

A DEVICE FOR DELIVERY OF AEROSOLIZED DRUG IN A PORTION OF A BODY

FIELD OF THE INVENTION:

This invention relates to the field of biomedical engineering.

Particularly, this invention relates to a device for delivery of aerosolized drug in a portion of a body.

BACKGROUND OF THE INVENTION:

Chemotherapy is the use of drugs to destroy cancer cells. It usually works by keeping the cancer cells from growing, dividing, and making more cells. Because cancer cells usually grow and divide faster than normal cells, chemotherapy has more of an effect on cancer cells. In chemotherapy, many drugs require injection directly into a vein; this is called intravenous (IV) treatment.

In comparison to intravenous (IV) treatment, intraperitoneal (IP) administration results in a several-fold increase in drug concentration within an abdominal cavity.

There is now growing evidence from clinical studies showing a survival advantage for IP chemotherapy in various tumor types, including ovarian, thoracic, gastric, and colorectal cancer. Efficacy of intraperitoneal (IP) chemotherapy is limited by poor distribution within the abdominal cavity and by poor tissue penetration.

Therefore, there is a need for a new way for administering intraperitoneal chemotherapy into an abdominal cavity.

Prior art technology which is termed as Pressurized Intraperitoneal Aerosol Chemotherapy (PIPAC) administers chemotherapy drug through laparoscopic access using two balloon trocars in an operating room equipped with laminar air flow. In a first step, a normothermic capno-peritoneum is established with a pressure of 12mmHg. In a second step, a cytotoxic solution (about 10% of a normal systemic dose) is aerosolized with a pressure injector into an abdominal cavity and maintained for 30 minutes. In a third step, the aerosol is then removed through a closed suction system.

However, there is a need to move away from the prior art technology of delivery of aerosol under pressure. Prior art mechanisms have to rely on third party pressure for delivery and hence are inefficient. These third-party pressure delivery mechanisms are injectors which create pressure for drug feeding into a nozzle of the prior art. These pressure injectors are bulky equipment, typically, available in bigger sized hospitals and predominantly used as a radiolucent dye injection in patient for CTs, MRIs, and CATHLAB departments.

This restricts such treatment in smaller size hospitals which doesn't have Pressure injectors

There is a need for a device, mechanism, apparatus, and / or system which does not rely on pressure and / or any pressure injector and / or any third-party equipment for delivery.

OBJECTS OF THE INVENTION:

An object of the invention is to provide a new way for administering intraperitoneal chemotherapy into an abdominal cavity.

Another object of the invention is to provide a device in order to deliver chemotherapy drug into an abdomen of a palliative patient in an aerosolized form and the drug delivery being of average nanometer size or smaller.

Yet another object of the invention is to provide a device in order to deliver chemotherapy drug, in an aerosol form, under ultrasound waves.

Yet another object of the invention is to provide an easier delivery mechanism for delivery of chemotherapy drug into an abdomen of a palliative patient.

Yet another object of the invention is to provide a safe operability of the device ensuring safety for OT/ OR personnel present, while delivering the aerosolized chemotherapy drug into an abdomen.

Yet another object of the invention is to provide possibility of safe maneuverability of the drug delivery nozzle while delivering aerosolized chemotherapy drug for better reach within the peritoneal cavities.

Still another object of the invention is to provide a device, which does not rely on pressure and / or any pressure injector and / or any third-party equipment; for delivery.

An additional object of the invention is to provide a device which is convenient to use and also at small sized hospitals.

SUMMARY OF THE INVENTION:

According to this invention, there is provided a device for delivery of aerosolized drug in a portion of a body, said device comprising:

- a nozzle comprising a head portion extending, distally, into an elongate shaft, said head portion comprising:
 - o one or more piezoelectric transducers mounted between a pair of electrically conductive electrode discs, said piezoelectric transducers configured to create capillary waves in a liquid film leading to atomization of drug/s while passing through said nozzle;
 - o an aperture, at an operative proximal end of said nozzle, through which tubing is connected, said aperture follows through with a passage ensconced in said elongate shaft, and passing through said piezoelectric transducers and said electrically conductive electrode discs in order to allow passage of drug received through said tubing; and
- said elongate shaft supporting a body member at its operative proximal end and having an opening at its operative distal end, said drug, received through said tubing, and passing through said passage, being dispensed through said opening.

In at least an embodiment, said piezoelectric transducers are disc-shaped piezoelectric transducers.

In at least an embodiment, said body member is a cylindrical body member with its flat operative top surface being configured to support said nozzle.

In at least an embodiment, fastening mechanisms is provided at operative top of said nozzle to hold said piezoelectric transducers from its operative top.

