Artificial Tear Delivery Device

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General Introduction

The dry eyes syndrome is a quite frequent syndrome in our society, especially when people get older than 40 years old. The number of people affected is estimated to 25-30 millions in the United States. It is more common in women than in men, with a 9:1 ratio, mainly because of hormonal changes. [1]

For the rare severe cases of dry eyes, there is no satisfactory treatment available, although several attempts have been made to find a solution. The most simple solution is manual application of artificial tears every 5-10 min in the most severe cases, but it is not convenient for the patient.

A very interesting project carried out by Professor Juan Murube led to the development of a fully implantable artificial lacrimal gland [2][3]. It consists of a pump and reservoir implanted in the abdomen, with a subcutaneous silicone tube driving the liquid to the eye. This project is in clinical trials, but the implantation surgery is quite complex, because a tube has to be inserted subcutaneously from the abdomen to the neck, ear and eye, without touching nerves or blood vessels. The refill of the reservoir is made with a syringe so it is quite invasive as well and can lead to infections, which would require revision surgery. Therefore, this solution does not seem optimal.

To overcome these issues, a new theoretical approach is proposed in this project, trying to find a balance between patient comfort, risk of infection and invasiveness of the device and implantation procedure.

1) Anatomy and Physiology

Because the eye is in continuous movement, the front of the eyeball and the cornea need to be constantly lubricated in order to decrease friction. The lubricant secreted in the eye also fulfills a cleaning function: it removes unwanted particles as well as prevents infections. Tears are produced in lacrimal glands, collected in ducts and then they reach the eye through multiple secretory ducts. When tears reach the surface of the eyeball, they are spread on the entire surface of the eye thanks to the movement of the eyelids. Tears then evaporate or drain into the nasal cavity through the lacrimal canals [4].

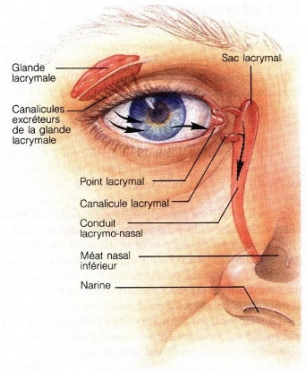

Fig 1 : Anatomy of the eye [5]

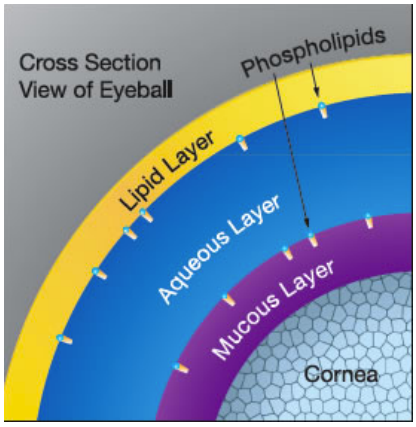

Fig. 2 : Layers of the tear film [6]

Tear composition is very diverse and matches its function: to clean and lubricate the eye. The eye's tears contain three main components: oil, water and mucus.

The **watery portion** of the tears is produced by the lacrimal gland. This gland lies underneath the outer orbital rim bone, just below the eyebrow. The aqueous component of tears provides defense against foreign organisms thanks to multiple of its components, such as lysozymes, immunoglobulins and beta-lysin. The **oily component** is produced by meibomian glands which lines the edge of the eyelids. This film coats the aqueous

layer and provides a protection that prevents evaporation of the aqueous layer. Finally the **mucous layer** is produced by goblet cells in the conjunctiva. It wets the microvilli of the corneal epithelium and provides a foundation allowing tears to adhere to the surface.

These different components of tears play major roles in the function and protection of the eye. Tear production is estimated to be around 1.5 mL/day in healthy patients. A lack of tear production is observed in multiple diseases. It can lead to many complications, which range from mild to severe depending on the level at which glands are affected.

2) Pathologies

The dry eye syndrome, also called keratoconjunctivitis sicca, can be linked to an insufficient tear production by the lacrimal glands or to a defect in tears composition that leads them to evaporate too quickly. If untreated, the insufficient hydration of the eyes can result in different complications. The most frequent are infections and scarring on the surface of the eye resulting in inflammation and ultimately vision damage (Fig 3).

Fig 3 : Inflammed or irritated conjunctiva [7]

This syndrome can have many different causes.
First, dry eyes are a side effect of many medications, such as antihistamines, antidepressants, certain blood pressure medicines, Parkinson's medications and birth control pills. A dry or dusty environment, as well as air conditioning and wind, can also cause dry eyes. Hormonal changes can also cause dry eyes. [8]
The Sjogren's syndrome is an important cause of severe dry eyes. This syndrome is a chronic autoimmune inflammatory disorder that induces dry eyes by atrophy of the secretory epithelium in lacrimal glands. It also affects salivary glands. In the case of secondary Sjogren's syndrome, it can be associated with rheumatoid arthritis, systemic lupus erythematosus or scleroderma.[9]
Xérophtalmia is a quite rare syndrom in industrialized countries. It is caused by lack of vitamin A, and induces dryness of the conjunctival epithelium. It is easily treatable with vitamin A when caught early. Otherwise, it can degenerate into corneal ulceration and blindness. [10]
Lacrimal gland tumours are another cause of dry eyes. They can be benign (dermoid cyst) or malignant (malignant mixed epithelial tumours). In both cases, the tumour needs to be removed, so in certain cases the remaining secreting epithelium is not sufficient to have a correct hydration of the eyes. Another important cause of lacrimal gland destruction is traumatism or accidents. Indeed, these cases can be the most severe if the lacrimal gland is completely destroyed.

