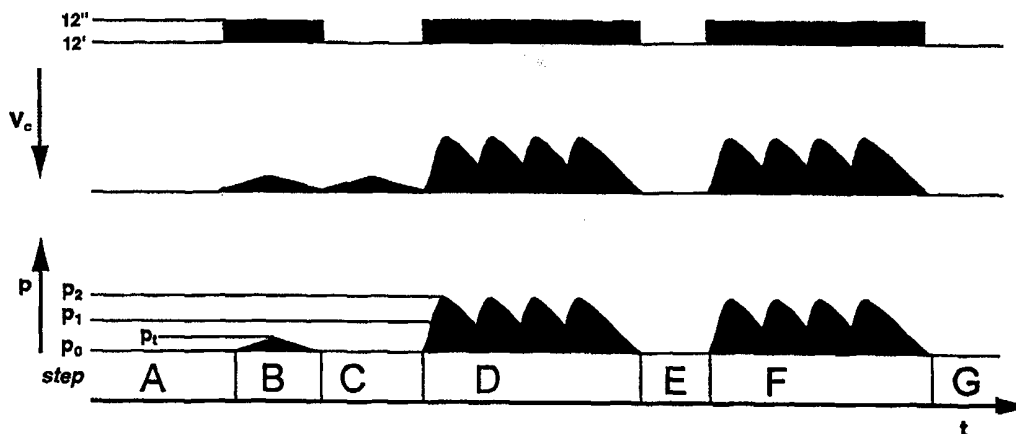




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁶ : A61F 11/00	A2	(11) International Publication Number: WO 00/01331 (43) International Publication Date: 13 January 2000 (13.01.00)
(21) International Application Number: PCT/SE99/01167 (22) International Filing Date: 29 June 1999 (29.06.99) (30) Priority Data: 9802422-7 6 July 1998 (06.07.98) SE (71) Applicant (for all designated States except US): PASCAL MEDICAL AB [SE/SE]; Attn.: Engvall, Daniel, Pilefelts-gatan 73, S-302 50 Halmstad (SE). (72) Inventors; and (75) Inventors/Applicants (for US only): DENSERT, Barbara [SE/SE]; Örnäsvägen 76, S-302 40 Halmstad (SE). ENGVALL, Daniel [SE/SE]; Hertig Knuts gata 37B, S-302 50 Halmstad (SE). NILSSON, Anders [SE/SE]; Rosentorpsvägen 21, S-302 44 Halmstad (SE). (74) Agent: CONIMAR AB; Gerhard Miksche, P.O. Box 2086, S-141 02 Huddinge (SE).		(81) Designated States: AU, BG, BR, BY, CA, CN, CZ, EE, HR, HU, IL, IN, IS, JP, KR, KZ, LT, LV, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, US, ZA, Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE). Published <i>Without international search report and to be republished upon receipt of that report.</i>

(54) Title: METHOD OF TREATING MENIERE'S DISEASE AND CORRESPONDING APPARATUS



(57) Abstract

In a method of treating Ménière's disease intermittent air pressure pulse trains are administered to an outwardly sealed external ear volume bordering to a surgically perforated tympanic membrane. In a pulse train air pressure is increased from ambient (p_0) to a first level (p_1) and from there repeatedly to a second level (p_2) and repeatedly decreased to the first level (p_1), and finally decreased to ambient (p_0). p_1 is from 4 to 16 cm H₂O, p_2 is from 8 to 16 cm H₂O, with the proviso that $p_1 > p_2$, the pressure increase rate is from 0 to 4 mm H₂O per millisecond, the pressure decrease rate is from 0 to 2 mm H₂O per millisecond, the modulation frequency is from 3 to 9 Hz, the intermittent time period is from 3 to 10 seconds. Also disclosed is an apparatus for carrying out the method.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

METHOD OF TREATING MÉNIÈRE'S DISEASE AND CORRESPONDING APPARATUS

FIELD OF THE INVENTION

5

The present invention relates to a method for treatment of Ménière's disease by producing variations in positive air pressure, which are transmitted to one of the ears of a patient, and to an apparatus for carrying out the method.

