25th International Congress on Modelling and Simulation, Darwin, NT, Australia, 9 to 14 July 2023
mssanz.org.au/modsim2023

Challenges of developing a digital twin of an in-vitro device that mimics swallowing

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Abstract: Dysphagia is a medical term used to describe difficulty in swallowing food, liquids, or saliva. It can have serious consequences, such as malnutrition, dehydration, and an increased risk of aspiration pneumonia and death. Texture-modified foods (TMFs) and thickened fluids are often utilized as a therapeutic intervention in management of dysphagia, particularly in the elderly population. The Gothenburg Throat (GT) is an in-vitro device that mimics swallowing, providing a risk-free and more economical alternative to in-vivo measurement for testing TMFs and thickener. It is unknown how well this device reproduces the important parts of swallowing, but physics-based simulation may provide insights into this. Here we present the first steps towards building a fully predictive digital twin of the GT device (DT-GT) that could both help evaluate the current design and be used to develop improvements that allow it to increasingly emulate real swallowing.

The development of the DT-GT involves multiple steps. First, a 3D computer aided design (CAD) geometry of the GT was supplied by RISE, Sweden. It includes the device's main pharyngeal channel, which is static, and moving parts including the artificial epiglottis and the syringe plunger that is used to deliver the bolus. Second, each CAD geometry component is converted to boundary surface meshes with regularly spaced nodes. Third, the bolus material is discretised into Smoothed-Particle Hydrodynamics (SPH) particles, which are evenly spaced throughout its volume. SPH is a powerful method capable of simulating large deformation and free surfaces for flow of fluids in complex deforming meshes. It is used to predict the bolus fluid dynamics as it interacts with the GT components. Simulation results are evaluated by comparing bolus transport timing through the device using boluses of varying viscosities.

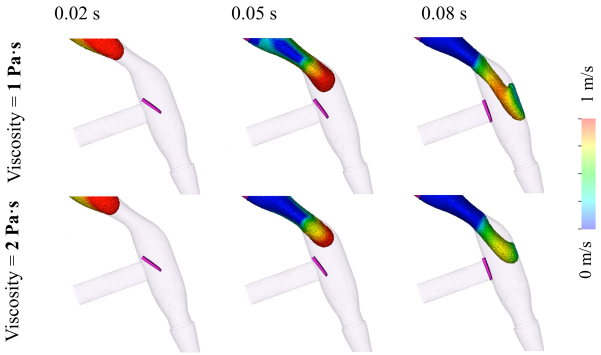

Figure 1. Comparison between the bolus transit profiles predicted by the DT-GT model for two viscosity cases for the first 110 ms. The bolus has been colour-coded to show speed

The DT-GT is used to replicate bolus transit profiles from two swallowing experiments conducted using the in-vitro GT device with varying viscosity of boluses (1 Pa·s and 2 Pa·s). In both simulation cases, the bolus flows at a high-speed (~1 m/s) through the syringe due to the pressure exerted by the plunger motion (Figure 1). Upon entering the pharynx, the front of the 1 Pa·s bolus continues with similar speed until partly adhering to the anterior side of the tube. While in the 2 Pa·s case the bolus slows down considerably following entry into the pharynx and mostly traverses over the posterior side of the tube.

The spatial distribution of the boluses in the DT-GT model matches the experimental results in the early stage but results subsequently deviated with the simulated bolus front failing to remain in contact with the upper pharynx surface for sufficient time. This resulted in substantially shorter transit times in both cases. Select model parameters may contribute to disparities between the model and the experiment. Some were tested using a sensitivity analysis approach. The initial location of the bolus midpoint inside the syringe and the distance to which the plunger is pressed were found to have a role in determining the initial direction of the bolus flow on entrance into the pharynx. Several other identified unknown model parameters, such as the variation in the apparent viscosity of the bolus due to shear-thinning, which can affect the model predictions are also discussed. The learnings highlight the benefit of explicitly incorporating a DT into experiment design to identify and quantify the actions of any mechanism influencing the performance of a device and improve its design outcome and effectiveness. The study also underscores the need for developing a DT in stages with dedicated "unit" experiments to validate the model and provide necessary model inputs.