When the dry eyes syndrome is not too severe, it can be easily treated with artificial tears so an implantable device is not necessary. Artificial lacrimal glands may be useful when the dryness is very severe and irreversible, particularly with Sjogren's syndrome, lacrimal gland tumour or traumatism, because they involve extensive damage of the lacrimal glands themselves that cannot be repaired.

3) Current treatments and limitations

Current treatments depend on the severity of the disease. The main treatment consists in delivering manually artificial tears [11]. They are applied multiple times a day with a frequency that depends on the patients. In the most severe cases, manual application of artificial tears has to be performed every 5-10 minutes, while at night no lubrication at all is provided. This solution is therefore not satisfactory for severe cases.

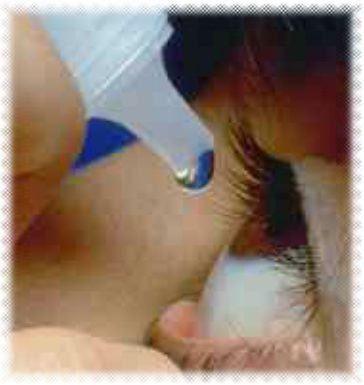

Fig 4 : Eye drops [12]

An alternative method used to improve comfort of the patients is solid inserts filled with a lubricating component (hydroxypropyl cellulose for Lacrisert inserts [13]). The insert is placed inside the lower eyelid, where it gradually releases lubricants during the day. As a result it reduces the number of applications of artificial tears required to ensure lubrication of the eyes.

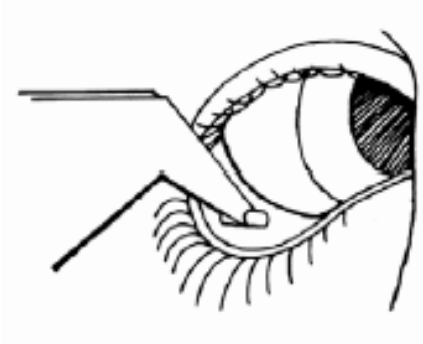

Fig 5 : Solid insert [14]

To further reduce the need for artificial tear, an option is to use Punctal plugs [15]. They are inserted in the drainage system of the eye, more specifically in the canals going from the eye to the lacrimal duct. It prevents tears from draining in the nose cavity, thus increasing the humidity in the eye.

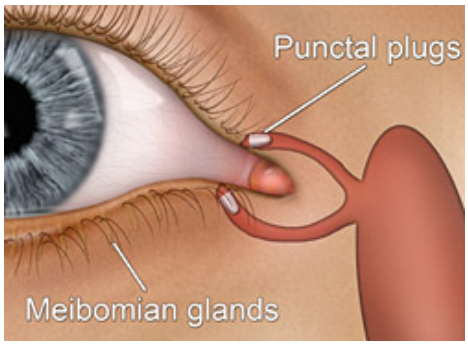

Fig 6 : Punctal plugs [16]

Those solutions are still not satisfactory for severe cases of dry-eye syndromes such as Sjogren's syndrome. For such severe cases, an artificial tear injection device implanted in the patient would provide the best treatment option and would greatly increase their quality of life.

4) Design of an artificial lacrimal device

a. General overview

The aim of the strategy described here is to develop a device against severe dry eyes that is more efficient and more convenient for the patient compared to current treatments.
The minimally-invasive approach chosen is based on the delivery of artificial tears from an external pump-reservoir unit to the eyes through a semi-implantable tubing system which is composed of an external part (from the pump-reservoir to an incision behind the ear) and a subcutaneous part (from the incision behind the ear to the eye).
The artificial tears are delivered to the eyes by two separate devices: each eye is connected to one device containing a pump and a reservoir. Another possibility is to deliver artificial tears to both eyes from the same device.

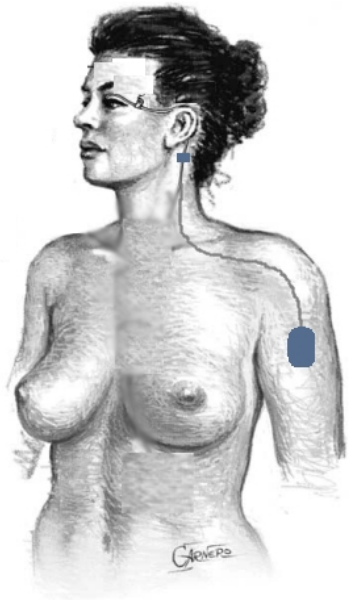

Fig 7 : General design [2]