10

BACKGROUND OF THE INVENTION

Ménière's disease can be treated by affecting the pressure in the internal ear, in particular the endolymphatic system.

15

WO 83/02556 teaches the treatment of Ménière's disease by a particular kind of air pressure pulses and an apparatus for their generation. Pulse trains of a low frequency, that is, short time periods of raised pressure interrupted by

20 similarly short time periods of 'normal' (ambient) pressure, are administered to the external ear of a patient that has been put in communication with the middle ear by means of a transmyringeal passage. The pulse trains resemble to a square wave and are separated by periods of ambient
25 pressure. Modulation pulses of a higher frequency are superimposed on the low frequency pulses. Via the middle ear the pressure pulses are transmitted to the internal ear where they reduce the excessive volume of liquid in the endolymphatic space.

30

EP 266 474 A1 discloses a total pulse amplitude of from 10 to 30 cm H₂O, a modulation amplitude of from 25 to 0 cm H₂O, a modulation frequency of from 3 to 15 Hz, a pulse length of from 0.5 to 5 seconds, the pulse train frequency of 4.5⁻¹ Hz

= 0.22 Hz, the length of a treatment session to be from 5 to 10 minutes. Until a clinical effect is seen the treatment is repeated every second hour: Thereafter the frequency of treatment is lowered to 3.4 per day.

5

WO 93/08775 discloses an air pressure generator for the treatment of Ménière's disease by pressure pulses of the following parameters: a minimum pressure which is 33 % of the maximum pressure; a maximum pressure of from 10 to 30 cm
10 H₂O; intervals between pulses of 5 seconds; a number of pulses per treatment from 1 to 18; a modulation frequency of from 1 to 10 Hz; a pulse length of from 0.1 to 2 seconds.

When applying square wave pulses to the internal ear in cats
15 with a patent cochlear aqueduct a pronounced rebound effect could be noted (Transmission of Square Wave Pressure Pulses through the Perilymphatic Fluids in Cats, B Densert et al., *Acta Otolaryngol.* Stockholm 1986). In humans the situation might be similar. The pressure changes in the internal ear
20 caused by the application of square wave pulses according to methods disclosed in the prior art thus could lead to results substantially differing from what was endeavoured. This provides a possible explanation of the fact that, in spite of various apparatus for the production and
25 transmission of such air pressure pulses having been devised over the past fifteen years, none of them has been put into practical use at a commercial scale. This delay in the implementation of an interesting therapeutic principle seems to be due not only to these apparatus having certain
30 drawbacks from a constructional point of view making them insufficiently adapted to the need of most outdoor patients but also to methodical shortcomings in regard of how to vary the pressure during a treatment such as to make it applicable to a large group of patients.

OBJECTS OF THE INVENTION

The present invention seeks to overcome these drawbacks and problems, and to provide an improved method of treating
5 Ménière's disease and a corresponding apparatus.

Other objects of the invention will become apparent from the following short description of the invention and a preferred embodiment of it, as well as of the appended claims.

10

SUMMARY OF THE INVENTION

According to the present invention is provided a method of treatment of Ménière's disease by intermittent
15 administration of air pressure pulse trains to an outwardly sealed external ear volume bordering to the tympanic membrane brought into communication with the inner ear by means of surgery, a pulse train comprising increasing air (gas) pressure from ambient pressure (p_0) to a first level
20 (p_1) above ambient pressure and from the first level (p_1) repeatedly increasing the pressure to a second level (p_2) and decreasing it to the first level (p_1) and, upon said repeated increase and decrease, decreasing the pressure from the first level (p_1) to ambient pressure (p_0), wherein p_1 is
25 from 4 to 16 cm H₂O, p_2 is from 8 to 16 cm H₂O, with the proviso that $p_1 \geq p_2$, the pressure increase rate is from 0 to 4 mm H₂O per millisecond, the pressure decrease rate is from 0 to 2 mm H₂O per millisecond, the modulation frequency is from 3 to 9 Hz, preferably from 5 to 7 Hz, the
30 intermittent time period being from 3 to 10 seconds, preferably about 5 seconds.