Keywords: *Swallowing, dysphagia, smoothed-particle hydrodynamics, Gothenburg Throat, digital twin*

1. INTRODUCTION

Swallowing, or deglutition, refers to the coordinated sequence of muscular contractions and relaxations that propel food and liquids from the mouth to the stomach. This is a complex process that involves the interaction of multiple muscles and nerves and occurs in four stages: oral preparatory, oral, pharyngeal, and oesophageal.

Among the different stages, the pharyngeal stage is the most critical as it involves the safe passage of food or liquid through the pharynx, which is shared by the airways to the lungs (McFarland et al., 2016). Impairment in the pharyngeal stage can lead to difficulties with swallowing (dysphagia), which can have serious consequences such as malnutrition, dehydration, increased risk of aspiration pneumonia and an overall reduction in the quality of life. Dysphagia affects a considerable proportion of individuals aged 65 years or older (Nawaz and Tulunay-Ugur, 2018), with estimates ranging from 7% to 13%. Those residing in assisted-living facilities, are particularly susceptible to dysphagia, with up to 50% of the latter group experiencing swallowing difficulties (Logrippo et al., 2017).

Texture-modified foods (TMFs) and thickened fluids are often utilized as a therapeutic intervention in management of dysphagia, particularly in the elderly population (Hadde and Chen, 2021; Munialo et al., 2020). TMFs involve altering the texture and consistency of food to make it easier to swallow, while thickeners are substances that can be added to liquids to increase their viscosity or thickness. Despite recent progress in characterizing the rheological properties of TMFs and thickeners, there is still limited research on optimal material properties and swallowing safety of these foods. A major challenge in developing new TMFs and thickeners is the difficulty and risk associated with conducting experiments on people using invasive methods such as X-ray or manometry.

Mackley et al. (2013) and Noh et al. (2011) assert that in-vitro devices which mimic swallowing provide a risk-free and more economical alternative for testing TMFs and thickeners than in-vivo approaches. Numerical simulation of swallowing can be used as another predictive tool that allows for precise control of organ movements and food bolus properties (Ho et al., 2017; Kamiya et al., 2019; Kikuchi et al., 2015; Michiwaki et al., 2018). Qazi et al. (2019) and Stading et al. (2019) developed such an in-vitro device called ‘Gothenburg Throat’ (GT) to examine the role of rheology in swallowing and to simulate the different swallowing malfunctions. Development of a digital twin of the GT is intended to help assess the performance of the existing design and identify/inform areas where improvements can be made.

The main benefits of developing the digital twin of GT (DT-GT) are two-fold. DT-GT can (1) enable detailed simulation of bolus transport experiments with different rheological properties of the bolus in a short time frame, the results of which can be used to design further experiments involving the GT; and (2) be used to examine the effects of different device settings on the bolus flow that cannot be easily assessed in the in-vitro devices. A digital twin could be similarly constructed for the real throat and comparisons with the DT-GT can be used to assess the realism of the GT experiments. Such models can then aid in verifying that the GT accurately replicates the diverse range of in-vivo conditions and muscular movements associated with bolus swallowing and dysphagia in the general population.

