Patient-Specific Bile Flow Simulation to Evaluate Cholecystectomy Outcome

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Abstract. Gallbladder disease has one of the leading positions by patients’ number in the World. About 16% of the adult population is suffering now from this disease. Cholecystectomy is believed to be a general surgical method of the gallbladder disease treatment, but the success rate is quite low because the surgeons do not take into account the patient-specific features during the treatment and cannot predict operation results. The main purpose of the paper is to create a computational tool for numerical evaluation of cholecystectomy outcome compared with healthy state and current pathological state based on the patient-specific patients’ data. The patient-specific features of the biliary tree were studied by 1-way FSI bile flow simulation. The extra-hepatic biliary tree geometries were extracted from MRI and after that imported to ANSYS CFX for the subsequent fluid dynamics analysis. It was revealed that in the pathology state, velocities were found to have lower magnitude while the pressures were higher. The patient-specific features have a dramatic influence on the bile flow patterns. Cholecystectomy leads to the decrease of bile flow rate in the extra-hepatic biliary tree. The proposed computational approach can be applied to medical practice to evaluate the circumstances of surgical interventions.

1. Introduction
Personalized medicine, taking into account the individual approach to the treatment of a particular patient, has considerable potential for improving the quality and effectiveness of medical care. The development of non-invasive diagnostic methods, modern mathematical and computer models allows us to describe the biomechanical processes occurring in the body with an increasing degree of accuracy. This circumstance increases the possibility of their use in improving existing and developing new personalized methods for diagnosing and predicting treatment.

In Russia, about 25 million people suffer from cholelithiasis and diseases of the biliary tract [1]. Gallstone disease is a multifactorial and multi-stage disease associated with the formation of stones in the gallbladder and / or biliary tract. The pathology of the biliary system is in third place in the World in the number of patients after cardiovascular diseases and cancer [2]. The presence of stones in the biliary tract and gallbladder can lead to various complications, ranging from inflammation of the ducts, ending with a fatal outcome due to malignant tumors of the biliary system [3].

For the treatment of patients with cholelithiasis, surgical removal of the gallbladder is usually used (cholecystectomy). There are about 2 million cholecystectomies (operations to remove the gallbladder) per year, including 320 thousand in Russia [4]. However, in 15% of cases, the results of this operation lead to postoperative complications [5,6]. One of the reasons is the use of subjective experience and the insufficient number of individualized biomechanical models for the analysis of surgical interventions [7]. It should be noted that there are few works on biomechanical modeling of the functioning of the biliary system in normal and pathological conditions [8].

Compliance of soft tissues walls plays a crucial role in the biofluids transport. In particular, the motor function alterations of the extra-hepatic ducts have an influence on the bile flow. Fluid flow in the elastic
and compliant vessels can be described by various models (for example, Windkessel model, peristaltic flow model, fluid–structure interaction, Navier–Stokes equations, e.t.c.).

**Study of the bile flow in the cystic duct**

The cystic duct geometry effect on the flow resistance with using of 2D- and 3D-models of bile flow was studied in paper [9]. The cystic duct was represented in the form of a straight pipe with baffles. Bile was assumed to be Newtonian, a fluid with a viscosity in the range of 1–4 mPa·s. Further, the results were compared with a more realistic two-dimensional model obtained as a result of processing the patient's cholangiogram. It was found that both the height and the number of baffles have a dramatic effect on the flow resistance. According to calculations, the channel geometry has a greater effect on the distribution of velocities and pressures in the duct than the change in viscosity.

Ooi et al. [9] and Al-Altabi, et al. [10, 11] conducted a series of experimental studies with a uniform arrangement of partitions. In experiments, the Reynolds number is Re > 50, which is significantly higher than in the human biliary system (Re~10). Thus, only qualitative comparisons between experiment and numerical simulation are currently available. However, for large Reynolds numbers, a good quantitative agreement between numerical results and experimental measurements was obtained by Al-Altabi et al. [12–14]. In these studies, the cystic duct was considered as a separate channel with rigid walls. Li et al. [15] constructed two one-dimensional T-shaped models of the cystic duct, common hepatic and common bile duct with rigid and elastic walls. The phases of emptying and filling were considered. Using the developed one-dimensional model, the effect of geometry, the elasticity of the wall of the cystic duct, the flow rate and viscosity of bile on the pressure gradient was studied in detail. It was found that many factors, including the elastic modulus and bile viscosity, can influence the pressure gradient. However, the influence of changes in the geometry of the cystic duct was still dominant. It was found that the number of baffles has a significant effect, because it causes large changes of the channel equivalent diameter. The pressure gradient also increases with a decrease in the Young's modulus of the cystic duct during emptying.

A series of works [7, 16–18] was devoted to aspects of the flow of bile in the cystic duct during pathology (presence of a stone, narrowing of the ductal lumen). Bile was considered as a non-Newtonian fluid (Herschel–Bulkley model) by analogy with [19].