It is preferred for the number of pulse trains to be from about 10 to about 50, more preferred of about 25 to about 35.

- 5 It is preferred to administer, during a treatment session, two to four treatments, in particular three treatments separated by from about 25 seconds to about 80 seconds.

In the method according to the invention the pressure pulses
10 are formed in an apparatus comprising an air (gas) pressure chamber being in sealing communication with said outwardly sealed external ear volume. It is preferred to vary the pressure by applying an electromagnetic force to a diaphragm forming a wall of the pressure chamber.

15

It is preferred for the electromagnetic force to be controlled by a control circuit comprising a microprocessor, power control means, and pressure monitoring means.

- 20 It is preferred for the power supply means to provide the coil with pulse modulated DC.

According to the present invention is also disclosed an apparatus for treatment of Ménière's disease by
25 intermittently increasing, in an air (gas) pressure chamber being in communication with an outwardly sealed external ear volume bordering to the tympanic membrane, air (gas) pressure from ambient pressure (p_0) to a first level (p_1) above ambient pressure and from that (p_1) repeatedly
30 increasing the pressure to a second level (p_2) and decreasing it to the first level (p_1) and, upon said repeated increase and decrease, decreasing the pressure from the first level (p_1) to ambient pressure (p_0), comprising:

a flexible diaphragm (membrane) forming a wall of the chamber; actuating means for displacing the diaphragm; pressure sensing means for monitoring the gas pressure in the chamber; pressure equalising means for equalising the
5 air pressure in the chamber with ambient air pressure; control means comprising a microprocessor, for controlling the displacement of the diaphragm and the pressure equalising means by signal input from the pressure sensing means.

10

It is preferred for the pressure equalising means to comprise valve means. It is preferred for the valve means to be in an open (equalising) position except during the generation of pulse trains.

15

It is preferred for the diaphragm actuating means to comprise an elongate actuating member having an axis and being fixed to the diaphragm at its one end and to an electromagnet, an electric coil for displacement of the
20 magnet along said axis in the direction of the chamber; means for providing the coil with electric power controlled by the control means; means for displacement of the diaphragm in a direction away from the chamber.

25 It is preferred for the means for displacement of the diaphragm in a direction away from the chamber to comprise resilient means not controlled by the control means; it is even more preferred for these displacement means to essentially consist of compressed air contained in the
30 chamber, the conduit, and the sealed external ear volume (the compressed air in the middle ear being disregarded from in this context).

To prevent the pressure to raise excessively in case of a software failure the inclusion of an hardware controlled extra safety means is preferred, breaking the current to the pressure equalising means and the pressure actuating means
5 if the chamber pressure is excess of 25 cm H₂O in regard of ambient pressure.

On the other hand it is important not to apply a pressure which would expose inner ear structures to suction, that is,
10 negative pressure. It is therefore preferred to provide the apparatus of the invention with a mechanical safety valve for protection of the patient against negative pressure opening at a pressure of about - 1 cm H₂O; the acceptance of a slightly negative pressure is due to design requirements
15 for such a mechanical safety valve. It is also preferred to provide the apparatus of the invention with a safety valve for protection of the patient against positive pressure opening at a pressure of about + 35 cm H₂O. The safety valves are purely mechanical and not controlled by the
20 control means. The pressure equalising means preferentially comprise on/off electromagnetic silent valve means working below a hearing level of 20 DB, in particular valve means provided with sealing faces comprising a resilient polymer.

25 The combined volume of the chamber and the conduit can be varied within a broad range but considerations of design and conditions of use suggest the combined volume to be preferably from about 20 ccm² to about 50 ccm².