2. GOTHENBURG THROAT IN-VITRO DEVICE

Figure 2A shows a schematic diagram of the in-vitro GT (Stading et al., 2019). It employs a programmable syringe to simulate the oral phase of swallowing by delivering a fixed volume bolus at a fixed speed, mimicking the tongue and gum thrusting actions. The bolus is delivered into an elliptical pharynx region with a length of 6.3 cm and width of 2.8-3.0 cm. To prevent bolus flow by gravity during syringe filling, a slide valve is kept closed until the syringe is filled. The valve is then briefly opened to allow bolus flow only due to syringe thrust. The epiglottis is a leaf-like tissue flap located at the upper part of pharynx that prevents food and liquid from entering the trachea or windpipe during swallowing. The GT epiglottis can close within 0.2 s with an angle of 60 degrees, preventing flow of bolus into the airway tube in GT model. The GT oesophageal channel is constructed as a transparent silicon tube. The junction between pharynx and oesophagus is controlled by an upper oesophageal sphincter (UES) which has an elliptical entrance and can be regulated by a pinch valve.

The velocity profile of the bolus in GT is measured using an ultrasound transducer (Wiklund et al., 2007) located in the pharynx wall in opposite side of the epiglottis (Stading et al., 2019). To measure the pressure variation during swallowing, pressure transducers were installed at key locations in the device. Finally, during each bolus transit, photographic images of the bolus flow were captured using a camera operating with a high framerate of 50 frames/s.

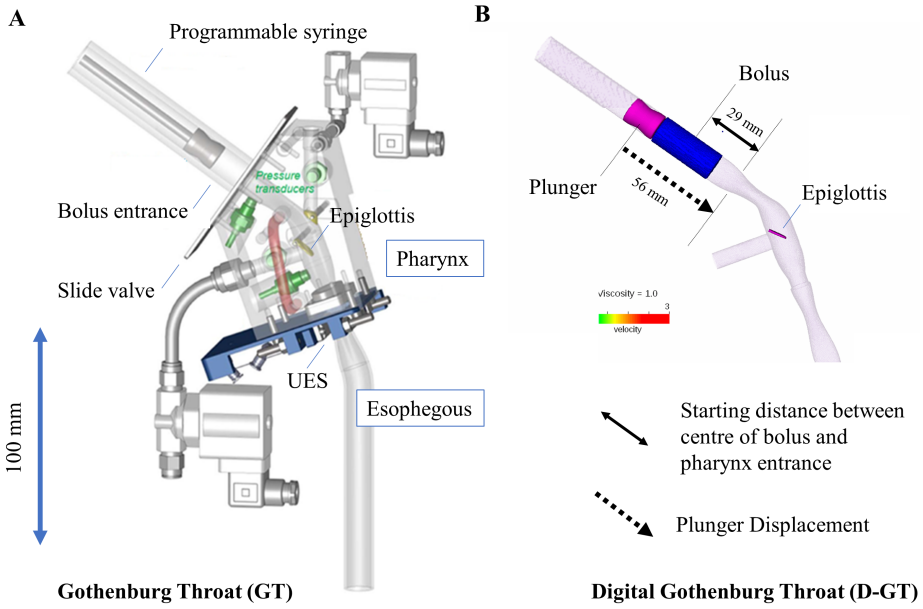

Figure 2. (a) Sketch of the GT model depicting its structure and various mobile components, adapted and altered from the one in Qazi et al., (2019), while ensuring compliance with the Creative Commons (CC) Attribution License, (b) Sketch of the DT-GT model with the mobile components highlighted in magenta. Dimensions of two device parameters which are not available in the original research papers are included

3. CONSTRUCTION OF THE DT-GT

3.1. Overview

The GT-DT is a physics-based predictive model that uses computational fluid dynamics methods to calculate fluid flow in a virtual representation of the GT geometry and using boundary and initial conditions that replicate its physical use. The GT-DT model is shown in Figure 2B. Its inputs include: (1) a 3D surface mesh of the static component of the device and its primary movable elements—the epiglottis and the plunger; (2) a Smoothed Particle Hydrodynamics (SPH) based model of the liquid bolus; and (3) the initial location, speed, and acceleration of the moving components within the device.

