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(54) **TEMPERATURE CONTROL**

(57) The invention relates to a device and a method for rapidly changing and controlling the temperature of diagnostic consumables and their contents in a diagnostic analyser system and provides a system for performing biochemical assays with a fluid, comprising a circular disc-shaped container with at least one compartment for taking up the fluid to be processed in the biochemical assay, wherein the circular disc-shaped container has a centrally arranged acceptance for an axis; a thermal chamber, comprising a housing for accommodating the circular disc-shaped container, wherein the housing comprises a flat upper surface and a flat inner bottom surface, and wherein a cold plate that is connected to a cooling element is arranged above the flat inner bottom surface inside the housing of the thermal chamber, and an inlet and an outlet for an air supply; and a drive comprising the axis with an upper end for its connection to the circular disc-shaped container by crossing a bottom surface of the thermal chamber's housing, wherein the axis is connected to a motor for rotating the axis, and wherein the axis is further connected to a motor for moving the axis vertically inside the thermal chamber.

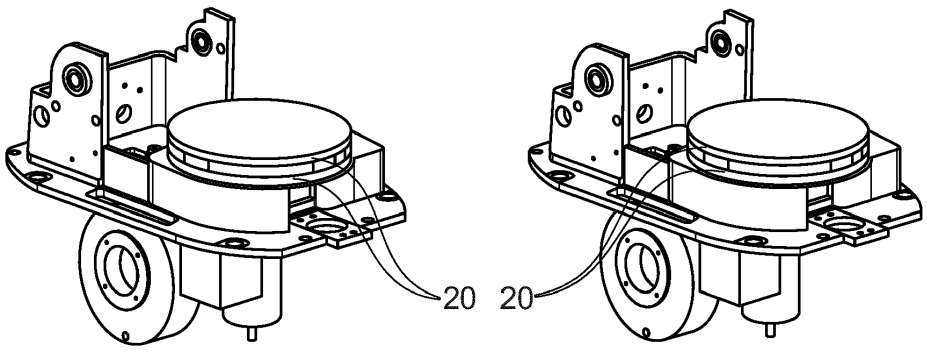

Fig. 3

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Description

Field of the Invention

[0001] The invention relates to a device and a method for rapidly changing and controlling the temperature of diagnostic consumables and their contents in a diagnostic analyser system.

Brief description of the related art

[0002] Automated analyser systems for use in clinical diagnostics and life sciences are produced by a number of companies. For example, STRATEC® SE, Birkenfeld, Germany, produces a number of devices for specimen handling and detection for use in automated analyser systems and other laboratory instrumentation.

[0003] STRATEC designs and manufactures diagnostic instruments with functional modules that have to process a various number of different reaction container like consumables or vessels with an also various number of different handling and processing steps. Such instruments are used for vitro diagnostics (IVD) comprising the crude extraction of nucleic acids and successive real-time polymerase chain reaction (PCR).

[0004] A consumable that has a disc shape is used in devices known from the prior art for solid phase heating and cooling. A metal disc holder is heated with radiation of light and cooled with ambient air. The temperature inhomogeneity of the disc holder during cooling and heating causes increased costs for spare parts and maintenance. In addition, variations in the ambient air temperature are leading to variations in cooling speeds and thus influence the assay or instrument performance.

[0005] Other available real-time PCR instruments use a single medium for tempering consumables containing reaction liquids. Some use gaseous media such as air, in which the consumables are moving in a heated or cooled airflow.

[0006] The use of liquid media for tempering consumables was commercially never successful due to the many technical drawbacks that came along with long-term handling of liquids (usually water) in automated systems.

[0007] Most systems use a solid phase for transferring temperature changes to a consumable comprising a reaction mixture. Usually, Peltier elements are used for heating and cooling in PCR devices, which change the temperature of vials or chips in a vial or chip holder mount on top of it. In this setup, there is no phase transfer since the solid consumable is directly connected to the solid mount. Since the tempered media (mount) does not cover the entire consumable, this design comes with a heated lid solution to prevent condensation. Many solutions taking advantage of this technology in the market for PCR and real-time PCR. In general, these are multiplate approaches, processing samples in a batch format.

[0008] Although an airflow in a system using a gaseous medium allows due to its low heat capacity for a fast change of the temperature in a reaction chamber, the temperature shift of reagents inside the PCR consumable is relatively slow and dependent on homogeneous consumables with minimal deviations of their wall thickness. This is in particular critical during cooling, when it is necessary to reach a precise annealing temperature in order to avoid unspecific amplification of similar targets. In addition, since these systems use ambient air, elevated outside temperatures prolong or even prevent successful PCR.