30 According to a preferred aspect of the invention it is preferred to store, in an E²PROM (electrically erasable and programmable read-only memory) or an equivalent media coupled to the microprocessor, the information for control of the apparatus in form of parameter sets, each set

comprising all parameters necessary to carry out a treatment, that is, the variation of pressure in the chamber with time during treatment. It is preferred to provide the apparatus of the invention with input means to allow a
5 parameter set to be replaced by another set. Input means not requiring an electrical connection, such as infrared (IR) input means, are preferred. The various parameter sets then are stored in PC or similar and transferred therefrom to the apparatus of the invention. It is also preferred to store
10 several parameter sets in the E²PROM, and to provide the apparatus with means for their individual selection. The apparatus of the invention thus comprises a fixed basic program stored in the PROM memory of the microprocessor and an exchangeable supplementary program stored in the E²PROM.
15 It is, of course, possible to chose functionally equivalent storage media for the fixed and/or the exchangeable software for controlling the apparatus of the invention.

In the following the invention will be explained in more
20 detail by reference to a preferred embodiment illustrated in drawing. The embodiment is however only described to exemplify the invention but not to limit it in any way.

SHORT DESCRIPTION OF THE DRAWING

25

Fig. 1 is a schematic function diagram of an apparatus according to the invention;

30

Fig. 2 is a schematic pulse diagram with a non-linear time axis.

The preferred embodiment of the apparatus according to the present invention illustrated schematically in Fig. 1

comprises an about cylindrical chamber 1 for generating pressure pulses by displacement of a flexible circular rubber diaphragm 4 forming one base of the chamber 1 wall, a piston 2 centrally fixed to the diaphragm 4 at its one end and at a ferromagnetic alloy core 22 at its other end, the core 22 being partially inserted into an field coil 3. The chamber 1 has a terminal section 5 provided with a 'silent' (hearing level <20 DB) on/off electromagnetic equalising valve 12 which puts it in communication with the atmosphere when in an open position.

Via a flexible plastic tube 10 (of polystyrene, polypropene or a similar material) the chamber 1 is put into communication with an air volume in the external ear bordering to the tympanic membrane of a patient sealed off by an ear plug 11. The tympanic membrane is penetrated by a microtube which has been applied by surgery; thereby the external and middle ear of the patient is put into communication. The pressure in the chamber 1 is monitored by a pressure sensor 8, the signal 20 of which is processed in a control unit comprising a microprocessor 16 and software 14. By input of sets of data 15 software parameters relating to pressure and time can be changed. Input is via an IR-link 17 from data stored in a personal computer. One output signal 18 from the microprocessor 16 controls the power supplied to the field coil 3 while another output signal 13 controls the equalising valve 12 by switching it between an open and a closed position. If, for some reason the chamber 1 pressure cannot be maintained within the physiologically acceptable interval the equalising valve is opened. If the chamber pressure exceeds the maximum treatment pressure by 25 cm H₂O a hardware controlled safety function breaks the power both to the equalising valve 12 and the field coil 3. As a further safety precaution mechanical safety valves 7,9

against negative pressure (opening pressure - 1 cm H₂O) excess positive pressure, respectively, are provided in addition.

- 5 The treatment data are stored in the microprocessor in form of one or several parameter sets. A parameter set contains all information in regard of pulse amplitude, frequency, pressure increase and decrease rate, etc. In addition each parameter set comprises data for the software controlled
10 safety functions.

In Fig. 2 a typical treatment sequence is shown, except for the number of pulse trains being reduced to two for the sake of simplicity. The chamber pressure (lowermost section of
15 the diagram, the chamber volume (central section of the diagram) and the mode of the equalising valve 12 (uppermost section of the diagram; 12' = open; 12'' = closed) are set off against time.

- 20 The various phases of the treatment sequence are identified by capital letters. During phase A the pressure sensor 8 is brought to a working temperature, the equilibrating valve 12 is in an open position, and the chamber 1 is at ambient pressure. Then follows a leak test in phase B during which
25 the valve 12 is kept closed while the pressure is gradually increased to a test pressure p_t of about 1 cm H₂O, and then again decreased to zero. In test phase C an openness test is carried during which the chamber 1 volume V_c is varied in the same way as in phase B but with valve 12 in an open
30 position. If the test pressure p_t deviates from the expected values the program will stop the apparatus from proceeding to the treatment sequence proper. During the first treatment phase D the chamber pressure p is gradually raised to an intermediate pressure p_1 and from there to the maximum