3.2. Smoothed particle hydrodynamics for digital twin predictive capabilities

The SPH is used as the compute engine inside the digital twin to simulate the flow of bolus in DT-GT. SPH is highly effective in modelling large deformations and free surfaces and can accurately represent fluid motion within complex deforming surface meshes. Previous studies (Cleary et al., 2021, 2007; Harrison et al., 2014)) have demonstrated the utility of SPH to simulate in-vivo oral processing (mastication) and estimate the values of mechanical parameters such as particle size distribution of chewed bolus. Such models could be used to develop an in-vivo digital twin incorporating chewing and swallowing.

3.3. Digital Gothenburg throat

To create a digital twin of the GT, first a 3D computer aided design (CAD) of the device was provided by RISE, Sweden (Figure 2B). The CAD geometry included models of the moving parts such as the epiglottis and plunger of the syringe used for delivering bolus. The 3D geometry was then imported into Hypermesh software (Altair Engineering, Inc, Detroit, USA) to create a surface mesh compatible with SPH. The average resolution of the mesh is 1 mm. During simulations of the DT-GT, the plunger of the syringe was prescribed with a uniform motion through the syringe channel, while the epiglottis was closed with a fixed angular speed. DT-GT did not include the slide valve mechanism.

Using the DT-GT, we attempt to reproduce the outcomes of two separate swallowing experiments utilizing the in-vitro GT device. These experiments are based on non-Newtonian (shear-thinning) boluses with two different viscosities - 1 Pa·s and 2 Pa·s, measured at a shear rate of at 50 s^{-1} (Qazi et al., 2019). As an initial investigation of the flow behaviour, both the boluses are modelled as Newtonian fluids and this model assumption is assessed by comparison of model results to those from the experiments. The SPH particle resolution used was 0.5 mm.

The boluses are initially located inside the syringe just below the plunger as shown in Figure 2B. Table 1 outlines the other material parameters and device configurations used in these two experiments. DT-GT simulations also incorporated some device parameters whose values were not precisely monitored in the experiments. These includes the initial axial distance from bolus midpoint to start of the sliding valve, as well as displacement of the plunger when fully pressed. Different values of these device parameters are simulated in the DT-GT model.

The main point of comparison between the results from GT and DT-GT model is the total transit time of the bolus through the pharynx. Additionally, photographic images of bolus ejection from the GT model are compared with 3D rendered images of bolus transit in the DT-GT (Figure 3).

Table 1. Key material and device parameter values for DT-GT simulations. Values marked with an asterisk (*) represent model assumptions which were tested using a sensitivity analysis approach.

Material parameters		**Device parameters**	
Viscosity	1 and 2 Pa·s	Plunger speed	1.25 ± 0.03 m/s
Density	~ 1014 kg/m^3	Bolus midpoint location	29 mm and 49 mm *
Bolus Volume	15 ± 2.5 mL	Plunger Displacement	56 mm and 13 mm *

