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Construction of a novel microfluidic experimental setup for testing recent glaucoma drainage devices

Abstract: Glaucoma is an eye disorder in which the optic nerve is damaged over time due to a sustained elevation of the intraocular pressure (IOP). Being the second leading cause of blindness according to the reports of the World Health Organization, glaucoma is not only a serious ocular disease that threatens individuals, but also a community health problem. In recent years, great improvement has been achieved in the technology of implants used in the treatment of the disease. Despite the great effort dedicated to the design and implementation of the glaucoma drainage devices (GDD), they still have unsolved problems and weaknesses.

Most of the currently employed GDDs are very simple and have major problems such as reversed flow, choking and a coarse interval of pressure control. Experiments must be devised to investigate the flow behavior inside these devices. In this study, an accurate microfluidics experimental setup is constructed to analyze and characterize the in-vitro performance of actively employed GDDs on the glaucoma treatment. Proposed setup includes a pressurized fluid reservoir, ELVEFLOW microfluidics flow rate measurement/control unit, microfluidics flow/pressure sensors, and data analysis system. In the setup, more precise measurements than experimental setups in literature is planned to be provided. It is estimated that the results showing consistency with in-vivo measurements will be obtained, behavior of the fluid passing through the GDDs will be observed and issues with design flaws will be addressed.

Keywords: Glaucoma, glaucoma drainage device, microfluidics, in-vitro experimental setup

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1 Introduction

Glaucoma constitutes the group of ophthalmic diseases caused by pressure in the eye above normal limits. This rise of pressure is seen as a result of the obstruction of the passageways of the flowing fluid, aqueous humour (AH), which fills the front (anterior) and back (posterior) chambers in the eye. This disease may end the sight partially or completely without showing any early warning. If left untreated, glaucoma may cause blindness. According to World Health Organization reports, it is the second cause of blindness. In 2010, it was predicted that the number of 8.4 million individuals who were blind from primary glaucoma would increase to 11.1 million in 2020. In addition, 60.5 million open-angle and closed-angle glaucoma cases in 2010 are assumed to be 79.6 million in 2020 [1].

Glaucoma can be treated in three different approaches: medical therapy, surgical treatment, glaucoma drainage devices (GDD). While alternative treatments to GDD are effective in a limited period of time, the drainage implant can be used for life after insertion. While none of these three methods yielded complete results, GDD surgery has been successful in the last 20 years due to design improvements.

An ideal GDD was not produced. With today's technology and practical approaches, Ahmed Glaucoma Valve (AGV) can be considered the closest device to the ideal [2]. However, as previously mentioned [3], the AGV acts as a flow blocker after implantation and it must be switched on and off at certain pressures such as a real valve. A numerical study was performed for AGV [4], thereafter microfluidic theory [5] has been performed for Venturi system of AGV.

No matter how effective the computational studies are [4, 5], the simulation results cannot be accurately reflected in reality if the numerical models are not fully defined. Experimental studies should be performed on GDD to verify these models. In-vitro experimental setups for GDD analyses are surveyed in literature and summarized in authors' recent article [6]. These experimental studies took into account the pressure drop occurring just after the installation of GDDs. However, the main considerations should have been:

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- Observing whether the device can continue its initial functionality after a period of time (e.g. one week),
- Testing how effectively it responds to postoperative complications such as hypotony and diplopia,
- Wide range of reversed flow, flow blockage, and pressure control commonly encountered in GDDs.

In this study, an accurate microfluidics experimental setup is constructed to analyse and characterize the in-vitro performance of actively employed GDDs on the glaucoma treatment. The gaps to be filled are listed below:

- Creating a more sensitive and faster response system than the syringe pump currently used in experimental setups,
- Testing different GDDs at the same setup and perform a comparative test,
- Providing comments about design errors,
- Suggesting a design that takes into account the exposure and ergonomics sensitivities that may occur during implantation of GDD.