b. Tube

General tubing system

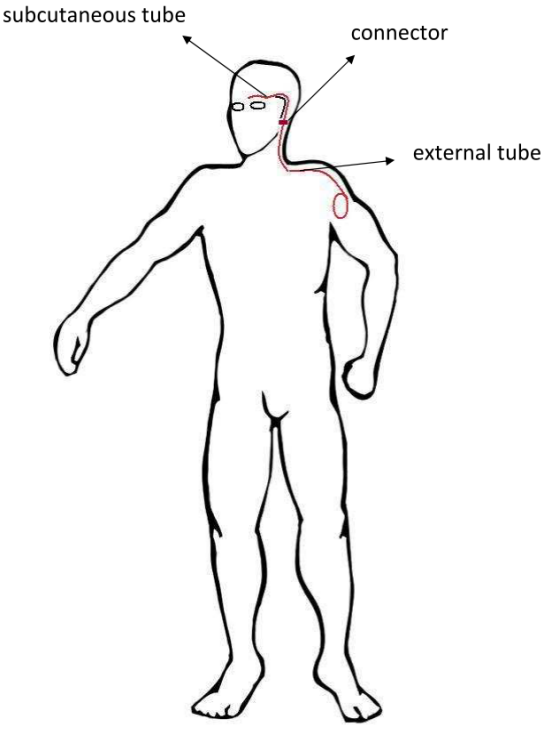

Fig 8 : General design

The tubing system designed to deliver artificial tears is composed of two parts. A first tube is implanted subcutaneously between the eye and an incision behind the ear, where it crosses the skin and is attached to a second tube. This second tube is then connected externally to the pumping device stuck on the arm for example (Fig 8).

Special attention should be paid to the region where the tube crosses the skin. In order to avoid an infection due to contact with the external environment, this region should be well insulated by using collagen sutures. Other medical procedures have already encountered such an issue but suturing techniques were developed to achieve an efficient insulation. An example is the colostomy, where a portion of the large intestine is brought to the surface of the abdomen to form a stoma by suturing the end to the skin. [17] [18]

Apart from being well insulated, the region where the tube crosses the skin has to be chosen carefully to help prevent inflammation due to frictions.

Several devices have also been developed for this purpose for the cases when a transcutaneous tube has to be used for very diverse medical applications. For example, fig. 9 shows a transcutaneous system with inflatable discs. This device was designed for medical drainage tubes and billary stents and avoids using sutures. We could imagine an adaptation to hold in place the transcutaneous silicone tube. Friction will then be decreased. [19]

Another existing possibility to help integrate the tube with the skin at the transcutaneous region makes use of collagen naturally present in the skin (fig.10). The surface of this device is a fibrous material with free collagen fibers that will be integrated with natural collagen fibers. This will decrease micromotion at the interface silicone/skin, thus solving part of the inflammation problem, and also decrease infections. [20]

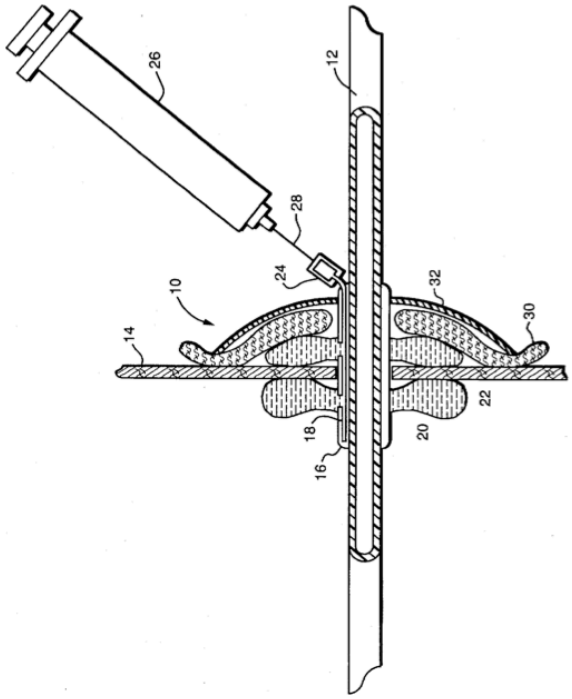

Fig 9 : Inflatable transcutaneous device [19]

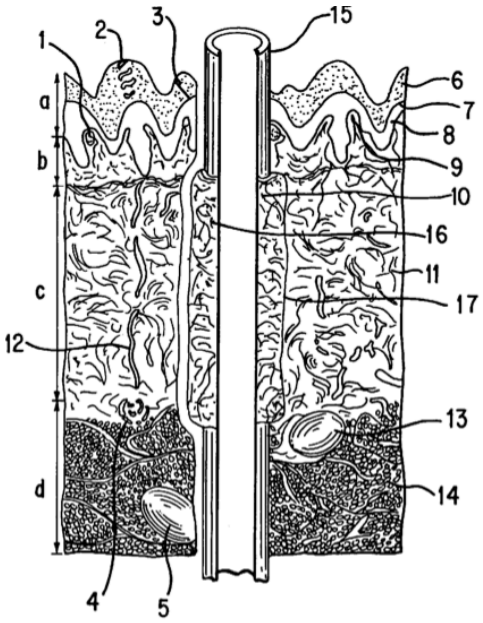

Fig 10 : Transcutaneous device with free collagen fibers [20]

The ocular end of the catheter reaches the original position of the lacrimal gland and is positioned along the upper conjunctival fornix, which is the fold connecting the conjunctival membrane lining the inside of the eyelid with the conjunctival membrane covering the eyeball (figure 11).

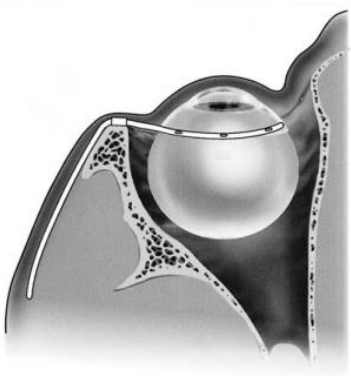

Fig 11 : Ocular end [2]

In order to avoid any retraction, the catheter is anchored to the temporal muscle fascia and the periosteum of the lateral orbital rim, as it was done by Murube's group [2][3]. Indeed, the temporal muscle is enveloped by a fascia, which is a tendonlike connective tissue rich in collagen fibers. Similarly, the orbital rim is covered by a dense fibrous membrane (the periosteum). The tube is sutured to these tissues thanks to fixing regions on the tube ocular end.