4. PREDICTIONS FROM DIGITAL TWIN

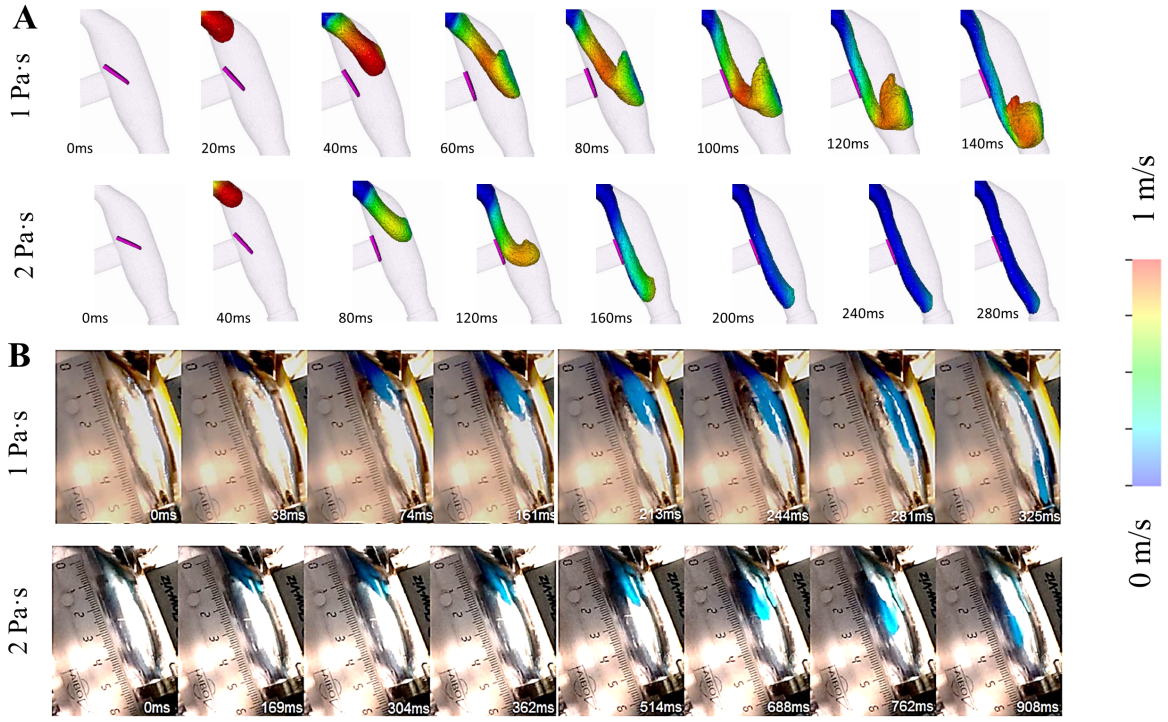

Figure 3. Comparison of bolus transit and profile for viscosities of 1 and 2 Pa·s. Images in each column represent similar location of the bolus front. **(a)** Bolus flow predicted by DT-GT, **(b)** Experimental bolus flow (coloured blue) from GT. The images were adapted and altered from published literature (Qazi et al., 2019), ensuring compliance with CC Attribution License

4.1. Comparison between numerical predictions for different viscosities

The results of bolus transit using the DT-GT model are shown in Figure 3A for two different viscosities. Initially the bolus flows rapidly through the narrow syringe (~1 m/s) due to the pressure from the plunger. When the bolus enters the pharynx at 20 ms, the front of the 1 Pa·s bolus maintains a high speed until it partially adheres to the anterior side of the tube at 60 ms. At this point, the front of the bolus in contact with the walls moves at a slower speed than the part of the bolus immediately behind it. A new front is subsequently created in the bolus, moving still at a speed of approximately 1 m/s towards the oesophagus, reaching it at around

150 ms. At this stage, different parts of the bolus contact different sides of the pharynx, resulting in strong velocity gradients.

In contrast, the 2 Pa·s bolus decelerates considerably after entering the pharynx and only moves along the posterior side of the tube. By 200 ms, the average bolus speed falls below 0.1 m/s with weak velocity gradients. Consequently, the transit time of the bolus through the pharynx is much longer for 2 Pa·s (280 ms).

4.2. Comparison between numerical predictions and experimental results

Figure 3B shows two sequences of photographs from the GT experiment. The spatial distributions of both the boluses in the GT model match closely with the predictions from DT-GT for the first 20 ms. However, as the transit progresses, the bolus fronts in the GT model remain strongly in contact with the pharynx surface. Conversely, in the DT-GT model, the bolus fronts do not remain in contact with the pharynx for long, resulting in free fall due to gravity for most of the bolus volumes until 80 ms. Consequently, the predicted transit times of the bolus by the DT-GT model are considerably shorter than those observed in the GT experiment (Figure 4).

Despite the difference in transit times, the trajectory taken by the bolus to reach the oesophagus appears to be consistent between the DT-GT and the physical GT. The 1 Pa·s bolus predominantly travels through the anterior side of the pharynx, while the 2 Pa·s bolus mostly adheres to the posterior side.

