells of a cancer patient) to the method of detecting MACs described in D1.
3.6 It follows that the subject-matter of claim 1 in any case does not involve an inventive step having regard to the teachings of D1 and D2 (Article 56 EPC), even if novelty were accepted by ignoring the fact that features of the claim appear to be implicitly disclosed in D1.

4. Claim B

4.1 Claim B is directed to a classifier. With reference to figure 8 of the application, the description explains that "a classifier 290 is a computer program that analyzes an object based on its feature values" (page 11, lines 21, 22). Decision T 1173/97 (OJ EPO 1999, 609) states that a computer program is not excluded from patentability under Article 52(2) and (3) EPC if it is capable of producing a "further technical effect" which goes beyond the normal physical interactions between program and computer (see the headnote). The Board needs however not to investigate whether the classifier of claim B produces such a further technical effect since, for the reasons indicated below, its subject-matter is in any case obvious.

4.2 Claim B recites the classifier features contained in claim 1 with the addition that data from the databases is used to develop a discriminant function that can discriminate between MAC-positive nuclei and MAC-negative nuclei. The feature "discriminant function" is not regarded as a further limitation since it is merely the name given for the set of rules used for detecting MACs. This interpretation is in line with the appellant's statement that claim B "claims the same
invention /as claim 1/" (letter dated 25 August 2006). Thus this claim must share the fate of claim 1. It may also be noted that D1 employs the expression "discriminant function" as well (column 5, lines 16 to 21).

5. It follows that the main request is refused.

Auxiliary requests 1-4, 8 and 10

6. Claim 1 of auxiliary request 1 is identical with claim 1 of the main request. Auxiliary requests 2 to 4, 8 and 10 contain claim B. These requests are therefore also not allowable.

Auxiliary requests 5-7

7. Claim 1 according to auxiliary requests 5 to 7 all contain the feature "determining the need for further investigation if the ratio exceeds the predetermined threshold". This feature has no basis in the application as originally filed. The description mentions that "/i/f the frequency of cells exhibiting MACs exceeds the threshold, the computer system can indicate that the patient is healthy at step 342 or likely has or will develop cancer" (page 13, lines 6 to 9). Probable as it may be that a physician will determine the need for further investigation if a patient has been found likely to develop cancer, this is in fact not stated. Therefore this feature has been added in contravention of Article 123(2) EPC and the requests must be refused.
8. It might be added that since the subject-matters claimed do not differ significantly from the invention of the main request, they are in the Board's view in any case unlikely to involve an inventive step.

Auxiliary request 9

9. Claim A according to auxiliary request 9 differs from claim 1 of the main request in that values in the second database are obtained from a "cancer patient" (rather than an "abnormal patient"). This amendment cannot overcome the objections against the main request since both D1 and D2 are concerned with the diagnosis of cancer. Thus this request must also be refused.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

P. Cremona S. Steinbrener