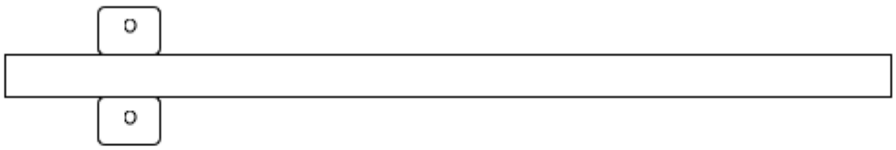

Fig 12 : Fixing regions on the tube

Biomaterials

The biomaterial selected for the tubing, especially for the subcutaneous tube, has to fulfill a few important requirements. First of all, the implant has to be biocompatible. In other words, it should perform its function without eliciting any undesired local or systemic immune reaction in the patient such as toxicity and allergic response. The biomaterial used also needs to have adequate mechanical and physical properties. In our case, the tube has to be elastic, resistant and long lasting (since the subcutaneous tube should require replacement as little as possible). Finally, the choice of the biomaterial has to take into account the manufacturability. Indeed, the biomaterial chosen should allow the production of tubing with the desired shape [21].

Silicone fulfills the requirements mentioned above and seems to be a good candidate for our tubing system. It is a polymer biomaterial characterized by a high flexibility, a low toxicity, chemical inertia and thermal stability, allowing it to be heat-sterilized. Silicone is widely used in medical applications such as in conjunctivodacryocystorhinostomy, a procedure for restoring lacrimal drainage when the canaliculi are occluded. This is done by implanting a tubular bypass prosthesis made of silicone (Murube tube), which provides higher stability than a tube made of Pyrex Glass (Jones tube) [22].

Characteristics of the tubes

The length of the tubes will depend on the patient's morphology and on the position of the adhesive patch. In general, the tube connecting the eye to the incision behind the ear is around 15-25 cm long, while the second part of the tubing system is around 35 cm long. The subcutaneous tube will have an external diameter of 1 mm and a wall thickness of 0.1 mm, while the external tube will have a higher wall thickness (for instance 0.5 mm) to provide better mechanical resistance.

The objective of the system is to achieve a homogeneous distribution of the artificial tears on the surface of the eye. Ideally, the small ducts deriving from the lacrimal gland could be kept and incorporated into the tubing system, but the surgery would be highly difficult and the probability of success is relatively small. Therefore, another possibility is to design a distal tube end having holes with increasing diameters (see section 4: Numerical models).

c. Liquids

The solution in the reservoir of the pump could be adapted to the patients. Indeed there are many different kinds of artificial eye drops available on the market and each patient has to test many of them before finding the appropriate one. Usually, artificial tears are protein free and contain water, polymers and salt. The polymers most commonly used in artificial tears are: methylcellulose, propylene glycol, glycerin, polyvinyl alcohol (PVA) and povidone [18]. Preservative free eye drops are preferred when they are used for long-term treatments.

Cleaning liquid enriched with lysozymes and bactericides could be considered in order to limit infections. Flushing the tubing system, with a syringe at the level of the connector, using a cleaning solution every day might be enough to prevent occlusion of the tube as well as infections.

d. Pump and reservoir

The injection system of the device is based on the technologies used for insulin pumps. The pump designed by Debiotech for insulin injection (Jewelpump) [23] could be adapted in order to match the needs for tear injection device. The pump contains a reservoir with a capacity of 4.5 mL. Since the daily tear needs in healthy patients is around 1.5 mL, the capacity of the reservoir is sufficient. A single reservoir could provide daily tear delivery for the two eyes. The minimal dose injected by the MEMS Nanopump is 0.2 uL, which is small enough to provide close to continuous flow rate. Assuming a flow rate around 1 ul/min, it would be equivalent to five injections of 0.2 uL per minute. Since the pump is directly programmable from a PDA device via Bluetooth, the flow rate can be adapted according to the needs of the patient. Its small size (60 x 40 x 13 mm) and its light weigh (22g) make it discreet, it can be attached anywhere on the skin thanks to an adherent patch. Since it is not cumbersome, patients can keep it even at night. They can also go into the water with it, thanks to its waterproof properties.

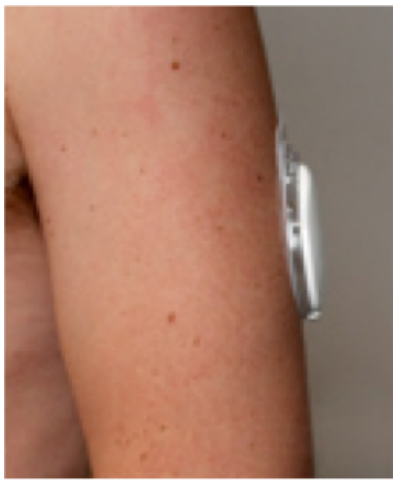

Fig 13 : Adhesive patch [24]

Fig 14 : Control system [24]

The pump is made of two parts, a non-disposable one that contains the electronics and a disposable one which contains the pumping system, the battery and the reservoir.