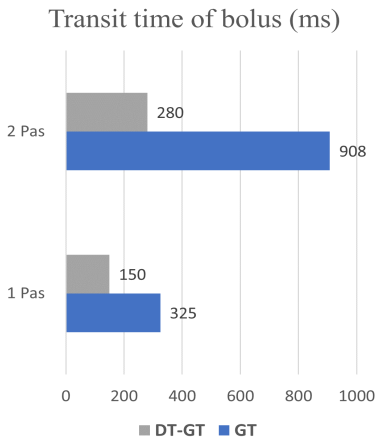

Figure 4. Comparison between the transit time of bolus through the pharynx predicted by the DT-GT model and observed during the GT experiment for two different viscosities

4.3. Variation in device parameters

A range of settings in the DT-GT model could contribute to disparities in the velocity of bolus flow and transit time between the digital and physical models. Two of these parameters (starting bolus midpoint location and plunger displacement) are given in Table 1 and were tested using a sensitivity analysis approach to understand their impact on the transit time for a bolus viscosity of 1 Pa·s.

The viscosity cases discussed in section 4.2 used a starting bolus midpoint location of 29 mm above the sliding valve location. This distance was chosen to ensure that the bolus initially remained approximately over the slide valve. Figure 5A presents another case where the bolus midpoint is located 49 mm above the entrance to the pharynx. In this case, the bolus front falls freely due to gravity through the centreline of pharynx for 80 ms and contacts the pharynx wall just a few mm above the oesophagus. As a result, the transit time of the bolus in this simulation was 110 ms compared to 150 ms in the previous simulation.

In Figure 5B, the DT-GT predictions are shown for a scenario where the full displacement due to the motion of the plunger was reduced. For the original results (in Figure 3A), the duration of the plunger motion was 45 ms. In Figure 5B, the plunger motion was only for 10 ms so that the full displacement of the plunger was 12.5 mm. Reducing the plunger travel distance increased the velocity of bolus flow in the pharynx and decreased the transit time to around 110 ms. This is mainly due to the bolus entering the pharynx with a direction of flow parallel to the pharynx walls. Because of this alignment, the bolus front does not come into contact with the walls for a significant time and instead falls freely due to gravity.

The results in Figure 5 collectively indicate that the pressure applied to the bolus by the plunger motion plays a key role in directing the flow towards the pharynx wall and away from the centre of the channel, resulting in slower flow velocities. Since the plunger is a GT model representation of pharyngeal muscles and tongue, the influence of muscular pressures may similarly direct bolus transit in-vivo to the rear of the throat away from the airways. This may indicate a potential new control mechanism for swallowing linking dysphagia and aging if muscular deterioration results in food distributed closer to the epiglottis during transit.