[0009] Peltier based thermocycler need a relatively massive heatsink for fast cooling. They further need a lot of space and energy to achieve homogenous heating and cooling. The edges of such devices are due to their increased surface related to a delayed reach of a temperature equilibrium so that systems using a solid phase for heat transfer are usually slower than systems which use a gaseous medium.

Object of the Invention

[0010] It is therefore the object of this invention to provide a device and a method for allowing a fast and reliable change of temperature of fluids comprised in a container.

Summary of the Invention

[0011] The present invention provides a system for performing biochemical assays with a fluid, comprising

- a circular disc-shaped container with at least one compartment for taking up the fluid to be processed in the biochemical assay, wherein the circular disc-shaped container has a centrally arranged acceptance for an axis;
- a thermal chamber, comprising a housing for accommodating the circular disc-shaped container, wherein the housing comprises
- a flat upper surface and a flat inner bottom surface, and wherein a cold plate that is connected to a cooling element is arranged above the flat inner bottom surface inside the housing of the thermal chamber, and
- an inlet and an outlet for an air supply; and
- a drive comprising the axis with an upper end for its connection to the circular disc-shaped container by crossing a bottom surface of the thermal chamber's housing, wherein the axis is connected to a motor for rotating the axis, and wherein the axis is further connected to a motor for moving the axis vertically inside the thermal chamber.

[0012] In a further aspect of the invention, the system's upper surface of the thermal chamber's housing comprises an optically transparent element for optical measurements.

[0013] Another embodiment of the invention relates to

a system comprising a heating element for air that is connected to the inlet and outlet of the thermal chamber's housing.

[0014] The cooling element can be a Peltier element.

[0015] The system may also comprise control electronics for the drive and the control electronics can be connected to the heating element.

[0016] The system may further comprise a housing for accepting the drive and the thermal chamber.

[0017] Another object of the invention relates to a method for thermal cycling of a fluidic sample, comprising the steps of

[0018] Providing the fluidic sample in a circular disc-shaped container with at least one compartment;

- Arranging the circular disc-shaped container on an axis that is connected to a drive for rotating, lifting and lowering the axis which crosses the bottom surface of a housing of a thermal chamber enclosing the circular disc-shaped container;
- Closing the thermal chamber;
- Lifting the circular disc-shaped container through the axis connected to it and rotating it in the thermal chamber while heated air is blown into the thermal chamber for raising the temperature to a first temperature in the thermal chamber;
- Stopping rotation of the circular disc-shaped container when the first temperature is reached and exchanging the heated air in the thermal chamber with ambient air;
- lowering the circular disc-shaped container onto a cold plate that is arranged at the inner bottom surface of the thermal chamber's housing through a downwards movement of the axis;
- Cooling the circular disc-shaped container onto the cold plat which is thermally connected to a cooling element to a second temperature;
- Raising the disc-shaped container through an upwards movement of the axis connected to the circular disc-shaped container; and
- Raising the temperature in the thermal chamber to a third temperature.

[0019] Another aspect of the invention relates to a method, wherein the third temperature is higher than the second temperature but lower than the first temperature.

[0020] The method may further comprise the step of the fluidic sample in the circular disc-shaped container being illuminated through an optically transparent part in the upper surface of the thermal chamber's housing and an optical measurement is performed.

[0021] In another embodiment of the method according to the present disclosure, the circular disc-shaped container provides more than one fluidic sample, wherein each fluidic sample is comprised in a separate compartment of the circular disc-shaped container

[0022] Still other aspects, features, and advantages of the present invention are readily apparent from the following detailed description, simply by illustrating preferable embodiments and implementations. The present invention is also capable of other and different embodiments and its several details can be modified in various obvious respects, all without departing from the spirit and scope of the present invention. Accordingly, the drawings and descriptions are to be regarded as illustrative in nature, and not as restrictive. Additional objects and advantages of the invention will be set forth in part in the description which follows and in part will be obvious from the description, or may be learned by practice of the invention.

Summary of the Figures

[0023] The invention will be described based on figures. It will be understood that the embodiments and aspects of the invention described in the figures are only examples and do not limit the protective scope of the claims in any way. The invention is defined by the claims and their equivalents. It will be understood that features of one aspect or embodiment of the invention can be combined with a feature of a different aspect or aspects of other embodiments of the invention, in which:

FIG. 1 shows the repeating cycling steps A, B, and C.