Al-Altabi et al. [20] presented an individualized model of the flow of bile in the cystic duct. Bile was considered a Newtonian fluid. The geometry was formed from plastic castings of real cystic ducts, surgically removed from patients and scanned using Model Maker W (3D Scanners, UK) to create three-dimensional geometric profiles. Simulations were performed to obtain quantitative indications for comparison with clinical measurements. The results showed that the dimensionless pressure gradient in the cystic duct is 4 times higher than in a straight round tube of equivalent length and average diameter.

**Study of the flow of bile in the common bile duct**

Mai and Misra [21] presented a model of peristaltic flow in a porous channel to study the influence of various factors (critical pressure, porosity parameter and bile velocity) on reflux. It was found that with the presence of gallstones, the rate of bile increases as the porosity parameter increases, and the critical pressure for reflux decreases as the porosity increases. A mathematical model of the pathological flow of bile as a Casson fluid in a channel with a stone was presented in paper [22]. A bile velocity profile versus time was obtained depending on the size of the lumen. In addition, the dependence of the pressure in the duct on the size of the stone was obtained. The created mathematical model allowed us to estimate the dynamics of the postoperative period and to predict the development of specific complications based on the values of bile pressures. Information about the size of the stone, obtained using cholangiography or ultrasound, makes it possible to calculate the daily consumption of bile entering the duodenum.

**Construction of three-dimensional individualized geometry of the bile ducts**

It should be noted that in the majority of works on modeling the flow of bile, only the movement of biofluid in individual segments was considered, and the complete flow model was not taken into account. Some attempts to examine the flow in the complete biliary system were made in [23, 24], but they did not take into account the individualized geometry of the ducts, their ductility, the influence of the gallbladder, and the peristalsis of the sphincter of Oddi. The first papers [25, 26] on the construction of individualized geometry were published in 2013.
Summary
Based on the above, when analyzing the numerical and mathematical modeling of the flow of bile in the biliary system, it was noted that only the individual elements of the biliary system were considered, and the entire system was not considered completely. The main segments in the simulation of the flow of bile were the cystic and common bile ducts. In this paper we present patient-specific modeling of bile flow to analyze bile flow in the healthy state, pathology, and cholecystectomy.

2. Materials and Methods

2.1. Image acquisition
MRI data of 14 patients were obtained using 1.5T Siemens scanner. The in-plane spatial resolution was 0.5 m. ITK-Snap open source software was used to create 3D models of extra-hepatic ducts for subsequent simulations.

2.2. Problem formulation
Mass and momentum conservation equations for an incompressible fluid can be expressed as

\[ \nabla \cdot u = 0, \]  
(1)

\[ \rho_f \left( \frac{\partial u}{\partial t} + (u - u_g) \cdot \nabla u \right) = -\nabla p + \nabla \cdot \tau \]  
(2)

where \( \rho_f \) is the fluid density, \( p \) is the pressure, \( u \) is the fluid velocity vector and \( u_g \) is the moving coordinate velocity. In the ALE formulation, \( (u - u_g) \) is the relative velocity of the fluid with respect to the moving coordinate velocity. Here \( \tau \) is the deviatoric stress tensor. This tensor is related to the strain rate tensor; if the fluid is incompressible and viscosity is constant across the fluid, this equation can be written in terms of an arbitrary coordinate system as

\[ \tau_{ij} = \mu \left( \frac{\partial v_i}{\partial x_j} + \frac{\partial v_j}{\partial x_i} \right), \]  
(3)

where \( x_i \) is the \( i \)-th spatial coordinate, \( v_i \) is the fluid's velocity in the direction of axis \( i \), \( \tau_{ij} \) is the \( j \)-th component of the stress acting on the faces of the fluid element perpendicular to axis \( i \). In the case of pure shear this relation reduces to

\[ \tau = \eta \gamma. \]  
(4)

For a healthy bile, which is considered as Newtonian fluid \( (\eta=0.001 \text{ Pa}\cdot\text{s}) \) [9]

\[ \eta = \text{const.} \]  
(5)

The Carreau’s equation, which is used for simulation of lithogenic bile, is written as follows

\[ \eta = \frac{\eta_0 - \eta_\infty}{(1 + (\gamma \cdot \tau)^\beta)} + \eta_\infty. \]  
(6)

The parameters of the Carreau’s equation were taken from [24]. The momentum conservation equation for solid body can be written as follows

\[ \nabla \cdot \sigma_s = \rho_s \dot{\epsilon}. \]  
(7)

where \( \rho_s \), \( \sigma_s \), and \( \dot{\epsilon} \) are solid density, solid tensor, and local acceleration of the solid, respectively.