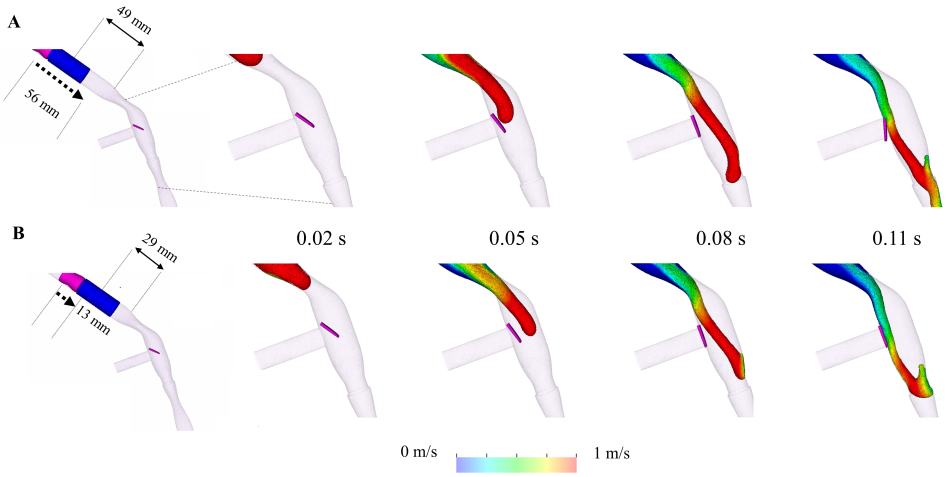

Figure 5. Effect of variation in device parameters of DT-GT on bolus flow. The first image in each row represents a given device setting, while remaining images show their impact on the bolus transport **(a)** effect of changing the starting bolus midpoint location **(b)** effect of decreasing the plunger displacement

4.4. Limitations and learnings for building digital twins

The presented results show that the DT-GT model was not able to accurately replicate bolus transit times recorded in the in-vitro GT device. A main limitation for the DT-GT was the treatment of the bolus rheology as a Newtonian fluid with fixed viscosity, whereas the liquids used in the GT experiments exhibited strong shear thinning behaviour meaning that their effective viscosity decreased under higher shear stress and vice versa. Qazi et al. (2019) suggested that shear rates could be much lower than 50 s^{-1} in slower moving regions with large increases in apparent viscosity. Conversely, high bolus speeds (> 1 m/s) at the pharynx entrance flow onto the anterior side creating a strong velocity gradient across the bolus thickness with the stationary wall producing shear rates up to 200 s^{-1} and greatly reduced apparent viscosity. The combination of the two flow behaviours may be responsible for the longer GT transit times and may explain the differences in bolus flow. In future iterations of the DT-GT, we aim to develop non-Newtonian fluid rheology models to enable more accurate representation of the complex shear thinning behaviour observed in the GT experiments.

Individual parts of the GT device may also have contributed to mismatch of DT-GT results. The slide valve was not modelled in DT-GT and was assumed to be always open. Measurement of the actual speed and timing of the slide valve, driven by an arm fixed on a stepper motor, was challenging to monitor in the GT experiments. Also, the slide valve may not completely open immediately after the plunger begins to exert pressure, resulting in partial obstruction of the bolus flow through the valve. Results in Figure 5 suggest that this can potentially influence the velocity profile of the bolus front and affect its eventual transit time through the pharynx. In addition, it was difficult to monitor the precise control of the plunger to ensure uniform speed. It is possible that there were significant accelerations and decelerations at the beginning and end of the plunger movement, which could further affect the bolus flow. Careful monitoring of these mechanisms in future GT in-vitro experiments may better inform the next generation of DT-GT to predict bolus flow more accurately.

Finally, back pressure due to the flow of air due to asynchronous timings between plunger movement and closure of various valves might also impact the bolus flow. Modelling a simultaneous flow of air and liquid bolus is another capability that could be incorporated in the DT-GT to improve the level of agreement with the physical analogue.

5. CONCLUSION

Here, we presented a digital twin of the in-vitro Gothenburg Throat, using SPH to simulate bolus transport through the device for different viscosities. It has been further used to show that initial location of the plunger inside the syringe and its total travel distance has a key role in determining the direction of the flow inside the pharynx. This may also be of biophysical significance as a control mechanism for preventing dysphagia if pharyngeal muscular control in-vivo plays a similar role in directing bolus flow away from the epiglottis and airways. These findings also indicate that accurate simulation of bolus flow and its transit time through the pharynx remain a challenge, owing to limitations in both rheological models of bolus as well as accurate

dynamic models of several mobile components of the device. However, with more comprehensive measurement of these mechanisms in future iterations of GT, the DT-GT model could potentially well replicate in-vitro swallowing experiments.

The experiences here highlight common issues for digital twins that need to be generically addressed: (1) to identify all necessary measurements that control the operation of the complete device. Any gaps in data required can cause major challenges in matching the digital and physical versions; and (2) to be wary of any untested assumptions arising from the experiments (such as start-up and stopping actions not being important).

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