FIG. 2 shows a schematic setup of a consumable disc within a thermal chamber and the drives for rotating and lifting the consumable disc.

FIG. 3 shows a more detailed setup of the ventilated thermal chamber in a mechanical integration.

Detailed Description of the Invention and the Figures

[0024] The technical problem is solved by the independent claims. The dependent claims cover further specific embodiments of the invention.

[0025] The core of the invention consists of a combination of different media to allow fast temperature shifts for objects that are moving in or on the surface of those media.

[0026] The present disclosure relates to a system and method for rapidly changing and controlling the temperature of a sample which is comprised in a container like a consumables for prcessing in a diagnostic analyzer system by altering the physical thermal contact by means of mechanical motion for tempering media with different states of aggregation. This allows fast temperature changes.

[0027] The system according to the present disclosure comprises a circular disc-shaped container as consumable which comprises at least one compartment for taking up a fluidic sample which has to be processed in a biochemical or diagnostic assay. A fluid may be a liquid, gas, or solid which flows under shear stress or gravitation.

[0028] The circular disc-shaped container is placed in-

to a further part of the system according to the present invention, a thermal chamber. Said thermal chamber may also have a circular shape. An axis spans through a bottom plate of the thermal chamber and rhe upper end of the axis is connected to the circular disc-shaped container. The axis can be actuated in two different ways. It may rotate so that a container which is connected to the upper end of the axis is rotating around the axis and the axis and respectively a connected container may be lifted or lowered by a vertical movment of the axis. The axis is connected to drives like a motor for performing said motions. A gearing mechanism may be used for transferring a drive's movement to the axis.

[0029] Hot air is introduced into the thermal chamber through an inlet of the thermal chamber, wherein the inlet is connected to a source for heated air like a fan for instance. The circular disc-shaped container is lifted and fast-spinning while the hot air is blown into the thermal chamber which can be designated as forced convection heating.

[0030] For cooling, the rotation of the circular disc-shaped container is stopped, and the disc-shaped container is lowered by a drive configured for said vertical movement. A cold plate which is arranged at the bottom of the thermal chamber is used for cooling the circular disc-shaped consumable by bringing the cold plate into contact with a solid heatsink. The lowered circular disc-shaped container is brought in contact with the cold plate that is thermally connected to the heatsink. When the cooling process is completed, the circular disc-shaped container is lifted again and the axis connected to the circular disc-shaped container starts to rotate agine the disc-shaped container again in hot air. One possible application that can be performed with such a device is polymerase chain reaction (PCR) which requires rapid changes between hot and cold temperatures of the sample in the conatiner.

[0031] The circular disc-shaped container or its compartments may be filled with fluidic reagents for real-time PCR, which can be rotated and moved in an up and downward direction (z-axis). This design allows free rotation for heating and signal measurement in a gaseous media (air).

[0032] FIG.1 shows the repeating cycling steps A, B, and C. In step A, the circular disc shaped container is lifted and the thermal chamber is filled with hot air while spinning the circular disc-shaped container. In step B is the circular disc-shaped container is lowered and pressed onto a heat sink for cooling. In step C, the temeraure is controlled and maintained so that an optical read-out may be performed. At the end of stepC, the circular disc-shaped container is lifted again and Step A is repeated so that a cycling of the sequence of steps A, B and C is achieved.

[0033] During step A in an assay for isolation DNA, the disc-shaped container is heated up towards denaturation temperature and is lifted and spined freely inside the thermal chamber. An increased temperature of the Peltier base located at the inner bottom surface of the thermal chamber is connected to a Peltier element. Additionally, heated air is introduced into the thermal chamber for raising the inner temperature of the thermal chamber and thus the temperature of the disc-shaped container's content. Circulating hot air is used for a forced convection heating of the disc-shaped container and to achieve an optimized homogeneity of the heating process.

[0034] For step B, the cold plate arranged at the inner bottom surface of the thermal chamber an connected to the Peltier element is cooled by the Peltier element down to the desired temperature, e.g. an annealing temperature appropriate for the respective DNA sequence indented for amplification. The thermal chamber is opened and the heated air inside the thermal chamber is ventilated out of the thermal chamber and replaced with ambient air. Afterwards the chamber closes again. The disc-shaped container stops spinning and is pressed onto the solid phase Peltier base at the inner bottom surface of the thermal chamber until it reaches a desired lower temperature level.

