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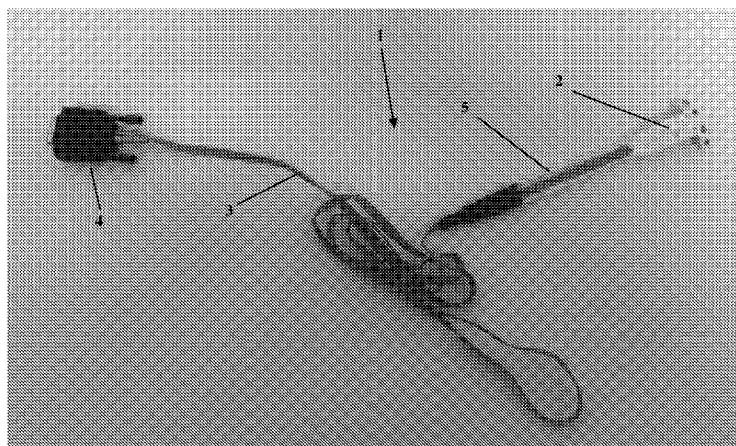
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(54) Title: A DEVICE FOR CHECKING THE STATUS OF INTEGRITY OF A CAVITY OF A PATIENT

**FIG. 1**



(57) Abstract: The present invention refers to an innovative apparatus (1, 10) for the check of a cavity of a human being, for example the oral, rectal or vaginal cavity. Such an apparatus comprises: - A generator for generating and injecting a predetermined input current (I1) in a person; - A long-shaped element (2, 5) suitable for being inserted in the cavity to be inspected and provided with at least two electrode (a, a', b, b') for receiving a return current (I2) following the input current (I1) injected in the person when said long-shaped element results to be inserted in the cavity with said electrodes in contact with one or more areas of the cavity to be inspected; - And wherein an apparatus (10) is further foreseen with which the long-shaped element is placed in communication in such a way as to transmit said current (I2) intercepted by the electrodes to said apparatus (10), the apparatus being programmed to process the values of current injected (I1) and those detected in return (I2).



TITLE**A DEVICE FOR CHECKING THE STATUS OF INTEGRITY OF A CAVITY  
OF A PATIENT**Technical field

The present invention concerns the technical field relative to medical instruments.

In particular, the invention refers to an instrument that allows the monitoring and check of anatomical cavities such as the oral, vaginal and rectal cavities, in order to identify, in an efficient manner, eventual injuries and alterations of the tissues in general and of the mucous membranes in particular.

Background art

A good check of the anatomical cavities such as the oral, vaginal and rectal ones, as known, is at the basis of the prevention of many pathologies, some of which are particularly serious, such as neoplasia.

In the prevention phase such a check is often only of visual nature and therefore subjective. The dentist or the gynecologist can be, for example, entrusted with it, who verify visually by means of probes, illuminators, optical fibers, the integrity of the mucous membranes and the presence of injuries.

In case of alterations or injuries, subjectively suspect, the doctor that does such a check can evaluate the seriousness thereof and decide whether to address the patient to a specialist for more thorough checks.

For example, with regard to the oral cavity, a common injury that for the patient can be interpreted as a surface scratch or a simple swelling of the mouth can instead be a sign of a rather serious infection, if not

even an injury of the neoplastic type.

In the current state of the art, however, the observation of the cavities is linked strictly to a visual system, since it is the doctor who inspects visually the areas of interest, eventually making use of auxiliary instruments for the acquisition of images.

Nevertheless, it is obvious that this type of inspection is not quantitative and does not allow to classify the nature or the presence of sub-clinic alterations of mucous membranes, inflammations and injuries that are at an initial state, and therefore of very reduced size.

Unfortunately, above all in the case of neoplasia, these result to be visible to the naked eye when they have already had a significant evolutionary process, the whole with a high risk for the patient and with difficulty in applying with success standard therapeutic treatments.

In principle, the need to have instruments that allow to make prevention screenings with a high degree of objectification and sensitivity is much felt.

It is therefore felt the need to make use of a specific apparatus that allows to inspect the anatomical cavities with extreme precision, thus being able to detect alterations of any nature and size, including micro-injuries that may be indicative also of a neoplasia.

Various devices are known in literature that, basing themselves on the injection of current through electrodes, measure a voltage and phase drop (intended as asynchrony between voltage and current) to obtain impedance values to be used for a medical analysis of the tissue.

For example, in WO2009/067658 an obstetrical forceps device is described which is configured to make an

exploration in the vaginal cavity, in particular a state of dilatation thereof in case of childbirth.

It is clear that an obstetrical forceps element is configured either for grasping or for divaricating an end and remaining fixed in a pre-established position, therefore allowing a local monitoring in a pre-determined point (in this case, precisely, a monitoring of an increase or decrease of volume or area).

Such a solution does not allow, however, to make a detailed exploration or inspective analysis of an entire area, in particular that relative to the oral cavity. The obstetrical forceps element, in a further embodiment, is substituted with an element having a sort of adhesive surface on which the electrodes are found and also this, therefore, is configured to be applied and remain fixed in a specific point.

The solution described, instead, in the publication WO2010/060152 describes the use of a siluride configuration system, for example suppository or cigar. Such conformations are ideal for the vaginal or rectal cavities but not, by virtue of the conformation thereof, for oral cavities since they cannot reach or detect efficiently zones such as the under-tongue, or the intra-jaw internal angles at least without causing annoyance or excoriations. Further, their shape impedes the tonometric exploration of small segments of the mucous membranes present inside cavities with very irregular morphologies, such as the oral ones.

#### Disclosure of invention

It is therefore the aim of the present invention to provide an innovative device that allows to solve said technical inconveniences.

In particular, it is the aim of the present

invention to provide a device that allows, in a fast and simple way, to inspect in full the oral cavity, allowing to identify eventual small injuries or alterations in general.

It is also the aim of the present invention to provide a device that results to be economical, simple to be used and whose use guarantees a high repeatability of the checks.

It is also the aim of the present invention to provide a device suitable for being substituted or sterilized or rendered even single-use and sterile, without incurring huge costs.

These and other aims are therefore reached with the present device (1) for the check of the oral cavity of a person, in accordance with claim 1.