Fig 15 : Subunits of the pump [24]

The working range of the Nanopump is between -100 mbar and +100 mbar. The total pressure required to inject the solution from the pump to the eye is equal to the hydrostatic pressure added to the pressure resulting from the fluidic resistance of the tube. For the hydrostatic pressure we consider a difference in height for the tube of 30 cm and a density of artificial tears similar to water which is 1000 kg/m^3.

$$P_{hydrostatic} = \rho g h = 10^3 \times 9.81 \times 0.3 = 2943\,Pa \simeq 30\,mbar$$

To obtain the pressure required to push the solution through the tube we use Poiseuille equation. Several assumptions are made. We assume a laminar, steady and developed flow, and we also consider the tube to be straight, with a constant diameter and a rigid wall. The tube used to inject the solution has an inner radius of 0.4 mm and a length around 60 cm. To calculate the hydraulic resistance of a channel of circular cross-section, the following expression is used:

$$R = \frac{8\eta L}{\pi(\frac{D}{2})^4}$$

Where R [Pa.s.m^{-3}] is the fluidic resistance, η [Pa.s] the viscosity of the fluid, L [m] the length of the tube, and D [m] the inner diameter of the tube.

$$R = \frac{8\eta L}{\pi(\frac{D}{2})^4} = \frac{8 \times 10^{-3} \times 0.6}{\pi(0.4 \times 10^{-3})^4} = 5.97 \times 10^{10} Pa.s.m^{-3}$$

The pressure required to push the liquid through the tube is equal to:

$$p = RQ = 5.97 \times 10^{10} \times 1.763 \times 10^{-11} = 1.053\,Pa \simeq 0.01\,mbar$$

Where p [Pa] is the pressure, R [Pa-s-m^{-3}] the fluidic resistance and Q [m^3.s^{-1}] the flow rate.
Using a flow rate of 1.5 mL/day (equal to 1.763x10^{-11} m^3/s) we obtain p = 0.01 mbar, which is negligible. Therefore the total pressure required for injection is equivalent to the hydrostatic pressure, around 30 mbar, which is in the working region of the pump.

The pump also contains pressure sensors that can detect occlusions, in which case a warning message is sent to a smartphone. The patient can be quickly aware of the problem and use temporary methods such as artificial tears from small bottles until the occlusion is removed. With the tubing design described in section 4b, any occlusion in the subcutaneous tube can be removed using a syringe, which contains saline solution. The syringe can be directly connected to the tube in order to flush the tubing and remove any occlusion.

An adaptation of this pump to tear injection can be imagined since it is less critical than insulin injection. A refillable reservoir would be of great interest since the battery can last 6 days and the current reservoir of JewelPUMP provides tears for up to three days.

There are multiple options that can be considered regarding the pump. An option is to use a Y-shaped tubing, delivering tears to both eyes, which would be connected to a single Nanopump. The problem with this option is that fluid chooses the path with less resistance. As a result it would be very difficult to deliver the same flow to both eyes. Another alternative would be to have one device containing two separate Nanopumps. There would only be one reservoir and each MEMS Nanopump in the device could be independently programmed in order to be adapted to each eye's tubing system. Therefore any change in fluidic resistance can be overcome by changing the flow rate. If modification of the pump is not possible, then each eye would be connected to an individual JewelPUMP.

5) Modelisation of the ocular tube end

In order to deliver homogeneously artificial tears to the eye surface, the ocular terminal of the catheter has three holes at a distance of 0.40mm from each other.
If the diameter of these three holes is the same, a major part of the inlet flow will exit in the first outlet, resulting in a reduction of the flow through the last holes. Since an uneven flow will reduce the quality of eye hydration and a low flow, in the more distal holes, might increase the risk of obstruction, a solution could be to increase the diameter of the holes.

a. Numerical methods

In order to test the feasibility of our approach, we used the software "COMSOL Multiphysics 4.1" to simulate the flow rate through each outlet of the tube and define their respective diameter.
COMSOL Multiphysics is a simulation package specifically aimed to couple Finite Element Methods (FEM), a numerical technique for finding approximate solutions of partial differential equations (PDE) as well as of integral equations. PDE are first approximated with a system of ordinary differential equations, and then they are numerically integrated.

b. System description

The purpose of the simulation is to determine the fluid flow delivery of an artificial lachrymal apparatus.

The **3D** graphical user interface is used to modeling the 3 dimensional flow through the tube.
Furthermore, laminar flow physic has the equations, boundary conditions, and volume forces for modeling freely moving fluids using the Navier-Stokes equations, solving for the velocity field and the pressure. So due to its fluid properties, we use **"Laminar Flow" physics** interface for our model simulation.
The 3D FEM analysis for the flow is done using the **stationary solve**r because of the steady-state condition in our model (all constraints are constant). The various physics interfaces of COMSOL provide different default settings depending on the study type so we decided to keep the default settings of the stationary solver to use a suitable solver and its associated solver parameters.