[0035] In step C, the temperature of the disc-shaped container and the thermal chamber is raised and adjusted to the desired elongation temperature for the PCR reaction. The disc is lifted again and starts spinning again. While the consumable disc spins, an optical measurement unit can illuminate and read-out every reaction compartment or cavity on the disc circumference when passing the unit.

[0036] FIG. 2 shows a perspective view onto a circular disc-shaped container 5 according to the present disclosure. The container comprises a centrally arranged acceptance for the axis of the drive (both not shown).

[0037] FIG. 3 shows a schematic setup of a circular disc-shaped container 5 arranged within a thermal chamber 20. The drives 30 for rotating and lifting the circular disc-shaped container 5 are arranged below the thermal chamber 20. The left part of FIG. 2 shows the disc-shaped container 5 freely rotating on a centrally engaged axis 31 in the thermal chamber 20. The arrow indicates the rotation. It is obvious for a skilled person that the circular disc-shaped container may rotate clockwise or counterclockwise.

[0038] Hot air is introduced into the thermal chamber 20, which is indicated by the arrowa at both sides of the thermal chamber 20, so that the circular disc-shaped container 20 and its content will be heated. The arrow on the right part of the chamber indicates a location for optical measurements through a transparent window in the upper surface 21 of the thermal chamber 20 for instance.

[0039] The right part of FIG.2 shows the circular disc-shaped container 5 set still within the meaning that no rotation takes place. The circular disc-shaped container 5 is lowered and thus pressed towards the Peltier element 25 tempered inner bottom surface 22 of the thermal chamber 20 for cooling it.

[0040] FIG. 3 shows a perspective view of of the ventilated thermal chamber 20 in a mechanical integration.

[0041] The design enables a fast heating and cooling, by taking advantage of low heat capacity of air to allow heating and a quick and homogeneous heat transfer to a steady state cooled bottom plate. Since many consecutive repeats of heat and cooling phases are necessary for this application is especially useful and timesaving.

[0042] This invention combines the positive aspects of fast heating with a gaseous medium and fast and homogeneous cooling on a solid phase block. A steady state tempered cooling plate allows fast cycling with a reduced space and energy consumption in comparison to state of the art thermocyclers.

[0043] Since the solid phase will not undergo repetitive temperature changes, it can use a high mass to allow an excellent temperature homogeneity, while accepting heat from the consumable quite fast. This will minimize or even prevent edge effects.

[0044] Moving the consumable into the gaseous phase, allows for fast heating. At the higher denaturation temperature, it is only necessary to reach a certain target temperature channel above the melting temperature of double stranded target DNA and below temperatures that harm taq-polymerases. In this situation, temperature deviations are tolerable

[0045] Alternative approaches may encompass different technical means for heating or cooling of the gaseous media and the solid phase. The consumable may have a different shape in comparison to the above-described disc shaped consumable. Device and method of the present disclosure may be used for other assays than PCR.

[0046] The foregoing description of the preferred embodiment of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise form disclosed, and modifications and variations are possible in light of the above teachings or may be acquired from practice of the invention. The embodiment was chosen and described in order to explain the principles of the invention and its practical application to enable one skilled in the art to utilize the invention in various embodiments as are suited to the particular use contemplated. It is intended that the scope of the invention be defined by the claims appended hereto, and their equivalents. The entirety of each of the aforementioned documents is incorporated by reference herein.

Reference Numerals

[0047]

5 circular disc-shaped container
7 acceptance for axis
20 thermal chamber
21 upper surface
22 inner bottom surface
25 Peltier element
30 drive
31 axis for roataion and vertical movement

Claims

1. A system for performing biochemical assays with a fluid, comprising

- a circular disc-shaped container with at least one compartment for taking up the fluid to be processed in the biochemical assay, wherein the circular disc-shaped container has a centrally arranged acceptance for an axis;
- a thermal chamber, comprising a housing for accommodating the circular disc-shaped container, wherein the housing comprises

i. a flat upper surface and a flat inner bottom surface, and wherein a cold plate that is connected to a cooling element is arranged above the flat inner bottom surface inside the housing of the thermal chamber, and
ii. an inlet and an outlet for an air supply; and

- a drive comprising the axis with an upper end for its connection to the circular disc-shaped container by crossing a bottom surface of the thermal chamber's housing, wherein the axis is connected to a motor for rotating the axis, and wherein the axis is further connected to a motor for moving the axis vertically inside the thermal chamber.