Such a device (1) comprises a generally long-shaped element (2, 5) suitable for being inserted in the oral cavity to be inspected.

In accordance with the invention, said element (2, 5) is provided with at least two electrodes (a, a', b, b') to detect a voltage drop following an input current (I1) that is injected in the person.

To that aim, in use, such a device is inserted in the oral cavity with such electrodes in contact with one or more internal zones of the cavity.

A current is injected in the person and, circulating in the body of the person, is withdrawn from said two electrodes of the device in question.

The device is also further configured to transmit such an intercepted voltage to an apparatus (10), for example a voltmeter and/or a phasemeter, programmed to process the values in indexes of resistance and of reactance.

Through known formulas it is therefore possible to

interpret the values of the current injected and of the current detected (in particular the voltage drop) in order to understand the status of integrity of the tissues and, from there, highlight with sensitivity and objectivity the presence of bio-electrical anomalies deriving from a possible pathology.

In such a manner, in an objective way, it is possible to solve all the said technical inconveniences since it is now possible, with such an instrument, to determine the health status of the tissues, disengaging from visual checks that are certainly less precise.

In accordance with the invention, said long-shaped element comprises a handle (5) and a head (2) on which the electrodes are positioned, said head being T-shaped, or fork-shaped, and configured to be moved, in use, inside the oral cavity with the electrodes in scraping contact with the walls of the oral cavity.

Alternatively, an O shape is also possible.

Such a T, O or fork-shaped solution is optimal for an oral inspection, allowing to reach zones that are not easily reached in another way, such as the under-tongue section.

Further advantages can be deduced from the other remaining dependent claims.

#### Brief description of drawings

Further features and advantages of the present device 1, according to the invention, will result to be clearer with the description that follows of some embodiments, made to illustrate but not to limit, with reference to the annexed drawings, wherein:

- Figure 1 shows a prospective view of a prototype of the apparatus in accordance with a first embodiment of the invention and particularly suitable for the inspection of

the oral cavity;

- Figure 2 shows just the part of the device that is inserted in the oral cavity and provided with handle to grasp it and manœuvre it;
- Figure 3 shows just the head in which two electrodes injecting current and two receiving electrodes are arranged;
- Figure 4 is a fork-shaped variant;
- Figure 5 shows the entire device that comprises also a processor and the current generator;
- Figures 6 and 7 show some graphics (nomograms with tolerance zones and confidence regions) on which the measurements detected are plotted in order to verify if the specific measurement made falls within a scope of normality or is indicative of an anomaly;
- Figure 8 shows a variant in which the head is provided with just receiving electrodes, while the electrodes that inject the current are arranged on an external device, such as transcutaneous electrodes of the pre-gelatine and adhesive type;
- Figures 9 and 10 show constructive solutions of the receiving electrodes, and applicable also to all the other solutions described;
- Figure 11 and figure 12 show an example of crossing of the current in the tissues in accordance with the solution relative to the head that comprises also the injecting electrodes;
- Having said that, figure 13 shows a constructive variant suitable for inspecting anal and vaginal cavities;
- Figure 14 is a further variant that allows the check of delimited and even point parts of area of cavity.

#### Description of some preferred embodiments

It is known that the knowledge of electrical parameters, such as the body reactance  $X_c$ , can help to

interpret the normality or not of pre-determined physiological status. For example, the reactance  $X_c$  and the resistance  $R$  have long been used in order to obtain the status of body hydration, while the phase angle is an excellent predictor of survival in different pathologies.

The same applicant has, for example, filed a preceding Italian patent application, ITFI20050202, which dealt precisely with determining the body hydration status.

To that aim, a generator was foreseen capable of generating a reference signal of alternate voltage at 50Khz or at two frequencies (5Khz and 100Khz) that was injected in a section of the body of the patient through pairs of plates or electrodes. In the case of plates, these were grasped by the hand of the patient through thumb and fingertip of the remaining fingers. In that manner, the electrical signal was injected from a plate and crossed the body that functioned as conductor to reach the opposite plate. In particular, the current injected crossed the plate on which the fingertips rested and was directed towards the other plate in contact with the other fingers. A discriminator calculated the deviation of the input signal (the one injected in a plate) with respect to the output signal (current that supervened to the opposed plate) after crossing such a part of the body. The deviation is, in fact, the non-synchrony between the current and the voltage that an electronic circuit is capable of quantifying visualizing it on the "display" as reactance and using an implementation of formulas already known.

The same solution could use electrodes of the caulked type applicable to the body.

The same inventor of the present patent application is, above all, the author of different scientific articles

in which the tetra-polar technique is discussed, which foresees the application of four electrodes, two at the hands and two at the feet, in order to inject sinusoidal alternate current at 50 kHz of innocuous intensity for the tissues (400  $\mu$ A) on one part and calculate a relative voltage drop in such a way that specific processors, adequately programmed, obtain the impedance value  $Z$  (module of the vector in Ohm) or also the two components of the impedance vector  $Z$  or resistance ( $R$ ) and reactance  $X_c$  in Ohm with devices sensitive to the phase. Continuous current (frequency zero kHz) is not used, which could not cross the cellular membranes. The article in question is entitled:

*"Sulle metodiche impedenziometriche"* ("On the impedentiometric methodicals")

and is available, for example, on the following website:

<http://www.life-beauty.com/Download/dispensaBiaVector.pdf>

In particular, the paragraphs of said article: "BIA VETTORIALE - Basi razionali della BIA vettoriale", "Analisi vettoriale con il Grafo Resistenza - Reattanza", "Interpretazione del Grafo Resistenza-Reattanza" ("VECTOR BIA - Rational bases of the vector BIA", "Vector analysis with the Resistance - Reactance Graph", "Interpretation of the Resistance - Reactance Graph") give all the mathematical bases to obtain the impedance vector  $Z$  with its displacement (therefore the components of resistance  $R$  and reactance  $X_c$ ) through the single or multi-frequency tetra-polar measurement injecting current and measuring the output voltage; all the bases are given relative to the interpretation of such data for the measurement of a hydration or body weight status.

Further, the method of the vector bivariate analysis of the R and Xc values in question has already been the object of other patents, such as in patent US20040167423 and to which we are directed for all the bases of interpretation of the same.