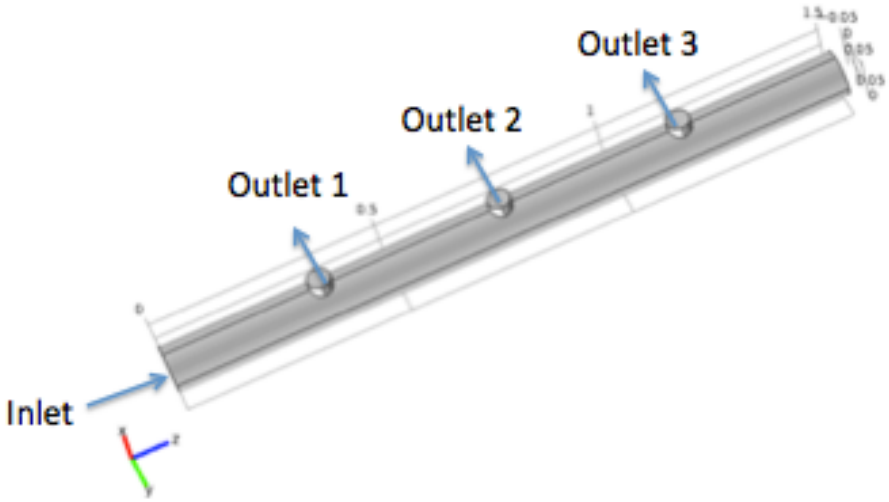

Fig 16 : Tube model used for the simulation

Geometry

The model is constituted of a 0.8 mm diameter cylinder with 3 holes.
The diameter of this cylinder corresponds to the internal diameter of the catheter used to the delivery of the artificial tears.

Parameters:
R = 0.4 mm, the radius of the tube
R1 the radius of the outlet 1
R2 the radius of the outlet 2
R3 the radius of the outlet 3
L = 1.5 cm, the length of the tube

The geometry of the model presents an axial symmetry; so half of the cylinder can be removed if a symmetry condition is defined on the half cylinder surface.

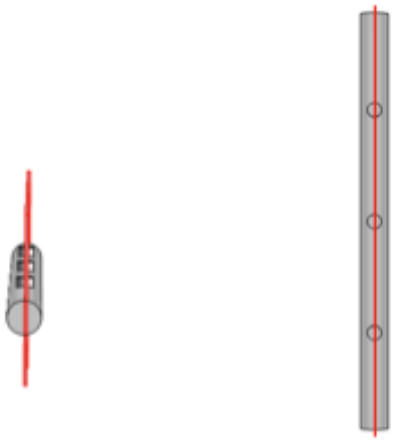

Fig 17 : Symmetrical plane

This simplification will result in a more precise model and a decrease of the calculation time during the simulation.

Model Implementation

Due to the relatively small difference between the inlet and outlet flow conditions of the fluid and its constant density, the fow of the fluid is considered as incompressible. Fluid is assumed to be water with a constant density ρ = 103 kg/m3 and viscosity η = 10−3 Pa·s; gravity effects are neglected.

Boundary conditions are imposed at the inlet and outlet boundaries:

- Inlet boundary condition: Flow rate Q = 1.5 ml/day
- Outlet boundaries conditions:
    - The flow rate should be the same through the three outlet holes
    - External atmospheric pressure P_0 = 1 atm
    - No viscous stress

To solve the incompressible fluid dynamics of our transient and steady state model, the incompressible Navier-Stokes interface of COMSOl is used.

Mesh

For 3D geometric model, the mesh generator discretizes the domains into tetrahedral, hexahedral, prism, or pyramid mesh elements. The boundaries in the geometry are discretized into triangular or quadrilateral boundary elements.

A **physics-controlled meshing sequence** is used during the simulation because it generates automatically the mesh elements and boundaries that fit the best to the tube model. Indeed, it examines the physics and automatically determines size attributes and sequence operations needed to create a mesh adapted to the problem of laminar flow.

To determine the mesh size, it is important to keep in mind that the mesh has to represent correctly the gradients and deformations of the model. Therefore a refining of the mesh density can be resolved to compare results between an extra fine mesh and a coarser mesh, just to ensure that there are less than 5% changes. Too many changes indicate a too coarse mesh so a refining is necessary.

For the tube model, the simulation is performed with a **normal mesh**. Indeed, results are similar (difference less that 0.5%) between an extremely fine mesh and a normal mesh simulation. So the normal mesh density is sufficient for the study of the flow through the tube.

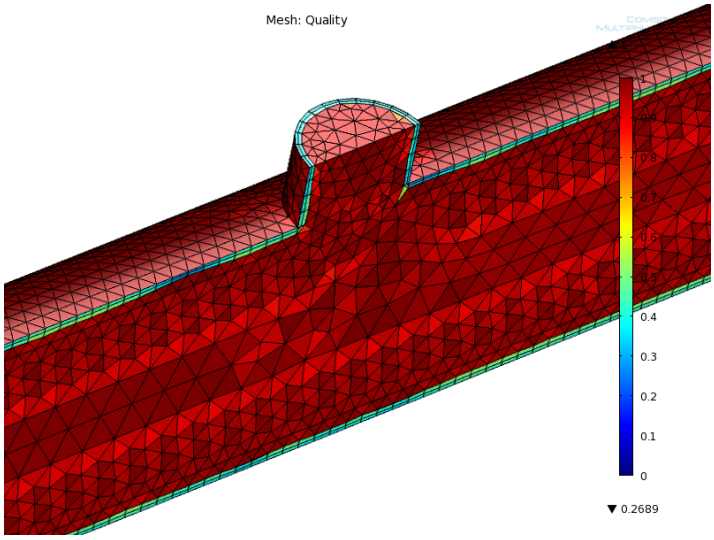

Fig 18 : Mesh

c. Results

The first simulation is done with a tube made of three outlets of same diameter, defined as R1 = R2 = R3 = 0.20 mm.