2 Proposed Experimental Setup

2.1 Setup components

The setups used in all of the in-vitro experiments [6] generally includes syringe pump, pressure transducer, three-way valve, insulated test tube (or box) with the GDD in it and an outlet tube. The working principle of the device can be summarized as follows: It is an open loop operation that starts by feeding the saline (similar to AH) solution inside the syringe pump to the implant by three-way valve control through the test tube that ends with the outlet pipe. If the outlet pressure is taken as atmospheric pressure, the relative pressure measured in the pressure column is equal to the pressure drop provided by the implant [7]. Lack of feedback of the currently employed setups in literature negatively affects the sensitivity. Furthermore, the characteristics of the syringe pump, the flexibility that may occur in the piping system and the use of a syringe pump that cannot produce the desired flow rate can cause unwanted vibrations in the release of the fluid. Finally, the stability and settling times of the syringe pumps [8] lead to longer tests and reduced reproducibility. A novel microfluidic experimental test setup is proposed in order to correctly handle these problems and to overcome them. In the proposed test setup, the following components are combined:

1. Pressurized fluid reservoirs,
2. ELVEFLOW microfluidic flow measurement/ control unit,
3. Pressure sensors,
4. Flow sensor,
5. Visual analysis by USB microscope,
6. Silicone pipes and insulated test boxes,
7. Data analysis unit (via computer).
8. Compressor,

The experimental test unit currently being set up is shown below.

Figure 1: Proposed test setup; (a) Reservoirs, (b) microfluidic flow measurement/ control unit, (c) pressure sensors, (d) flow sensor, (e) USB microscope, (f) insulated test box, (g) compressor

The apparatus will allow testing of any GDD in an artificial (in-vitro) environment similar to human eye environment. The loop starts by the pressurized air from the compressor (Fig. 1(g)). The flow control system is connected to the flow sensor (Fig. 1(d)) through the pressurized fluid (inlet) reservoir (Fig. 1(a)) at the beginning of the assembly. The pipe coming out of this sensor is connected to the inlet pipe of the test box. The inlet pipe directs the flow into the insulated box (Fig. 1(f)) in which the GDD is located. AH-like, saline solution is transferred to the outlet reservoir open to the atmosphere through the outlet pipe.

The pressurized air sent by the computer controlled system (Fig. 1(b)), feedback based on the constant value of the flow rate read by the flow sensor, allows the saline solution to pass through the microfluidic test apparatus under constant pressure. The pressure sensors (Fig. 1(c)) are connected to the input and output of the test box so that the pressure drop generated by the GDD can be detected. A USB microscope with a 20x-90x magnification range (Fig. 1(e)) is used in addition to the microfluidic device to closely investigate the saline solution passing through the GDDs. The snapshots and videos captured will be analysed in order to observe the path and behaviour of the flow as it passes through the tested GDDs. In this way, more than just the

1. Pressurized fluid reservoirs,

output of the data generated from graphs and tables will be obtained.

2.2 Calibration of the pressure control unit

The first thing to do when setting up any experimental device is to perform calibration. In this study, two types of calibration are applied: Firstly, when the pressure control unit is connected to the computer for the first time, the pressure input is calibrated to the desired 2 bar maximum output. Secondly, if the pressure output passes beyond the limit during the experiment, pressure regulator is calibrated. Details of the calibration procedure can be found in the user guide of ELVEFLOW [9].

After successful calibrations, the pressurized air versus flow rate graph is drawn to correctly categorize needed pressure for needed flow rate of the fluid. The graph can be used to select needed pressure of air through the experimental setup for the desired flow rate of the saline solution.

3 Discussion

Experiments must be devised to investigate the flow behaviour inside GDDs. The main purpose in this study is to analyse and characterize the in-vitro performance of actively employed GDDs on the glaucoma treatment by constructing an accurate microfluidics experimental setup. In the setup, more precise measurement than experimental setups in literature will be provided, results showing consistency with the measurements done in vivo (eye) will be obtained, behaviour of the fluid passing through the GDDs will be observed and issues with design faults will be inferred. In the light of these results, how to manufacture the projected novel GDD will be envisioned.

Experimental setup is aimed to be operated more precisely than the generally used duo of syringe pump and pressure transducer. Design of an experimental setup is crucial to compare the currently employed GDDs objectively. Required pressure intervals will be constituted in order to obtain most precise and accurate results. Response time of the proposed setup will shorten in proportion to generally used syringe pumps, besides stable results will be accomplished.

Keeping in view of originality of the proposed setup, in the light of emergent results, the future work is; to construct

and to test an exact size model of an improved implant preventing undesirable reversed flow and choking, providing a level of IOP control superior to that of currently used devices.

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