Having said that, although the determination of some electrical measurements of the body and their interpolation is known in order to determine some human physiological parameters (for example, hydration and nutrition status), there is no device known suitable for being introduced in the oral cavity, in order to detect specific electrical measurements and in order to interpret and use these same measurements to find pathological alterations.

The instrument described in ITFI20050202 is not in fact structured to result to be insertable in the oral cavity, or in other cavities, and therefore it is not suitable for being used for obtaining measurements in the cavities of the patient. Moreover, though doing some electrical measurements, these are not interpolated in order to identify alterations of the bioelectrical parameters in zones or sections of the oral cavity or of the cavities where inserted.

Figure 1 shows in an axonometric view a device 1 in accordance with a first embodiment of the invention.

Given its shape, the device described in the figures from 1 to 4 is particularly suitable for an inspection of the oral cavity.

The solution of figures 13 and 14, like also the solutions of figures 8, 9 and 10, are instead suitable for the inspection not only of the oral cavity but of other cavities such as the vaginal, rectal or nasal ones.

The expert in the field will be able to appreciate how it is possible to adapt different shapes and sizes in

order to render an inspection of any human cavity possible.

Going to figure 1, the device 1 comprises a head 2 that is connected to a handle 5. The handle terminates with an electrical wire 3 of connection to an electrical press 4 which, as better clarified below, is connected to a further instrument 10, such as a processor.

For example, figure 3 shows a solution of a T-shaped head at whose end are placed four metallic electrodes (or of other conducting material) in the shape of spheres of small diameter. The spheres are connected each one to an electrical wire and the assembly of such wires runs along the handle to terminate on the press 4. In this manner, as better clarified below, it is possible from each wire to inject a current (I) and receive in return a voltage (V).

A further constructive solution is shown in figure 4 in which the head can be fork-shaped and foresees at its ends four electrodes (a, b, b', a') through which to inject the current and detect the measurement thereof in volts and/or phase.

In a further variant it can also be O-shaped.

In particular, the head foresees four conducting elements (a, b, b', a'), preferably crossbow-like, and that terminate preferably with four spheres (a, b, b', a') of small diameter or with four small plates of a shape idoneous to rest internally on different points of the oral mucous membranes or on the tongue. Also in this case each conducting element terminates and is connected with an electrical wire and the assembly of such electrical wires terminate in the press 4.

In both the cases described it is possible to measure with the tetra-polar technique the impedance and phase values at a single frequency (typically 50khz) or at more frequencies (from 4 to 1000Khz).

The head 2 has such a size as to be inserted in the mouth in such a way as to be able to inspect it. It can have the size of a fork or of dental instruments of common use in such a way that the doctor can insert it in the oral cavity without creating big encumbrances to the patient and bringing the electrodes in contact with all the parts to be inspected such as the palate, tongue, under-tongue, gums, cheek, etc., by simply moving the head 2 inside the oral cavity.

It is also possible on the same to foresee on the part of the electrodes, or on the opposite side, also a small mirror that can facilitate the inspection.

The schematization of figure 5 shows the wire 3 that connects to an electronic processor 10, for example a PC 10 or anyway a device idoneous to the tetra-polar technique, through which the current injection can be controlled and the voltage or phase can be analyzed. The injection of current can take place through a specific generator that can be included in the structure of the processor or can be an independent external apparatus and that is connected to the handle of the instrument to send the current to the two pre-placed electrodes.

A voltmeter or systems sensitive to the phase allow to determine the measurements of impedance, resistance and reactance.

Alternatively, the handle can comprise inside it a generator of current.

In fact the wire 3, as explained above, although indicated with a single wire, foresees two output wires to inject the current from the generator to the two electrodes (a, a') and two return wires to obtain the reading of the voltage from the electrodes (b, b') to the processor.

The return signal is then interpreted as described

below.

In particular, the current ( $I_1$ ) in exit from the electrodes (a, a') arrives in contact with the mucous membrane that conducts current. The status of conduction varies obviously on the basis of the physiological status of the mucous membrane, inflammatory status or other and re-enters displaced of a pre-determined quantity ( $\phi$ ) to the electrodes (b, b') in the shape of current ( $I_2$ ).

The displacement ( $\phi$ ) depends on the physiological status of the mucous membrane or of the tissues in general. A pre-determined pathology, such as an inflammation, alters the tissues and their content of liquid and therefore the electrical conductivity.

The values of  $R$  and  $X_c$  deriving from the voltage and the asynchrony versus current arrive to the PC, which is programmed according to known formulas to calculate the regions of confidence and zones of tolerance, exactly as described in the known art with the denomination of measurement technique of the bio-impedance with 4-wire vector analysis tetra-polar system (BIVA). In particular, the voltage drop is detected from which a voltmeter detects the impedance  $Z$ , while systems sensitive to the phase allow to determine its components.

The processor calculates reactance  $X_c$ , resistance  $R$  and displacement of current ( $\phi$ ) once the current injected and the current in return are known, in particular the voltage drop.

A graph can therefore be interpolated experimentally, as that of figure 6 (bi-variate statistical analysis) in which the area A1 represents an area obtained through experimental measurements of reactance  $X_c$  and resistance  $R$  on a specimen of population used as healthy checks with measurements of the anatomical cavities (oral, vaginal, rectal). The measurements

obtained are plotted and a graphic is obtained that delimits an area A1 of normality (fiftieth percentile of the healthy checks), while the area A2 represents a zone of deviation from the norm (that can also be delimited in ellipses that englobe the seventieth and ninetieth percentile).

The graphic can be created just once initially as a fixed datum and can be memorized and used by the processor.

In particular, once a measurement is made on a patient, the resistance and reactance values obtained through a distance between the constant electrodes, and therefore expression of specific resistivity ( $\Omega\text{m}/\text{cm}$ ), are positioned in said graphic, verifying a position inside the area of normality or not. In this manner, in an immediate way, it is verified on the screen if the patient examined falls within a condition of normality (area of the 50%) or not and it can be verified exactly the point in which there is an anomaly zone indicative of a possible injury.

In particular, the doctor can pass the instrument in contact in the various parts of the cavity under exam and verify on the display if each point that he examines (and of which the processor obtains reactance and resistance) falls within the area of the graphic A1 or not.