2. The system of claim 1, wherein the upper surface of the thermal chamber's housing comprises an optically transparent element for optical measurements.

3. The system of claim 1 or 2, further comprising a heating element for air that is connected to the inlet and outlet of the thermal chamber's housing.

4. The system of any one of claims 1 to 3, wherein the cooling element is a Peltier element.

5. The system of any one of claims 1 to 4, comprising control electronics for the drive.

6. The system of claim 5, wherein the control electronics are connected to the heating element.

7. The system of any one of claims 1 to 6, further comprising a housing for accepting the drive and the thermal chamber.

8. A method for thermal cycling of a fluidic sample, comprising the steps of

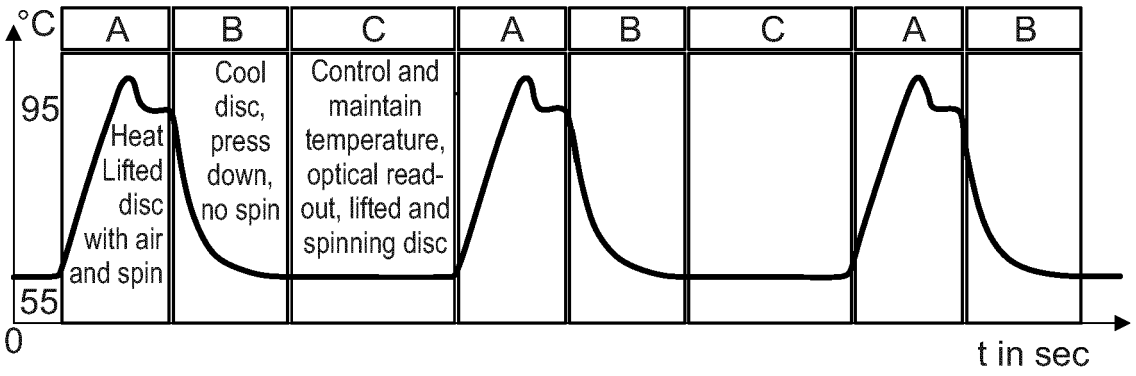
- Providing the fluidic sample in a circular disc-

shaped container with at least one compartment;
- Arranging the circular disc-shaped container on an axis that is connected to a drive for rotating, lifting and lowering the axis which crosses the bottom surface of a housing of a thermal chamber enclosing the circular disc-shaped container;
- Closing the thermal chamber;
- Lifting the circular disc-shaped container through the axis connected to it and rotating it in the thermal chamber while heated air is blown into the thermal chamber for raising the temperature to a first temperature in the thermal chamber;
- Stopping rotation of the circular disc-shaped container when the first temperature is reached and exchanging the heated air in the thermal chamber with ambient air;
- lowering the circular disc-shaped container onto a cold plate that is arranged at the inner bottom surface of the thermal chamber's housing through a downwards movement of the axis;
- Cooling the circular disc-shaped container onto the cold plat which is thermally connected to a cooling element to a second temperature;
- Raising the disc-shaped container through an upwards movement of the axis connected to the circular disc-shaped container; and
- Raising the temperature in the thermal chamber to a third temperature.

9. The method of claim 2, wherein the third temperature is higher than the second temperature but lower than the first temperature.

10. The method of claim 8 or 9, wherein the fluidic sample in the circular disc-shaped container is illuminated through an optically transparent part in the upper surface of the thermal chamber's housing and an optical measurement is performed.

11. The method of any one of claims 8 to 10, wherein the circular disc-shaped container provides more than one fluidic sample, wherein each fluidic sample is comprised in a separate compartment of the circular disc-shaped container.