In at least an embodiment, body member is provided at operative bottom of said nozzle to hold said piezoelectric transducers from its operative bottom.

In at least an embodiment, said tubing is connected to said nozzle, through said aperture, by means of a luer connector.

In at least an embodiment, said tubing is a gravity-fed tubing.

In at least an embodiment, a cable applies electric potential to said piezoelectric transducers.

In at least an embodiment, said cylindrical body member extends away from said discs to form an elongate shaft having a diameter substantially lesser than the diameter of the cylindrical body member.

In at least an embodiment, a conical surface is provided adjacent to said opening, said conical surface tapers such that it is narrowest adjacent to said opening of said elongate shaft.

In at least an embodiment, a step is provided at an operative distal end of said elongate shaft adjacent to said opening.

In at least an embodiment, a controller is provided to control frequency of vibration of said piezoelectric transducer which, in turn, atomizes drug from its liquid form into a nano-particle mist before being dispensed through said opening.

In at least an embodiment, working frequency of said device is in the range of 20 – 80 KHz.

BRIEF DESCRIPTION OF THE ACCOMPANYING DRAWINGS:

The invention will now be described in relation to the accompanying drawings, in which:

Figure 1 is an isometric view of a nozzle of the device of this invention;

Figure 2 is a top elevation view of the nozzle illustrated in Figure 1;

Figure 3 is a cross-sectional view of the nozzle constructed in accordance with the present invention showing the principal elements thereof;

Figure 4 illustrates a block diagram for the working of the device of this invention;

Figure 5 illustrates that smaller particle size ranging from 46 nm to 176 nm sizes enhances the absorption of drug in the tissue; and

Figure 6 illustrates increased depth of drug penetration up to 800µm in the tissue due to smaller drug particle size.

DETAILED DESCRIPTION OF THE ACCOMPANYING DRAWINGS:

According to this invention, there is provided **a device for delivery of aerosolized drug in a portion of a body.**

This device, of this invention, facilitates a new way in the application of administering intraperitoneal (IP) chemotherapy in the form of aerosol, typically, into the abdominal cavity.

Figure 1 is an isometric view of the nozzle.

Figure 2 is a top elevation view of the nozzle illustrated in Figure 1.

Figure 3 is a cross-sectional view of the nozzle constructed in accordance with the present invention showing the principal elements thereof.

In at least an embodiment, the device comprises a **nozzle (100)**. The nozzle (100) comprises one or more **piezoelectric transducers (104, 106)** that creates capillary waves in a liquid film leading to atomization of drug/s while passing through the nozzle (100). Typically, the nozzle (100) comprises one or more disc-shaped piezoelectric transducers (104, 106) mounted between a pair of electrically conductive electrode discs (103, 105). An electric potential is applied through a RF coaxial cable (113).

Referring to the drawings, and in particular to FIG. 1, the nozzle 100, in accordance, with this invention is illustrated. Nozzle (100), which forms a head portion, comprises a disc shaped piezoelectric transducer (104, 106) mounted between a pair of electrically conductive electrode discs (103, 105) and a flat surface of a cylindrical body member (107) (being a support member). An electric potential is applied through RF coaxial cable (113). Cylindrical body members (107) and fastening mechanisms (102) are holding bodies (top and bottom) of piezoelectric transducer (104, 106). There is an aperture (101) on a rear body member (111) of the nozzle (100) through which a tube (112) (which may be an IV set) is connected with the help of luer connector. Aperture (101) has a passage (300) through which drug flows. The cylindrical body member (107) extends away from the discs (103, 105) to form an elongate shaft (108) having a diameter substantially lesser than the diameter of the cylindrical body member (107). An opening (109) is provided at an operative distal end of the nozzle (100) i.e., at the

free end of the elongate shaft (108) (nozzle stem); through which drug is dispensed. A conical surface (110) is provided adjacent to the opening (109); the conical surface (110) tapers such that it is narrowest adjacent to the opening (109) of the elongate shaft (108). For flow rate and nozzle co-relation, the nozzle's conical surface (110) is sandblasted to lower cohesive force between liquid atoms by making the surface rough which results in fine atomization at even higher flow rate.

Referring to FIG. 3, passage (300) within the elongate shaft (108) allows for drug to flow before being dispensed through the opening (109). Reference numeral 301 refers to a curvature of a nozzle (100) to accommodate for change in diameter from cylindrical body member (107) to its connected elongate shaft (108). At the distal end, a step (302) is provided.