What has been described is valid exactly also for the constructive solution of figure 13 or 14, which is identical to the preceding one except for its shape, which is particularly idoneous for the insertion in cavities such as the vagina or rectum.

In particular, a cigar-shaped or suppository-shaped body can be selected, particularly extracted and with round ends.

Four electrodes, as usual, are foreseen arranged in

circular form around the perimeter of the body, or semi-perimetral electrodes or simply at small "spots" for rendering them idoneous to observe just a side or a minimum portion of the cavity.

Precisely to that aim the schematization of figure 14 is foreseen, which highlights "spots" that allow to observe only well-determined sides or points of the cavity.

Other forms can naturally be foreseen, without for this moving apart from the present inventive concept.

Alternatively, the interpolable graphic can be created on the basis of the phase ( $\varphi$ ) as per figure 7 and that defines always an area of normality A1 and an area of non-normality A2.

Exactly as for the preceding case, the instrument is inserted in the oral cavity to detect measurements of punctual reactance, resistance and phase which are plotted on the memorized statistical graphic to show in video if all the values measured fall within an area of normality or not.

A further variant of the invention is described in figure 8. It is obviously applicable both for the instrument with specific shape for the oral cavity and for the instrument with specific shape for the other cavities.

In that sense, the example of application to the mouth, as per figure 8, is not to be considered limiting.

Having said that, said variant differs from the preceding ones in that the injection of current does not take place through two electrodes arranged in the body of the instrument but through an external apparatus.

In particular, figure 8 shows schematically a patient in which the current is injected through an external generator provided with two electrodes that can be comfortably applied to the cheeks and therefore are not

integrated in the head 2 (in the case of check of the oral cavity).

The input current (I1) circulates among the tissues of the oral cavity and is measured in voltage and phase (current I2) displaced of the value detected by the two single electrodes present in the head 202.

Also in this case, exactly as described above, the electrodes (b, b') present on the head 202 can be of different shapes.

For example, figure 9 shows a solution in which the electrodes can be compared to buttons ("spot" solution).

The solution of figure 10 instead shows a conducting ring obtained on a part (semi-ring) or the entire perimeter of the head (entire ring).

The solution in which the head foresees two single receiving electrodes has the advantage of allowing to obtain a head of reduced size.

Moreover, a further advantage is in the precision of the measurement for the following reason.

In the case of the solutions described in which the head includes both the electrodes injecting the current and the receiving electrodes, obviously the modality of injection changes locally on the basis of the position in which the head is inserted in contact with the mucous membranes. According to the angulation of insertion of the electrodes (a, a') these can result to be parallel to the tissues, or with respect to them, orthogonal or inclined.

Figure 11 and figure 12 schematize two possible opposed situations.

The figures show a section of tissue in which the strips in black represent the muscular fibers.

It is clear that, according to the angulation of insertion of the instrument, the current injected can be

found parallel or transversal with respect to the fibers, with consequent variation of the norms of reactance.

The current runs parallelly to the muscular tissues (band) and is however possible to observe it transversally by means of the positioning of the fork and this modifies significantly the capacitive measurement (reactance). In the case of injecting electrodes placed on an external device, device connected to the current generator as per figure 8, its positioning is substantially always the same and therefore the modality of crossing of the current in the tissues is always the same.

What has been described is valid for all the embodiments, also for the instruments with such a shape that an inspection of the other cavities is made. In this case, it will be necessary to foresee a specific external generator and injector of current.

All the solutions described can be of the single-use and/or sterilizable type.

For instance, with reference to the solution for the inspection of the oral cavity, the head and the handle can be integral in a single piece and in a sterilizable and low cost material (for example plastic, PVC, etc).

The wire 4 can, for example, be detachable from the electrodes in such a way that the head and handle can be inserted in a sterilization apparatus.

Alternatively, the head can be detachable from the handle in such a way that the handle is, for example, sterilizable and the head is single-use.

Also the solution of figure 13 can be in the shape of a handle that is connected to a head of an idoneous shape, for instance, detachable and/or sterilizable as described.

In all the embodiments, nothing would impede to make head and handle in a single piece and single-use,

therefore disposable.

CLAIMS

1. A device (1) for the check of the oral cavity of a person and comprising:
  - A generally long-shaped element (2, 5) for being inserted in the cavity to be inspected;
  - Said element (2, 5) being provided with at least two electrodes (a, a', b, b') for detecting a voltage drop when inserted in the cavity with said electrodes in contact with one or more internal areas of the cavity and following an input current (I1) injected in the person;
  - The device being further configured to transmit said voltage drop to an apparatus (10) programmed to process the values of current injected (I1) and the relative voltage drop to determine impedance and/or resistance and/or reactance and/or phase parameters;
  - **Characterized in that** said long-shaped element comprises a handle (5) and a head (2) on which the electrodes are positioned, said head being T-shaped, or in the shape of a fork, or O-shaped, and configured to be moved, in use, inside the oral cavity with the electrodes in scraping contact with the walls of the oral cavity.
  
2. A device (1), as per claim 1, wherein said long-shaped element (2, 5) comprises at least two electrodes (b, b') for measuring the voltage drop and at least two electrodes (a, a') through which to inject the current (I1).
  
3. A device (1), as per claim 1, wherein at least two electrodes (a, a') are foreseen through which to inject the current (I1), said electrodes belonging to

a device for the injection of the current separated from the long-shaped element (2, 5).

