

## Shear stress during embryo transfer

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### ABSTRACT

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**Purpose:** This study was designed to analyze the influence of injection speed on the shear stress acting on the embryo during the ejection phase of embryo transfer.

**Methods:** Computational fluid dynamics was applied to calculate shear stress for the following injection speeds: 0.01, 0.1, 1, 6, 12 and 20 m/s. A 3D geometrical model of the flow domain was created in ANSYS Modeler. The computations were carried out using the CFD code Parallel ANSYS Fluent 12.1 with the segregated solver SIMPLE (Semi-Implicit Method for Pressure-Linked Equations). The model was solved in double precision on a control volume unstructured 3D mesh made in ANSYS Mesher.

**Results:** The results of the present study indicate that shear stress increases with the rise of the injection speed. Furthermore, shear stress is lower when the embryo is positioned in the midstream of the catheter instead of in proximity to the catheter's wall.

**Conclusions:** Taking these results into consideration, it is advised to transfer embryos with minimal injection speed because the strength of shear stress increases with the injection speed of the transferred load.

**Key words:** Catheter, embryo, embryo transfer, fluid velocity, shear stress.

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## INTRODUCTION

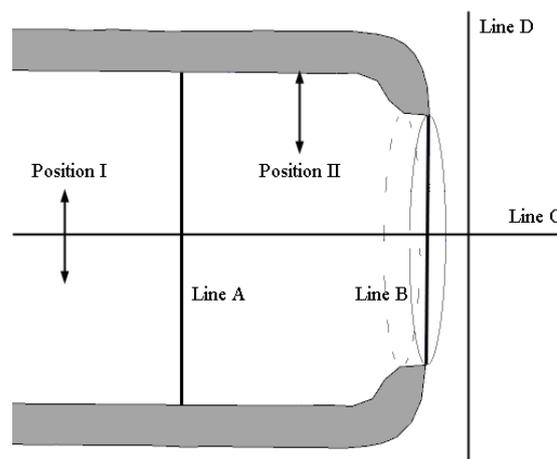
Embryo transfer (ET) is a major element of the in-vitro fertilization process. During ET, a newly formed embryo is placed within the uterus by means of a catheter. Successful ET includes one, a smooth and atraumatic passage of the ET catheter through the cervix, and two, the deposition of embryos to a site in the endometrial cavity where the chance of implantation is greatest [1-4]. Apart from embryo quality and operator experience, the properties of the ET catheter are the most important for successful ET. The fact that high rates of fertilization in the laboratory result in a relatively low rate of take-home babies has led investigators to blame various features of the ET procedure [1-4]. So far, little attention has been placed on the physical forces acting upon the embryo in the process of embryo transfer. Therefore, for this study, we have analyzed the shear stress acting on embryo during the injection phase of ET. At the end of this report, we discuss the possible impact of the shear stress on embryo viability.

## MATERIAL AND METHODS

A numerical approach using computational fluid dynamics (CFD) was implemented during the present study.

To complete the experimental approach presented in a previous article [5], a numerical model of the ET catheter ending and a model of the uterus were studied during the injection phase of ET. The entire period of injection lasted for 0.02s. Water, being a model of the medium of embryo culture, was injected at a time interval of 0.01s at a linear rising rate into the uterus model, which contained glycerin at rest. The water flow rate was then reduced to zero. The diameter of the inner compartment of the catheter used for the experiments and simulations was 0.4 mm. The tip narrowing was assumed to be 20% of the diameter of the inner compartment. Embryo culture medium properties were assumed to be those of liquid water, (density  $\rho=998.2 \text{ kg/m}^3$  and dynamic viscosity  $\mu=0.001003 \text{ kg/(m}\cdot\text{s)}$ ). In order to mimic the viscous uterine fluid, the uterus model was filled with glycerin of density  $\rho=1236.25 \text{ kg/m}^3$  and dynamic viscosity  $\mu=0.799 \text{ kg/(m}\cdot\text{s)}$ , which has similar density as that of the uterine fluid [6]. A 3D geometrical model of the flow domain was created using ANSYS DesignModeler.

The shear stress was computed for positions I and II (see Fig. 1). Calculations were performed for the following mean velocities: 0.01, 0.1, 1, 6, 12, and 20 m/s.