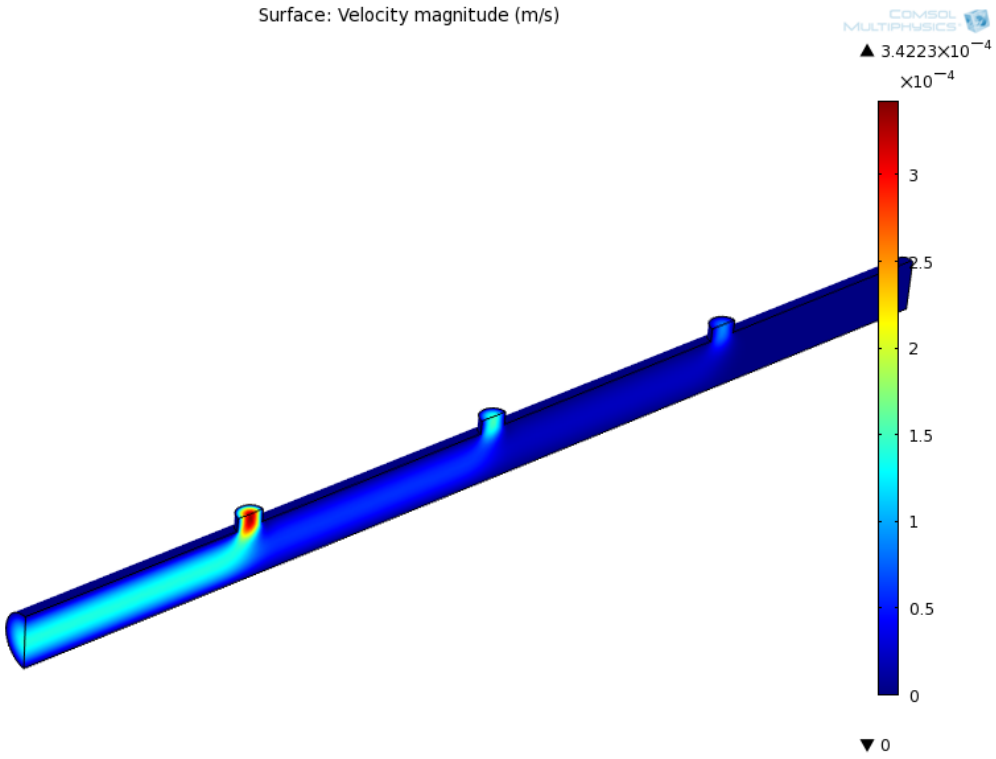

Fig 19 : Model simulation with constant diameter

As shown in Fig.19, the maximum velocity magnitude of the flow in outlet 1 is around 3.3×10^{-4} m/s while it is less than 8×10^{-5} m/s in outlet 3. As expected, the flow rate (Q) of the fluid through the different outlets 1, 2 and 3 is also completely different:

- Flow rate through outlet 1 = Q1 = 0.806 ml/day
- Q2 = 0.39 ml/day
- Q3 = 0.22 ml/day

Thus, more than half of the inlet flow (Q=1.5ml/day) exits through the first outlet. Then, Outlet 3 receives less than 15% of the inlet flow, leading to a higher risk of obstruction.
The design of a tube with increasing diameters outlets is a good approach to equalize the flow rate. The inlet flow is around 1.5 ml/day; so considering that the tube is constituted of three holes, the desired flow rate through each hole must be around 0.5ml/day.
By varying the diameter of the outlets independently until the desired results of 0.5ml/day, the simulation has allowed to find how to increase the rays.