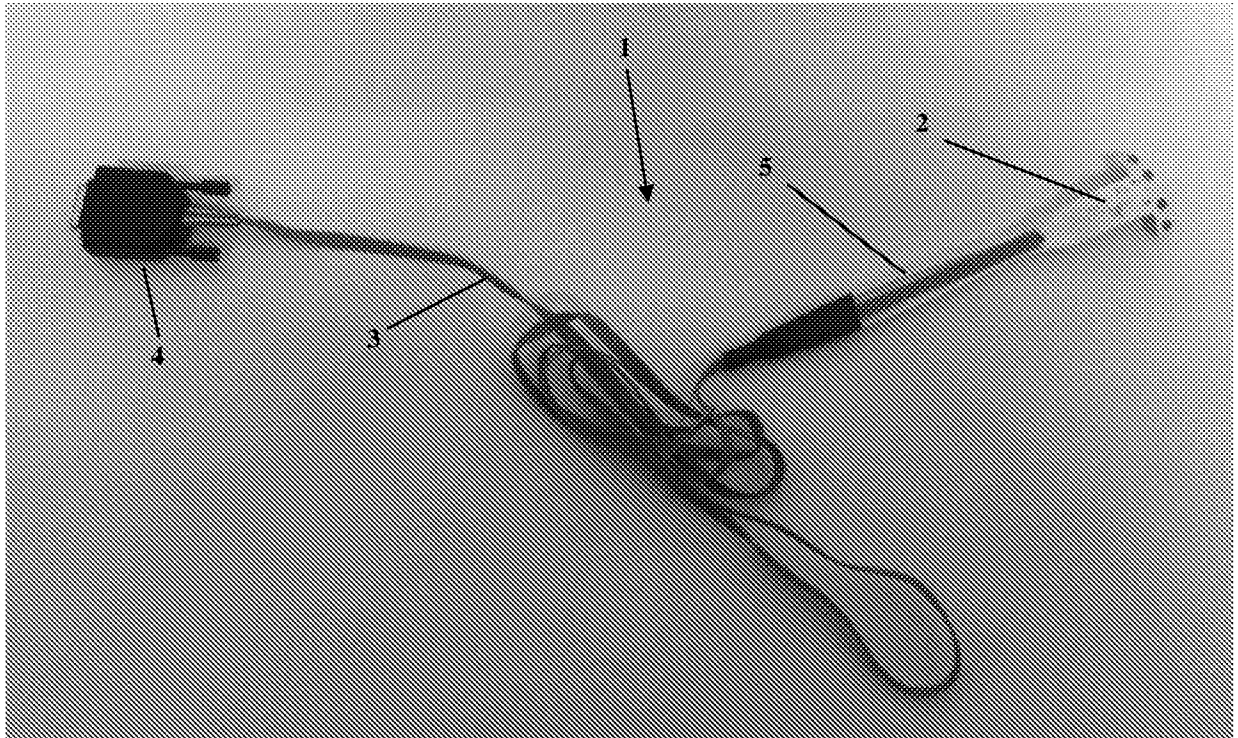
4. A device (1), as per one or more of the preceding claims, wherein a generator for generating the current (I1) is foreseen.
5. A device (1), as per one of more of the preceding claims, wherein a processor (10) is foreseen that is connected to the long-shaped element for processing the measurements of current injected (I1) and the relative voltage drop.
6. A device (1), as per one of more of the preceding claims, wherein said processor is in combination with a voltmeter and/or with systems sensitive to the phase.
7. A device (1), as per one or more of the preceding claims, wherein the handle (5) is at choice:
  - Detachable from the head (2), the head being a single-use one and the handle preferably of the sterilizable type;
  - Integrated to the head (2) and, preferably, handle and head of the sterilizable type.
8. An apparatus (1, 10) for the check of the oral cavity of a person and comprising:
  - A generator for generating a pre-determined input current (I1) to be injected to a person;
  - A long-shaped element (2, 5) for being inserted in the oral cavity and provided with at least two electrodes (a, a', b, b') for measuring a voltage drop following the input current (I1) injected in the person when said long-shaped element results to be

inserted in the cavity with said electrodes in contact with one or more areas of the cavity to be inspected;

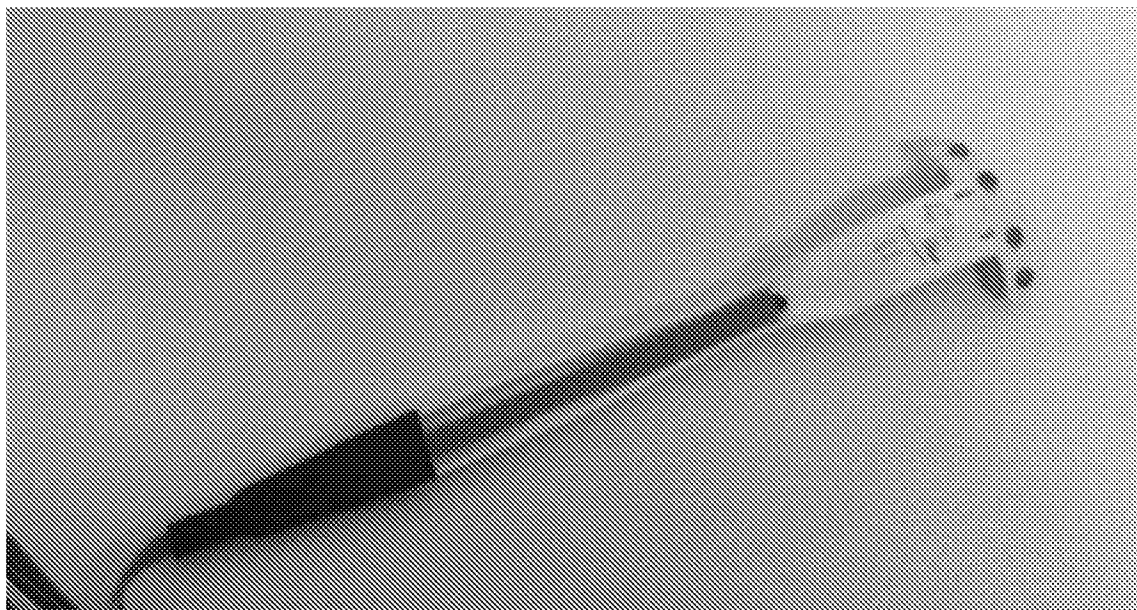
- And wherein an apparatus (10) is further foreseen with which the long-shaped element is placed in communication in such a way as to transmit said voltage drop intercepted by the electrodes to said apparatus (10), the apparatus being programmed to process the values of current injected (I1) and the relative voltage drop to determine impedance and/or resistance and/or reactance and/or phase parameters;
- **Characterized in that** said long-shaped element comprises a handle (5) and a head (2) on which the electrodes are positioned, said head being T-shaped, O-shaped, or in the shape of a fork, and configured to be moved, in use, inside the oral cavity with the electrodes in scraping contact with the walls of the oral cavity.