°C
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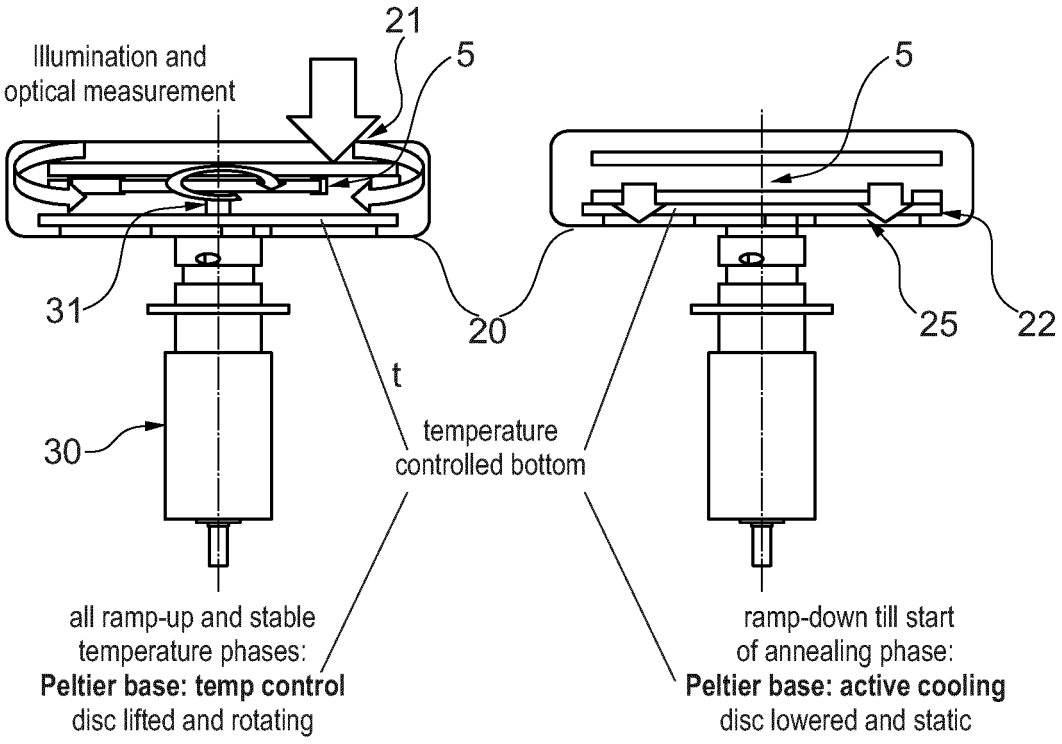
Heat Lifted disc with air and spin
Cool disc, press down, no spin
Control and maintain temperature, optical read-out, lifted and spinning disc
t in sec

Fig. 1


Illumination and optical measurement
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t
30
temperature controlled bottom
all ramp-up and stable temperature phases:
Peltier base: temp control
disc lifted and rotating
ramp-down till start of annealing phase:
Peltier base: active cooling
disc lowered and static

Fig. 2

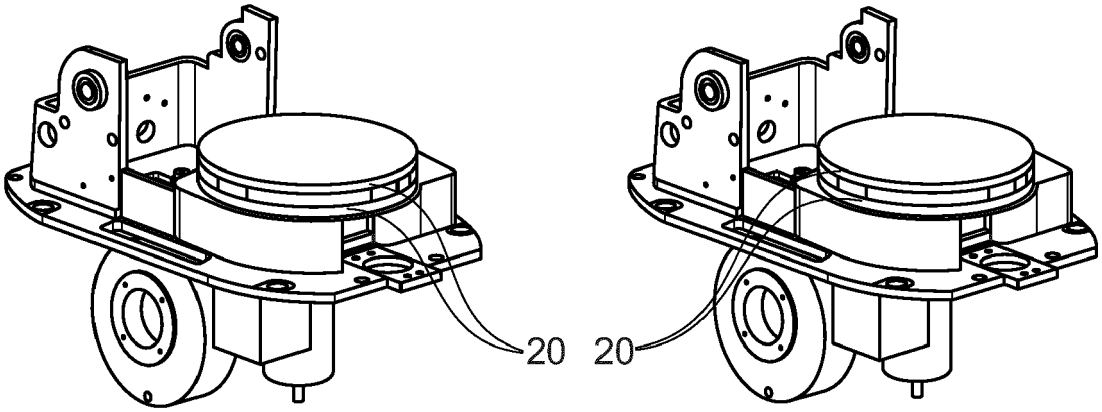

Fig. 3

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EUROPEAN SEARCH REPORT

Application Number
EP 22 19 7262

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A	WO 2005/118144 A1 (ABACUS DIAGNOSTICA OY [FI]; NURMI JUSSI [FI] ET AL.) 15 December 2005 (2005-12-15) * page 13, line 1 - page 14, line 16; figures 2a,2b * -----	1,8	

TECHNICAL FIELDS SEARCHED (IPC)

B01L

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
The Hague	9 February 2023	Vlassis, Maria

CATEGORY OF CITED DOCUMENTS

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