In at least an embodiment, the device comprises a **controller** which can be used to control frequency of vibration of the **piezoelectric transducer (104)** which, in turn, atomizes the diluted drug from its liquid form into a nano-particle mist which can be then sprayed / delivered into an abdominal cavity through the nozzle (100) of this invention. The nozzle is customized or tailor made to be compatible to the controller and specific to the stated application

The size of particles generated by the device, of this invention, depends on the frequency of vibration, surface tension, and viscosity of the liquid. The particle size is inversely proportional to frequency and, thus, the frequency can be increased to reduce the particle size. In this device, liquid is not forced through a small orifice but flows through a large channel in which ultrasonic waves produce the aerosol.

In at least an embodiment, the nozzle (100) is connected to the controller unit through the coaxial RF cable (113); through which an electric potential is applied. A tubing (110) is connected through a **luer connector** connected on the nozzle (100). Cylindrical body members (107) and fastening mechanism (102) depict a holding body of the piezoelectric transducer (104, 106). There is an aperture (101) on the rear body member (111) of the nozzle (100) through which the tubing (112) is connected with the help of luer connector.

The nozzle stem (108) comprises a conical surface (110), at its operative distal end, such that the nozzle stem's (108) narrowest part is adjacent to the opening (109). Reference numeral 300 refers to a passage for drug flow.

In at least an embodiment, actuation by the controller, it starts identification of the nozzle (100). This phase checks the status of the nozzle i.e., being used already or a fresh nozzle (100). Upon again acknowledging the identification phase and pressing the key, the controller starts delivering power to the nozzle (100). A pinch valve, which is present in the tubing (112), is to be opened, and drug starts atomizing from the tip of the nozzle (100).

Typically, this device's working frequency is in the range of 20 – 80 KHz.

In at least an embodiment, using the device of this invention, drug flows under gravity through the tubing (112); therefore, there is no need of a pressure injector or any third-party equipment.

The device, of this invention, is configured for creating and delivering aerosol under ultrasound waves. Compared to prior art, this is far more effective and much easier to set-up and deliver. This device does not rely on third party pressure injectors. Since procedures, in respect of palliative care, are repetitive procedures, this device is more conducive to be used, since there is cost reduction, on account of it being an independent, non-third-party-dependent, device.

Preferably, RFID technology is used to prevent the reuse / misuse of the same nozzle, multiple times.

Preferably, the entire device is made of Titanium for the acoustic properties that it lends to the construction of this device.

Figure 4 illustrates a block diagram for the working of the device of this invention.

According to a non-limiting exemplary embodiment, therapy procedures such as PIPAC are to be repeated after every 6 weeks for a palliative patient and for over 6-8 times. Prior art mechanisms require a huge setup; therefore, they cannot be set up in a small-sized hospitals. This prohibits a patient to obtain better care due to availability and affordability issues.

The device, of this invention, however, is independent, and portable; therefore, it is convenient to be used. Thus, this device can be used even in small sizes hospitals; thereby, overcoming availability and affordability issues of the prior art.

It was also observed, by the inventors, that, prior art mechanisms deliver, at the start, few non-aerosolized drops of diluted chemotherapy, as it is, which is not at all desired. In contrast, the device, of the current invention, delivers an aerosolized

drug right from the first instance of delivery; there is no lag for delivery of the right particle sized drug.

It was also observed, by the inventors, that, in prior art mechanisms, the average particle size, delivered in an abdomen is in Microns (Micrometers) in size, due to the pressure-based technique of aerosolization. In contrast, average particle size, delivered in the abdomen, using the NAC (Nano Aerosolized Chemotherapy) technique with the device of the invention, is Nanometers in size. Thus ensuring higher depth of penetration in the tissue, better drug concentration in the tissues and better drug distribution on the tissues.

Typically, volume of particles $\geq 3\mu\text{m}$ is 97.5% and 2.5% of particles $\leq 3\mu\text{m}$; using the prior art mechanism, whereas volume of particles $\leq 150\text{ nm}$ is 95% and 5% of particles $\geq 150\text{ nm}$ but $\leq 500\text{ nm}$ using the device of this inventions. All particles are in nanometer range.

It was further observed by the inventors that larger droplets are primarily deposited by impaction and gravitational settling onto a peritoneal surface facing the aerosolizing device of the prior art, leading to poor drug distribution within a peritoneal cavity. In contrast, using the device of the current invention, particles being in nanometre size, ranging from 46nm to 176nm; hence can uniformly disperse within the abdominal cavity and can spread even to inaccessible areas; this improves bioavailability and enhances therapy performance.

Figure 5 illustrates that smaller particle size ranging from 46 nm to 176 nm sizes enhances the absorption of drug in the tissue.

Figure 6 illustrates increased depth of drug penetration up to 800µm in the tissue due to smaller drug particle size.