9. An apparatus (1, 10), as per claim 8, wherein the long-shaped element (2, 5) foresees said two electrodes (b, b') for measuring the voltage drop following the input current (I1) injected in the person and two further electrodes (a, a') through which the current generated by the generator is injected.
10. An apparatus (1, 10), as per claim 8, wherein said electrodes (a, a') through which to inject the current (I1) belong to a device for the injection of the current separated from the long-shaped element (2, 5).

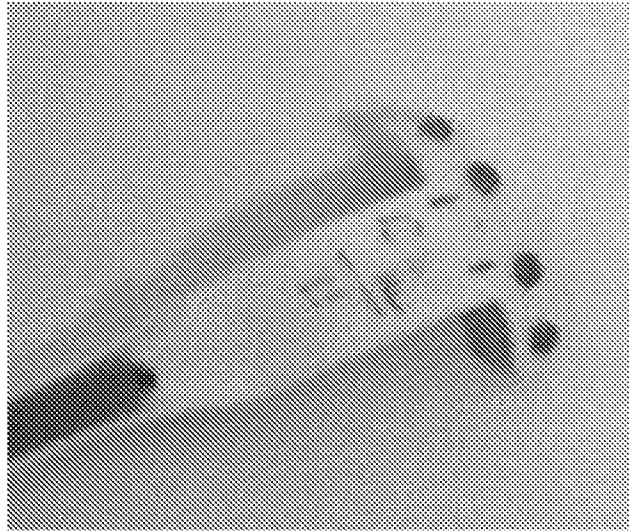
**FIG. 1**



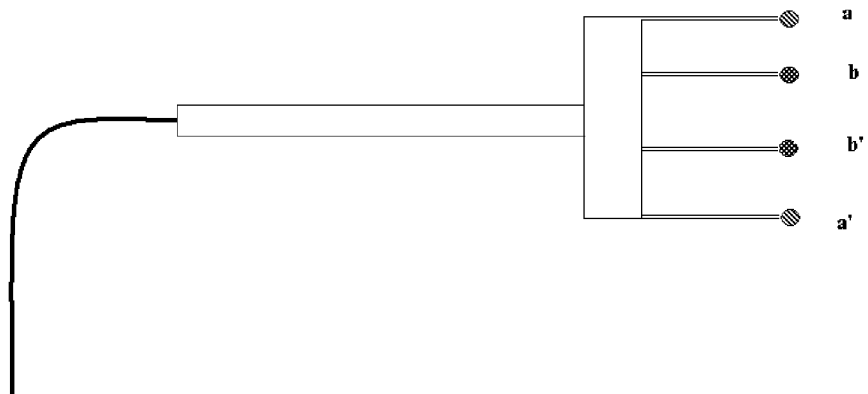
**FIG. 2**



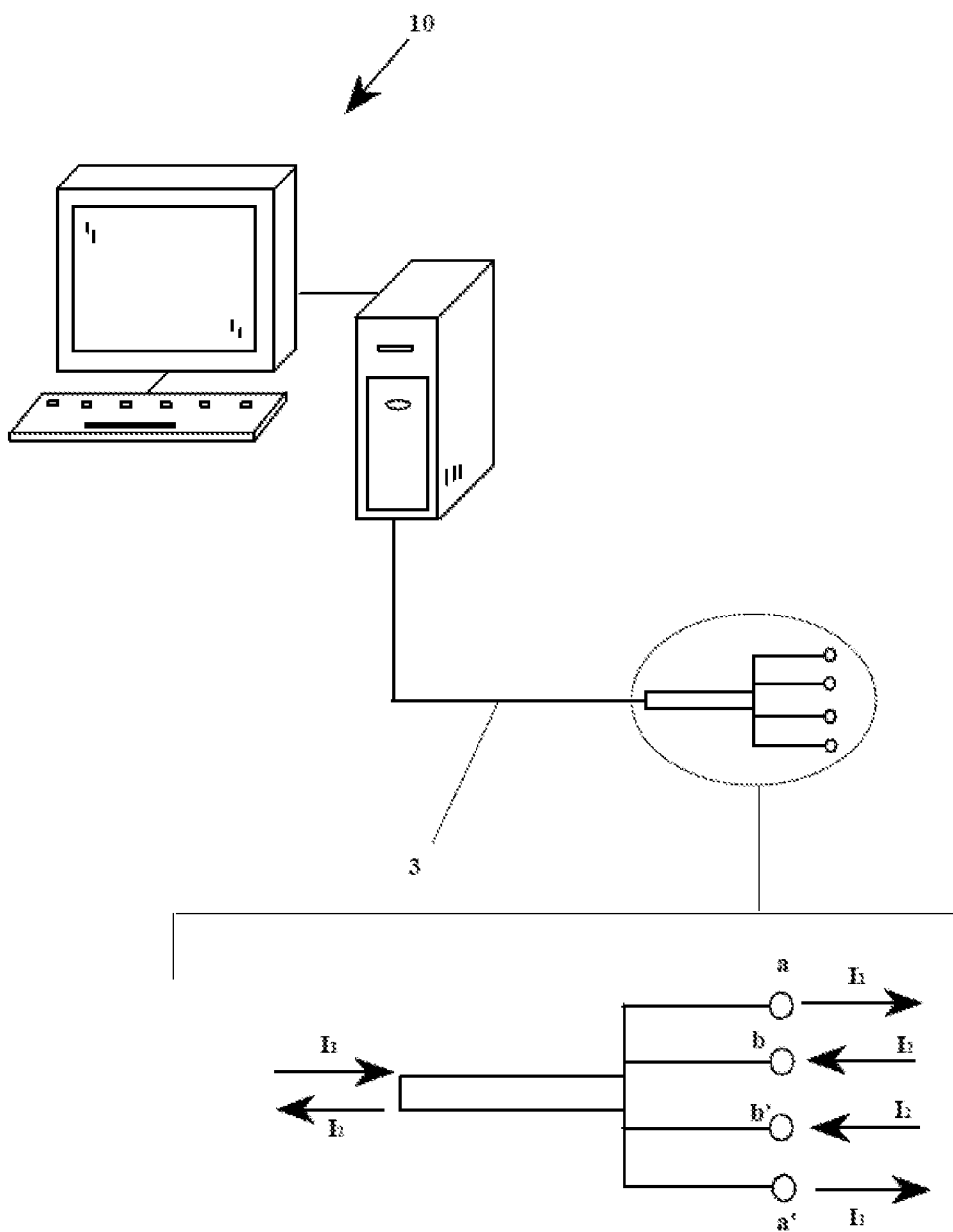
**FIG. 3**



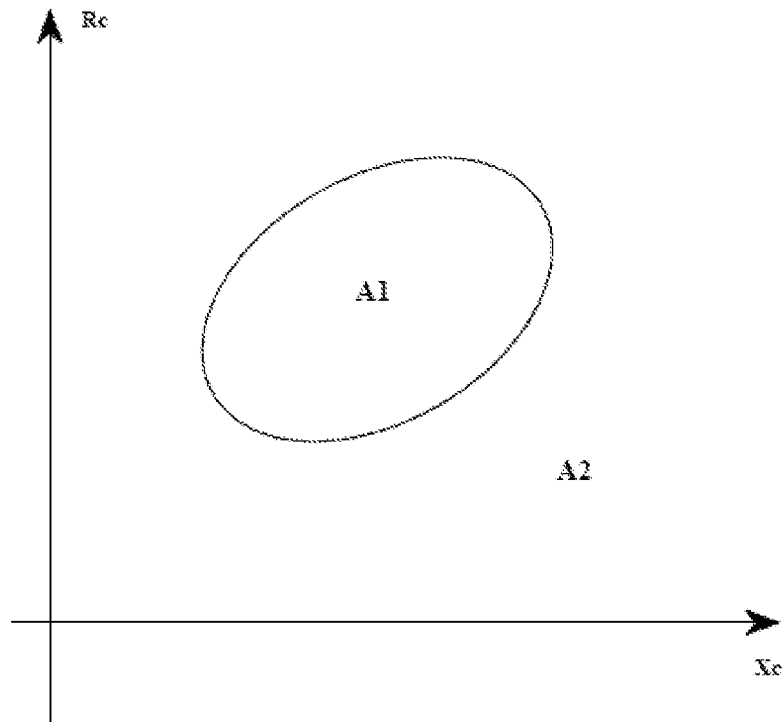
**FIG. 4**



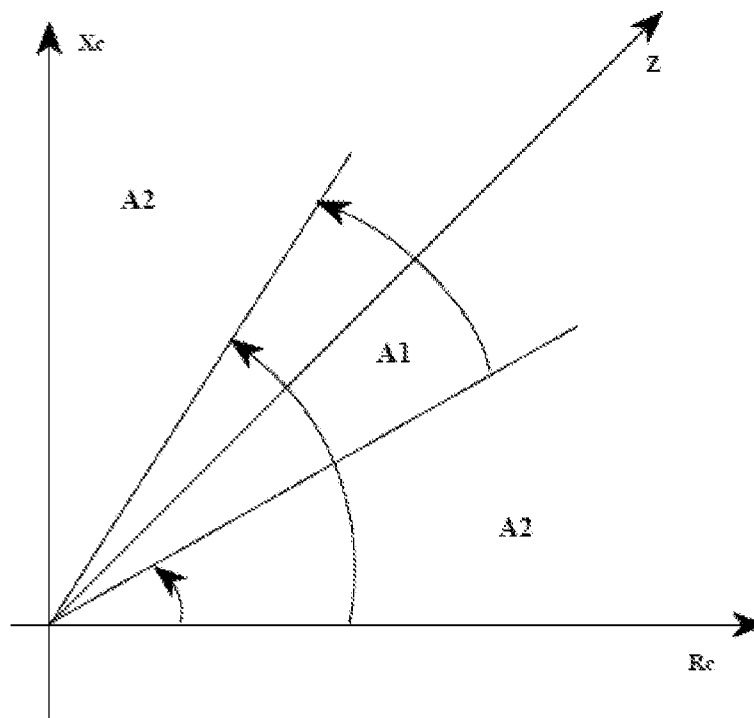