It is known that blood vessels can be described as hyperelastic material [27]. Due to similar anatomical composition, the bile ducts can be also considered as hyperelastic materials. For hyperelastic materials, the stress-strain relation is written as follows

3
\[ \sigma_s = \frac{\partial W}{\partial \epsilon} \] (8)

The Mooney-Rivlin hyperelastic potential is taken in the form

\[ W = c_{10} \left[ I_1 - 3 \right] + c_{01} \left[ I_2 - 3 \right] + \frac{1}{d} \left[ J - 1 \right]^2, \] (9)

The FSI interface conditions are written as follows. At first, it is necessary that displacements of the fluid and solid domain must be compatible:

\[ \delta_s = \delta_f, \]

secondly, the tractions at this boundary must be at equilibrium:

\[ \sigma_s \cdot \hat{n}_s = \sigma_f \cdot \hat{n}_f, \]

and at the last, the no-slip condition for the fluid is

\[ u = u_s, \]

where \( \delta, \sigma \) and \( \hat{n} \) are, respectively, displacement, stress tensor and boundary normal with the subscripts ‘f’ and ‘s’ indicating a property of the fluid and solid, respectively.

Boundary conditions are shown in figure 1. Boundary conditions correspond to emptying phase. During the gallbladder emptying, the bile comes out from the gallbladder and the liver at the same time. Bile pressures and initial velocity were applied to inlets and outlet. Following Howard et al. [28], who measured the mean flow rate of the bile from the gallbladder (2.0–3.0 ml/min) after meal, we recomputed it as the boundary condition as 3 mm/s. Pressure in the outlet was taken equal to the pressure in the duodenum (0.96 kPa [29]).

2.3. Mesh and numerical procedure

Fluid mesh consisted of 120869 nodes and 609969 elements. Solid mesh consisted of 78830 nodes and 78660 elements.

![Figure 1. Boundary conditions.](image)

One-way FSI (fluid–structure interaction) algorithm was adopted. The FSI simulation was performed using ANSYS Workbench 13.0 (ANSYS, Inc., Canonsburg, PA, USA). The two solvers (ANSYS Mechanical and ANSYS CFX) were coupled and solved iteratively within each time step until the specified maximum residual is reached. The convergence criterion for the fluid solver and the solid
solver were $10^{-4}$ and $10^{-3}$, respectively. Within one-time step of the FSI simulation, the forces acting on the body were interpolated from the converged solution provided by the fluid solver, and transferred to the solid domain to attain the effect of the acting forces, namely the wall displacement, from the converged solution of the solid solver.

**Figure 2.** Velocity distribution during the gallbladder emptying. (a) healthy bile, (b) lithogenic bile, (c) cholecystectomy, (d) in the case of the stone in the cystic duct.
The displacements at the wall boundary between solid and fluid domain were then interpolated to the fluid domain to generate a deformed fluid mesh. This step closed one inner loop of the FSI simulation and, these steps were repeated until the changes in the flow forces and the structural displacements fell below the convergence criterion.

3. Results and Discussion

The difference between velocity and pressure distributions was examined for four cases in different patient-specific biliary tree geometries. The considered cases were: healthy bile flow (which is considered as Newtonian fluid) and lithogenic bile (which is considered as non-Newtonian Carreau fluid) at the same boundary conditions. Moreover, we tested cases of lithogenic bile flow in the biliary tree with a stone in the cystic duct and flow in the biliary tree after cholecystectomy.

Velocity distribution for lithogenic and healthy bile is shown in figure 2. When gallbladder empties, the bile flows out the gallbladder via cystic duct and common bile duct. At the same time, bile flows out the liver via hepatic ducts and common bile duct. We simulated this physiological phenomena in the model. From figure 2 one can see that the peak of velocity is observed in the distal part of the common bile duct, where bile accelerates to come to the duodenum. It can be noticed also that the geometry of the biliary tree has a dramatic influence on the bile flow character.

![Patient 5](image1)

![Patient 7](image2)

![Patient 11](image3)

Figure 3. Pressure distribution during the gallbladder emptying. (a) healthy bile, (b) lithogenic bile, (c) cholecystectomy, (d) in the case of the stone in the cystic duct.
The pressure distribution for lithogenic and healthy bile flow is shown in figure 3. The pressure values in the case of lithogenic bile flow are higher. The maximum pressure occurs in the gallbladder neck, and it decreases along the cystic duct. In the case of healthy bile flow, the pressure in the common bile duct is equal to approximately 1.1 kPa, which corresponds to the known medical data [30]. The changes in bile viscosity and gallbladder presence play a great role in pressure distribution. The lithogenic bile case shows that pressure values are higher in the case of healthy bile flow because of bile viscosity increase in the case of pathology. The stone presence leads to an increase in pressure values in the extrahepatic biliary tree, which is approved by medical evidence in the paper [31].

4. Conclusion
The effect of bile pathology on the velocity and pressure distributions in the patient-specific extrahepatic biliary tree was investigated by FSI approach. Comparisons were made for healthy and lithogenic bile in terms of fluid flow. There was no significant difference for velocities between the healthy bile and lithogenic bile cases. Thus, bile rheology changes play an important role in the changes of the pressures, which can lead to the gallbladder disease progress. Cholecystectomy leads to the decrease of bile flow rate in the extrahepatic biliary tree. The proposed computational approach can be applied to medical practice to evaluate the circumstances of surgical interventions. The proposed model may help the surgeon to evaluate velocity and pressure distributions to assess the cholecystectomy results for the current patient and compare them to normal values.

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