It was further observed that, by using the device of this invention:

- uniform drug distribution within the abdominal cavity because of possibility of maneuverability of the nozzle and greater drug concentration in the tissue enhancing the bioavailability of the drug;
- no need of a third-party pressure injector for performing procedure, hence can be done in a small sized hospital setup enhancing availability / accessibility to every needy patient; and
- tighter particle size bandwidth.

Even though this specification may be written in relation to chemotherapy, it is to be understood that any for of drug can be used in connection with this device.

The **TECHNICAL ADVANCEMENT** of this invention lies in providing a device which provides ultrasonic atomization of drug for IP therapy; this drug delivery has a much tighter droplet size distribution than prior art's pressurized atomization. Here, atomized drug, under the influence of ultrasound waves, has particle size in nanometers. There is greater depth of penetration, using the device of this invention, and, hence, there is better absorption of drugs; thus, ensuring increased efficacy of the system and better patient outcomes. The flow of drug, using the device of this invention, is gravity fed; this eliminates the need of costly, bulky, and non-portable pressure injector systems typically found in bigger hospitals only and, typically, required by prior art mechanisms. Furthermore, due to narrow bandwidth of nano-particle size, drug distribution, using the device of this invention, is deposited all throughout an abdomen cavity and in a uniform manner.

While this detailed description has disclosed certain specific embodiments for illustrative purposes, various modifications will be apparent to those skilled in the art which do not constitute departures from the spirit and scope of the invention as defined in the following claims, and it is to be distinctly understood that the foregoing descriptive matter is to be interpreted merely as illustrative of the invention and not as a limitation.

CLAIMS,

1. A **device for delivery of aerosolized drug in a portion of a body**, said device comprising:
 - a **nozzle (100)** comprising a head portion extending, distally, into an **elongate shaft (108)**, said head portion comprising:
 - one or more **piezoelectric transducers (104, 106)** mounted between a pair of **electrically conductive electrode discs (103, 105)**, said piezoelectric transducers (104, 106) configured to create capillary waves in a liquid film leading to atomization of drug/s while passing through said **nozzle (100)**;
 - an **aperture (101)**, at an operative proximal end of said nozzle (100), through which tubing (112) is connected, said aperture (101) follows through with a passage (300) ensconced in said elongate shaft (108), and passing through said **piezoelectric transducers (104, 106)** and said **electrically conductive electrode discs (103, 105)** in order to allow passage of drug received through said tubing (112); and
 - said **elongate shaft (108)** supporting a **body member (107)** at its operative proximal end and having an **opening (109)** at its operative distal end, said drug, received through said tubing (112), and passing through said passage (300), being dispensed through said opening (109).
2. The device as claimed in claim 1 wherein, said piezoelectric transducers (104, 106) are disc-shaped piezoelectric transducers (104, 106).
3. The device as claimed in claim 1 wherein, said nozzle's conical surface (110) being a sandblasted conical surface (110) to lower cohesive force between

liquid atoms by making said surface rough resulting in fine atomization even at higher flow rates.

4. The device as claimed in claim 1 wherein, said body member (107) being a cylindrical body member (107) with its flat operative top surface being configured to support said nozzle (100).
5. The device as claimed in claim 1 wherein, fastening mechanisms (102) being provided at operative top of said nozzle (100) to hold said **piezoelectric transducers (104, 106)** from its operative top.
6. The device as claimed in claim 1 wherein, body member (107) being provided at operative bottom of said nozzle (100) to hold said **piezoelectric transducers (104, 106)** from its operative bottom.
7. The device as claimed in claim 1 wherein, said tubing (112) being connected to said nozzle (100), through said aperture (101), by means of a luer connector.
8. The device as claimed in claim 1 wherein, said tubing (112) being a gravity-fed tubing (112).
9. The device as claimed in claim 1 wherein, a cable (113) applies electric potential to said piezoelectric transducers (104, 106).
10. The device as claimed in claim 1 wherein, said cylindrical body member (107) extends away from said discs (103, 105) to form an elongate shaft (108) having

a diameter substantially lesser than the diameter of the cylindrical body member (107).

11. The device as claimed in claim 1 wherein, a conical surface (110) being provided adjacent to said opening (109), said conical surface (110) tapers such that it is narrowest adjacent to said opening (109) of said elongate shaft (108).
12. The device as claimed in claim 1 wherein, a step (302) being provided at an operative distal end of said elongate shaft (108) adjacent to said opening (109).
13. The device as claimed in claim 1 wherein, a **controller** being provided to control frequency of vibration of said **piezoelectric transducer (104, 106)** which, in turn, atomizes drug from its liquid form into a nano-particle mist before being dispensed through said opening (109).
14. The device as claimed in claim 1 wherein, working frequency of said device being in the range of 20 – 80 KHz.