**FIG. 5**



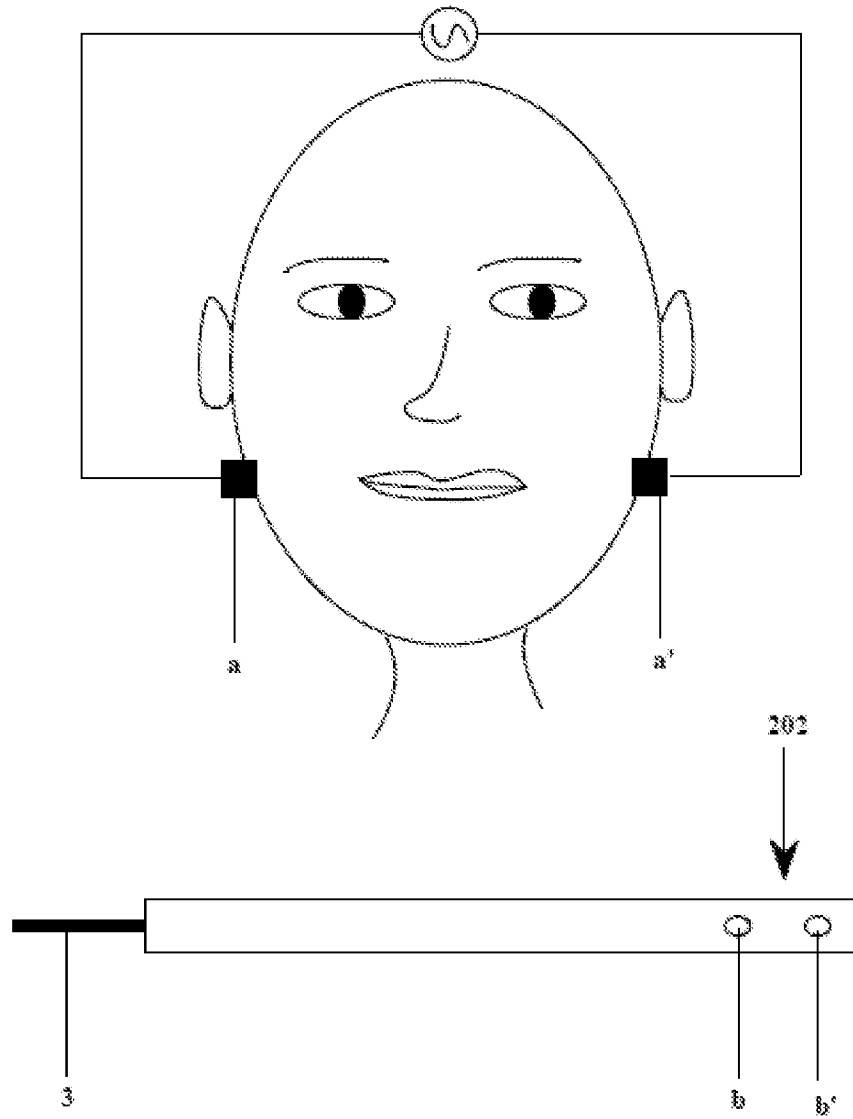
**FIG. 6**



**FIG. 7**



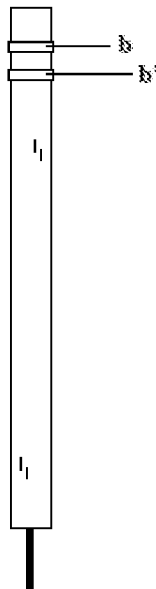
**FIG. 8**



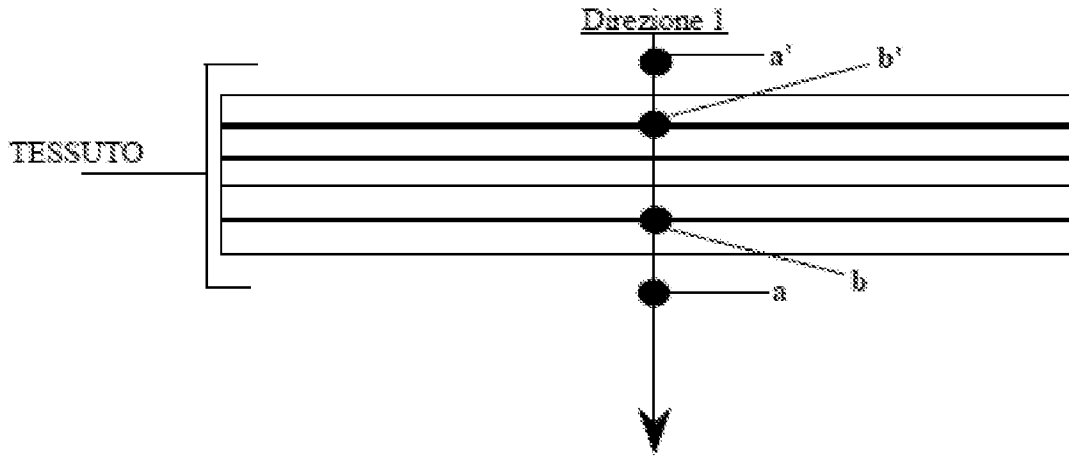
**FIG. 9**



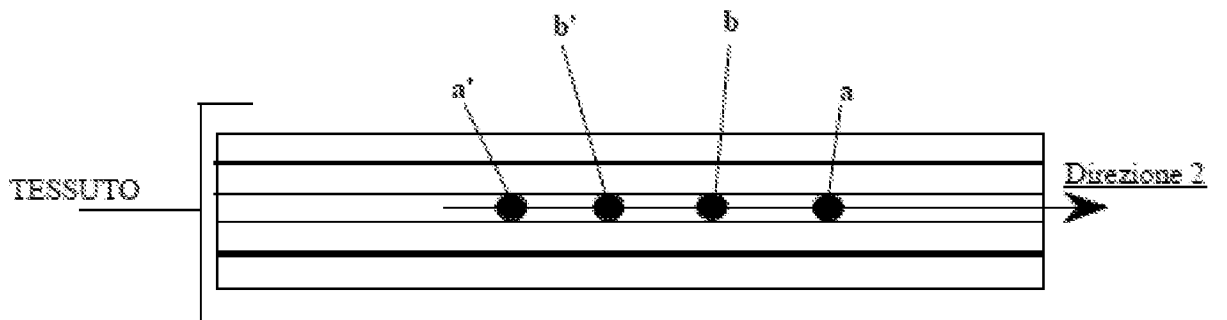
**FIG. 10**



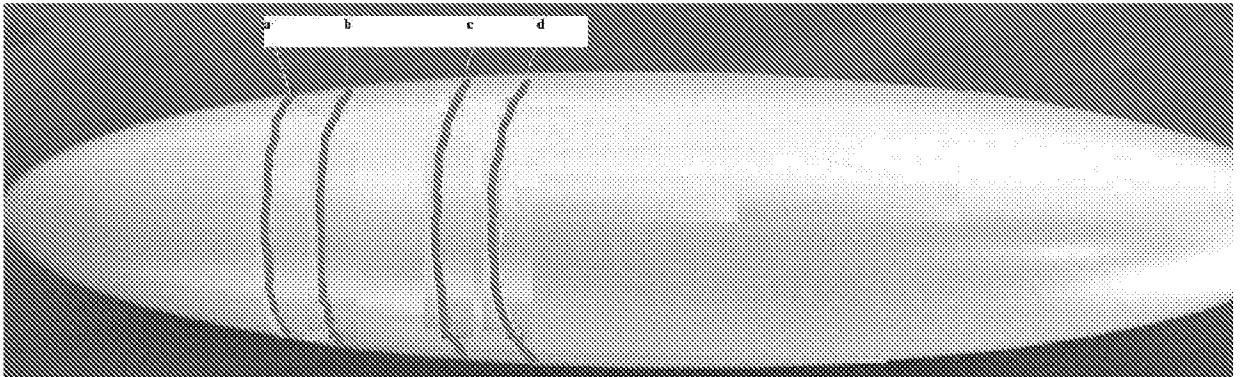
**FIG. 11**



**FIG. 12**



**FIG. 13**



a-d = infezione  
b-c = lettera

**FIG. 14**