**Figure 1.** The cross-section of the embryo transfer catheter tip.

The flow was assumed to be transient, incompressible, and turbulent, as described by the Reynolds-averaged Navier-Stokes equations (RANS) with the SST  $k-\omega$  turbulence model. The computations were carried out using the CFD code of Parallel ANSYS Fluent 12.1 with the segregated solver SIMPLE (Semi-Implicit Method for Pressure-Linked Equations). The model was solved in double precision on a control volume, unstructured, 3D mesh of 3,961,001 control volumes made using ANSYS Meshing.

The study was approved by the local ethics committee.

## RESULTS

The results of the present study indicate that shear stress acting on the embryo during the ejection phase of embryo transfer is lower when the embryo is positioned in the midstream of the catheter instead of in proximity to the catheter's wall. Furthermore, the shear stress increases with the rise of injection speed independently from the position of the embryo inside the catheter.

With an injection velocity of 0.01 m/s at the level of line A, the shear stress acting on the embryo in position I (0.1 Pa) was lower than in position II (0.2 Pa). With an injection velocity of 0.1 m/s at the level of line A, the shear stress acting on the embryo in position I was 1 Pa, while in position II it was 2 Pa. With an injection velocity of 1 m/s at the level of line A, the shear stress acting on the embryo in position I (7 Pa) was more than 3 times lower than in position II (23.5 Pa). With an injection velocity of 6 m/s at the level of line A, the shear stress acting on the embryo in position I (11 Pa) was approximately 20 times lower than in position II (210 Pa). With an injection velocity of 12 m/s at the level of line A, the shear stress

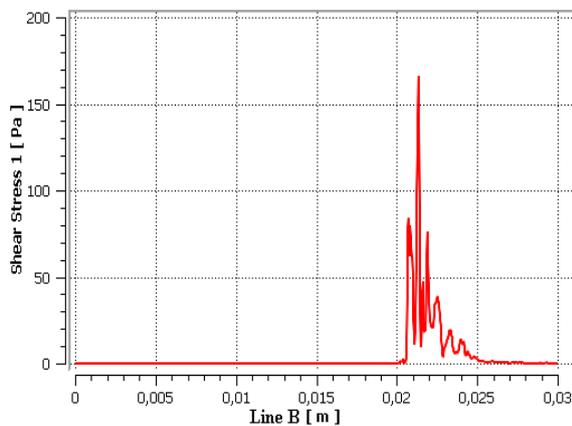
**Table 1.**Relation between average fluid velocity and pressure at point A and B of embryo transfer catheter (Figure 1).

Injection speed [m/s]	0.01	0.1	1	6	12	20
Shear stress difference at position I [Pa]	0.104	1.05	7.27	11.05	8.9	31.8
Shear stress difference at position II [Pa]	0.204	2.06	23.47	209.9	557.5	1640

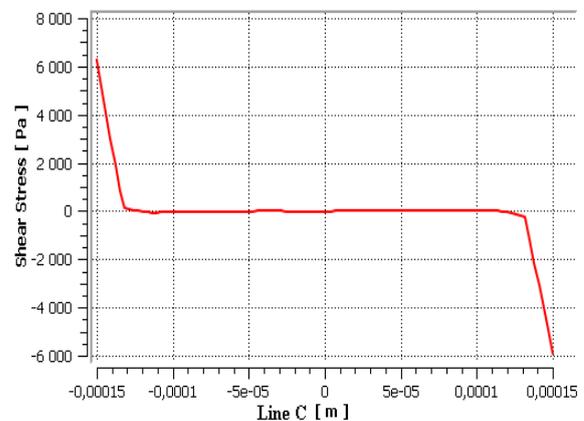
acting on the embryo in position I (8.9 Pa) was approximately 60 times lower than in position II (557.5 Pa). Finally, with an injection velocity of 20 m/s at the level of line A, the shear stress acting on the embryo in position I (32 Pa) was approximately 50 times lower than in position II (1640 Pa).

Table 1 presents detailed data on shear stress for the particular injection velocities.