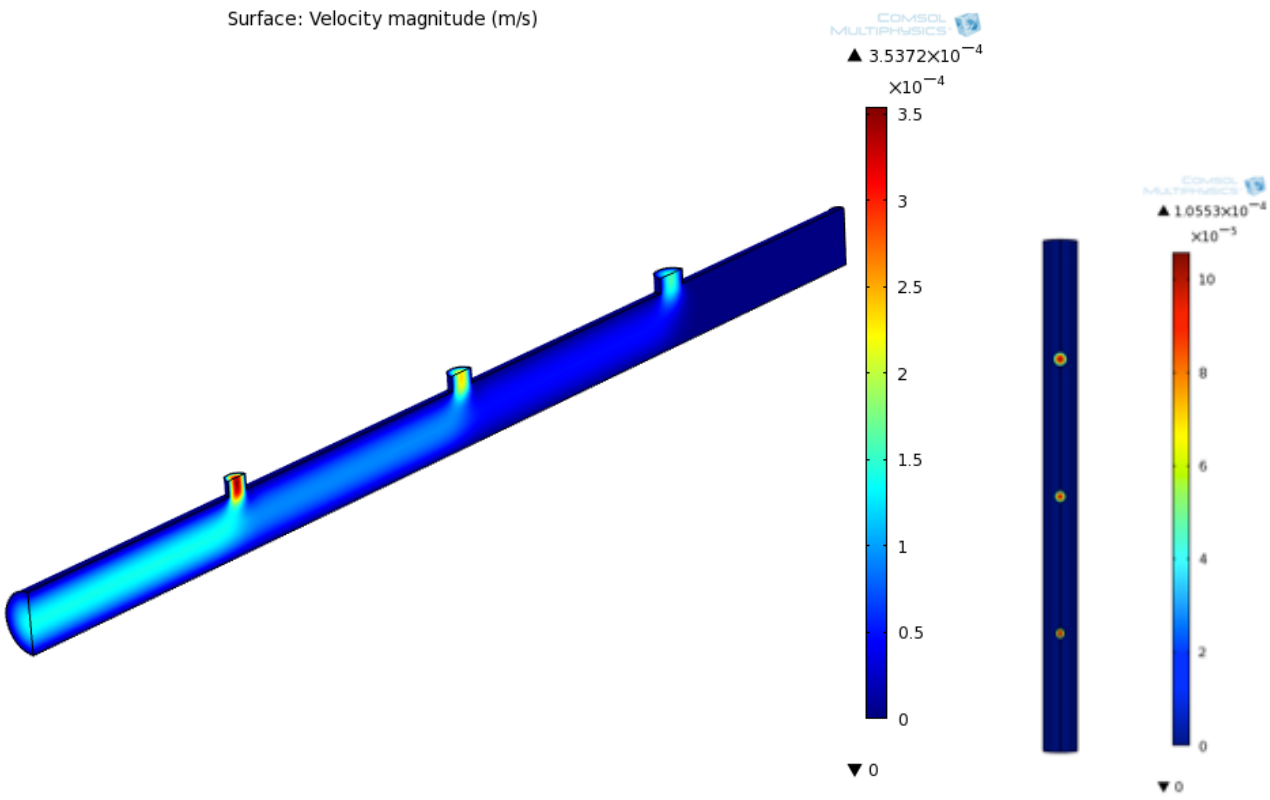

Fig 20 : Model simulation for constant flow

The simulation with COMSOL allows us to find the radius of each hole of the catheter, in order to have a continuous flow at each outlet and a uniform tear delivery to the ocular surface:

- **R1 = 0.15mm**
- **R2 = 0.18mm**
- **R3 = 0.22mm**

The obtained outlet flow rates in simulation are all around 0.5ml/day as desired:

- Q1 = 0.487 ml/day
- Q2 = 0.479 ml/day
- Q3 = 0.499 ml/day

d. Validation of the model

Fisrt, the inlet flow rate calculated by the simulation is Q = 1.5ml/day, which corresponds exactly to the defined theoretical boundary condition and to the physiological need of the patients.
Furthermore, by adding the three outlet flow rates together, the result of the simulation is close to the theory: Q1 + Q2 + Q3 = 1.465 ml/day ≅ 1.5 ml/day.

Then, by comparing the simulation of the model with and without symmetry, we see that the symmetrization of the problem is efficient. Indeed, the solution time for the symmetrical model is lower: with our computer, the computation time is 410 sec for the model with symmetry instead of 454sec for the model without. Furthermore, with a normal mesh, although the model without symmetry has a surface twice larger than the model with symmetry, the number of degrees of freedom solved decreases only from 250957 to 232993. So the mesh is finer for the symmetrical model.

6) Advantages and limitations

The main advantage of this device is that the surgical implantation procedure is minimally invasive compared to other techniques already existing to treat severe dry eyes, for example the subcutaneous abdominal pump-reservoir developed by Juan Murube [2][3]. Indeed, only two small incisions are required to insert the tube between the eye and the ear. However, similar cares need to be taken during the procedure to avoid facial nerves and subcutaneous blood vessels.

The replacement of the pump and reservoir every 2-3 days prevents complications and allows an easy access to the device if needed. The infection problems in the tube, as well as tissue ingrowth and mucus plugging are minimized because the external tube is disposable and the subcutaneous tube can be cleaned. If required, the patient can disconnect the external tube behind the ear and inject a saline solution enriched with lysozymes and bactericides using a syringe.

The design is relatively discreet: the dimensions of the subcutaneous tube allow it to be invisible under the skin and the external tube can be easily hidden behind the hair and the clothes. This is an advantage compared to other designs that could include for instance a behind-the-ear pump.

The risk of infection and fibrosis in the transcutaneous region are the main problems of this approach. Indeed, the contact of the soft tissue with solid silicone tube induces stress that causes cellular damage at the interface. This favours immunological reactions associated to inflammation and recruitment of macrophages that can be anchored to the silicone surface. To prevent that kind of problem, the entry site must be optimized and the interface should be carefully cleaned and disinfected on a regular basis.

Another limitation of this design is the discomfort that could occur during the night. Indeed, the behind-the-ear transcutaneous region as well as the adhesive pump on the arm could disturb the patients while sleeping. However, this is not a major issue since the patient can easily get used to sleeping in an appropriate position.

7) Future improvements

A sensor could be added at the end of the tube to measure in real time the quantity of tears in the eye. The information can be sent to the pump to continuously adjust the flux. The sensing can be done indirectly, for example by measuring the impedance of the liquid covering the eye, which will depend on the non-water components concentration in tears. This concentration is inversely proportional to the quantity of tears. This sensor has to be very small and cause as little discomfort as possible to stay in the eye permanently.

The other major improvement would be to find a way to minimize friction at the interface between the skin and the silicone tube. This would avoid cellular damage and minimize inflammation. Another way would be to find a material that is much smoother, to prevent microbial development in niches created by microfissures and other irregularities.

Conclusion

So far, current treatments against severe dry eyes have failed to provide satisfactory results. The artificial tears delivery device described here is a very promising solution. The device has high therapeutic potential and would significantly improve the quality of life of the patients on a long-term basis with high benefits compared to risks. Indeed, the system overcomes many issues encountered by people suffering from severe dry eyes and is a minimally invasive, convenient and discreet device. Commercialization of the device would require further investigation and optimisation, especially regarding the transcutaneous part, which is the critical aspect of this design [19][20]. As long as a tissue engineering approach to replace damaged lacrimal glands is not fully developed, this device may be the best solution to treat the symptoms of the dry eyes syndrome.

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