pressure p_2 , followed by a decrease to the intermediate pressure p_1 ; the $p_1 \rightarrow p_2 \rightarrow p_1$ cycle is repeated trice, followed by lowering the pressure to ambient pressure p_0 . After an interval E of about 5 seconds a second pulse train 5 (phase F) similar to the one in phase D is generated. This is followed by a second interval at p_0 (phase G) and 10 to 30 further pulse trains (not shown) with corresponding intervals. This first treatment section of equally spaced 12 - 32 pulse trains is followed by a rest period of about 40 10 seconds, and second and third treatment sections also spaced by a corresponding rest period. For optimal effect the treatment should be repeated several times a day.

C l a i m s

1. A method of treating Ménière's disease by intermittent administration of air pressure pulse trains to an outwardly sealed external ear volume bordering to the tympanic membrane brought into communication with the inner ear by means of surgery, a pulse train comprising increasing air pressure from ambient pressure (p_0) to a first level (p_1) above ambient pressure and from the first level (p_1) repeatedly increasing the pressure to a second level (p_2) and decreasing it to the first level (p_1) and, upon said repeated increase and decrease, decreasing the pressure from the first level (p_1) to ambient pressure (p_0), wherein p_1 is from 4 to 16 cm H₂O, p_2 is from 8 to 16 cm H₂O, with the proviso that $p_1 > p_2$, the pressure increase rate is from 0 to 4 mm H₂O per millisecond, the pressure decrease rate is from 0 to 2 mm H₂O per millisecond, the modulation frequency is from 3 to 9 Hz, the intermittent time period being from 3 to 10 seconds, preferably about 5 seconds.
2. The method of claim 1, wherein the modulation frequency is from 5 to 7 Hz.
3. The method of claim 1 or 2, comprising administering, during a treatment session, two to four treatments, in particular three treatments, separated by from about 25 seconds to about 90 seconds.
4. The method of any of claims 1-3, wherein the pulse trains are formed in an apparatus comprising an air (gas) pressure chamber being in sealing communication with said outwardly sealed external ear volume and provided with an electromagnetic force actuated diaphragm and an equilibration valve controlled by a microprocessor.

5. An apparatus for treatment of Ménière's disease by intermittently increasing, in an air (gas) pressure chamber being in communication with an outwardly sealed external ear volume bordering to the tympanic membrane, air (gas)

5 pressure from ambient pressure (p_0) to a first level (p_1) above ambient pressure and from that (p_1) repeatedly increasing the pressure to a second level (p_2) and decreasing it to the first level (p_1) and, upon said repeated increase and decrease, decreasing the pressure from

10 the first level (p_1) to ambient pressure (p_0), comprising: a flexible diaphragm forming a wall of the chamber; actuating means for displacing the diaphragm; pressure sensing means for monitoring the gas pressure in the chamber; pressure equalising means for equalising the air

15 pressure in the chamber with ambient air pressure; control means comprising a microprocessor, for controlling the displacement of the diaphragm and the pressure equalising means by signal input from the pressure sensing means, wherein p_1 is from 4 to 16 cm H₂O, p_2 is from 8 to 16 cm H₂O,

20 with the proviso that $p_1 > p_2$, the pressure increase rate is from 0 to 4 mm H₂O per millisecond, the pressure decrease rate is from 0 to 2 mm H₂O per millisecond, the modulation frequency is from 3 to 9 Hz, the intermittent time period is from 3 to 10 seconds.

25

6. The apparatus of claim 5, wherein the modulation frequency is from 5 to 7 Hz.

7. The apparatus of claim 5 or 6, wherein the pressure

30 equalising means comprise on/off electromagnetic silent valve means working below a hearing level of 20 DB provided with sealing faces comprising a resilient polymer.

8. The apparatus of any of claims 5 to 7, wherein the valve means are controlled to be in an open position except during the generation of pulse trains.