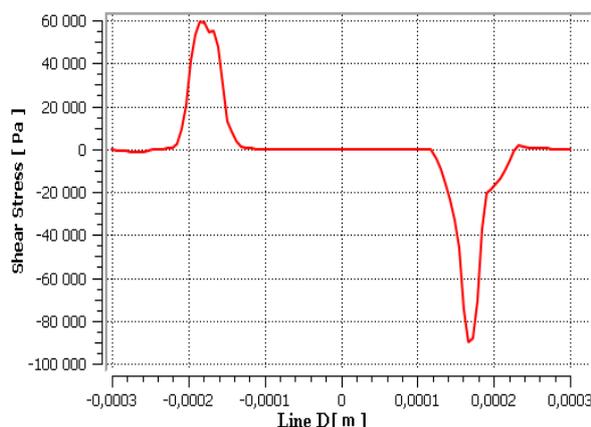
Figures 2, 3, and 4 present the shear stress at the level of the catheter outlet, outside the catheter outlet, and along the central line of the catheter, respectively.



**Figure 2.** Shear stress at the level of the catheter outlet (line B, Fig.1) for the ejection speed of 12 m/s.



**Figure 4.** Shear stress along the central line of the catheter (line C, Fig.1).



**Figure 3.** Shear stress 0.04 mm from the catheter outlet (line D, Fig.1).

## DISCUSSION

The aim of this study was to investigate the influence of the ejection speed of the transferred load on the shear stress acting on embryo during ET. The results of the present study indicate that shear stress increases with the rise of the injection speed. Furthermore, the shear stress is lower when embryo is positioned in the midstream of the catheter than in proximity to the catheter's wall.

According to the concept of the fluid flow inside a tube with a circular cross-section, the fluid in the central region moves faster than in the peripheral region of the catheter lumen. The fluid flow velocity gradient exerts shear stress on any object placed inside the fluid. Based on the results of the present study, it is evident that the embryo positioned in proximity to the catheter wall is exposed to higher shear stress than one that stays in the midstream, where fluid flow velocity gradient and shear stress is lower. The strength of the shear stress increases with the injection speed of the

transferred fluid. With high enough injection speeds, the shear stress can be strong enough to injure the vital cell's organs and impair embryo viability. In the literature, there are some evidences for cell damage caused by local pressure fluctuations. Key and coworkers noticed that a pressure gradient, not exposure duration determined the extent of the epithelial cell damage in a model of pulmonary airway reopening [7]. Furthermore, Bilek et al investigated surface-tension-induced lung epithelial cell damage in a model of airway reopening and they concluded that the steep pressure gradient near the bubble front was the most likely cause of the observed cellular damage [1]. An abrupt pressure fluctuation in the cell environment may influence many vital aspects of the cell anatomy and physiology. For example, the cell membrane of the pulmonary epithelial cells could be disrupted by the steep pressure gradient appearing during airway reopening [1, 7]. Furthermore, cytoskeletal damage *in vitro* was demonstrated after the impact of 16 MPa (120 000 mmHg) on a human renal carcinoma cell line [8]. It was also demonstrated that the high pressure could inactivate intracellular enzymes [9, 10]. It is certain that positive pressure does not actually cause damage to the cells but the steep increase in pressure (compression), followed by negative pressure (decompression), does cause damage since biological structures can only be damaged by shear or extension and not by positive pressure [11, 12].

It is very easily to achieve high shear stress in the transferred volume during ET with the standard syringe–catheter complex. The main reason is that the plunger of the insulin syringe has a diameter of 4.75 mm with a corresponding surface of 17.34 mm<sup>2</sup> while the diameter of an inside of the catheter used for the experiments has a diameter of 0.4 mm with a corresponding surface of 0.125 mm<sup>2</sup>. It is easy to note that the diameter of the syringe is up to 10 times higher than that of the catheter. This means that the movement of the plunger during the ejection steps, causes an important increase of the speed of the transferred fluid which is related with both the pressure applied on the plunger and the difference between the internal diameters of the syringe and of the catheter. The immediate consequence of those data is that when insulin syringe plunger moves by 1 mm, it transports about 140 times more volume of medium than catheter. Therefore, the catheter connected to the syringe can determine a speed of the transferred fluid very high.

## CONCLUSIONS

Taking these results into consideration, it is advised to transfer embryos with minimal injection speed because the strength of shear stress increases with the injection speed of the transferred load.

## Conflicts of interest

The authors have declared no conflicts of interest.

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