5 9. The apparatus of any of claims 5 to 8, wherein the means for displacement of the diaphragm in a direction away from the chamber essentially consist of compressed air contained in the chamber, the conduit, and the sealed external ear volume.

10

10. The apparatus of any of claims 5 to 9, comprising safety means for breaking the current to the pressure equalising means and the pressure actuating means if the chamber pressure is excess of 25 cm H₂O in regard of ambient
15 pressure.

11. The apparatus of any of claims 5 to 10, comprising a mechanical safety valve for protection of the patient against negative pressure.

20

12. The apparatus of any of claims 5 to 11, wherein the information for control of the apparatus is stored in form of parameter sets in an E²PROM coupled to the microprocessor or an equivalent media.

25

13. The apparatus of claim 12, wherein a parameter set is replaceable by another parameter set.

14. The apparatus of claim 13, wherein replacement is by
30 IR input means.

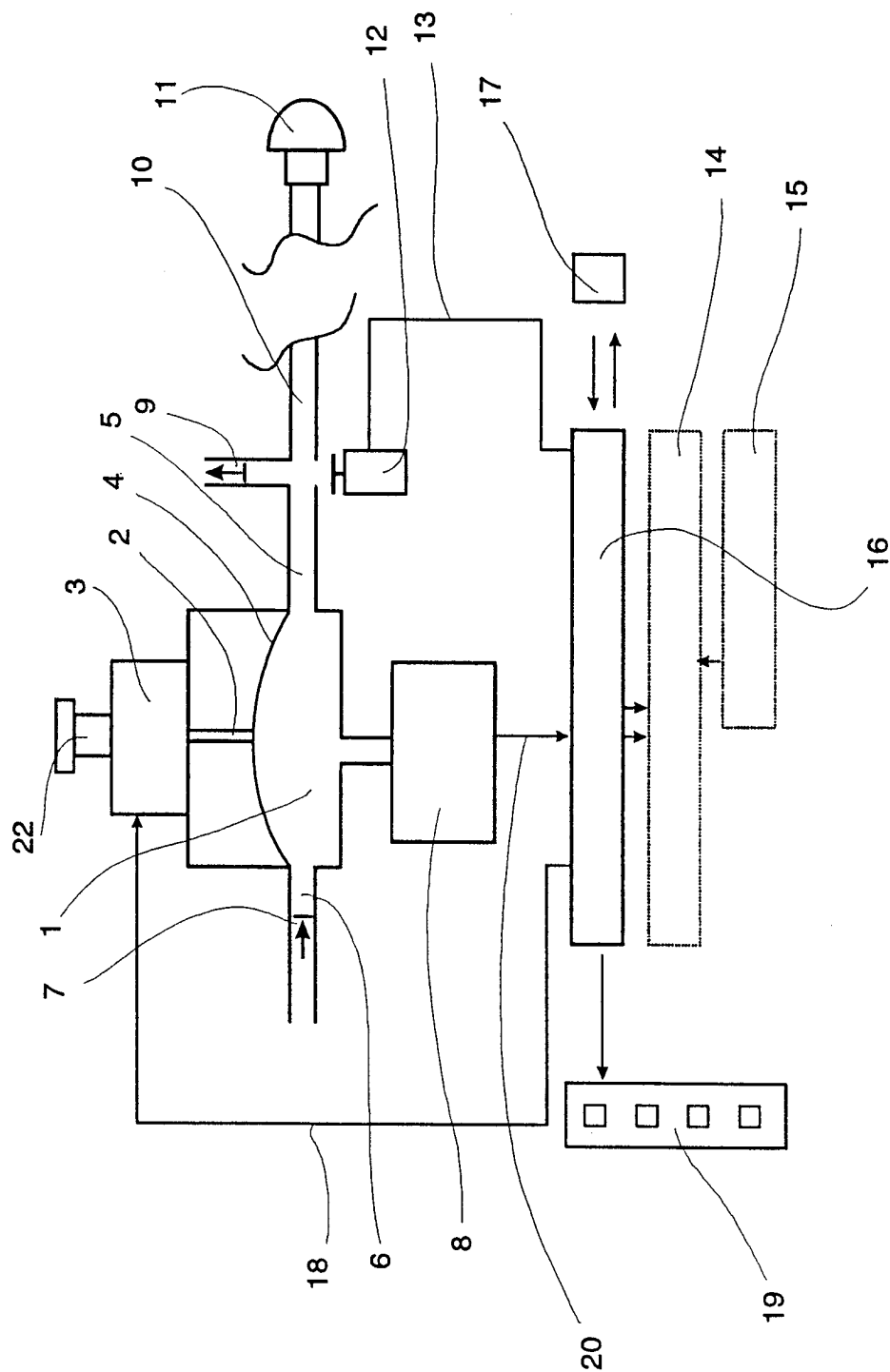


Fig. 1

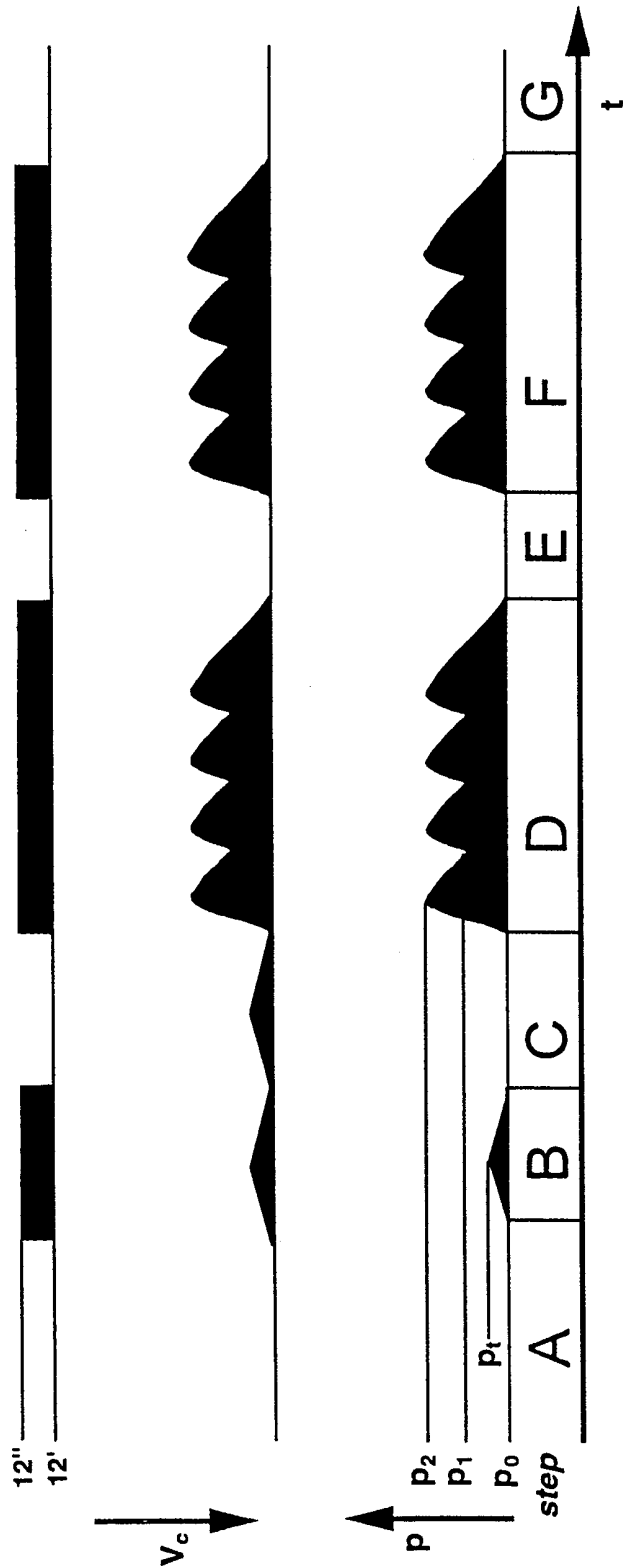


Fig. 2