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Computational fluid dynamics analysis of salivary flow and its effect on sialolithogenesis

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Abstract

OBJECTIVE—Sialolithiasis is a common disease caused by intraductal stones, formed by reduction in salivary flow, salivary stagnation, and metabolic events. We used computational fluid dynamics to investigate changes in salivary flow field around parotid stones of different shapes.

MATERIALS AND METHODS—Three-dimensional configurations of the Stensen's duct were reconstructed from computed tomography sialographic images. Fluid dynamics modeling was used to analyze the salivary flow field around stones under unstimulated and stimulated conditions.

RESULTS—The majority of sialoliths were oval-shaped (59/98), followed by irregular (24/98) and round (15/98). Salivary velocity was significantly higher around streamlined stones, compared with round ($P = 0.013$) and oval ($P = 0.025$) types. Changes in salivary flow field around sialoliths were found to affect the pattern of mineral deposition in saliva. The area of low velocity around the round stone was double the size observed around the streamlined stone during the unstimulated state, whereas in the stimulated state, local vortexes were formed on the downstream side of round and oval stones.

CONCLUSIONS—Salivary flow field around sialoliths plays an important role in the progression of multicentric stones, and analysis of the salivary dynamics during sialolithiasis may provide deeper understandings of the condition and aid in developing successful treatment strategies.

Keywords

sialoliths; saliva; flow field; computational fluid dynamics; lithogenesis

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Author contributions

Yue Xu designed the study and revised the paper. Ping Zhu and Yi Lin conducted the experiment, analysed the data and drafted the paper. Han Lin and Yi Han also contributed to the data analysis and experiment. Qingyin Zheng revised the paper.

Introduction

The formation and development mechanisms of calculi have been explored, mainly from a microperspective, since the beginning of the 19th century (Sabot *et al*, 2012). Calculi development in the salivary extraglandular system frequently causes salivary gland obstruction, which manifests as pain and swelling (Jardim *et al*, 2011). Generally, the etiologies of sialolith retention can be divided into morpho-anatomic (Nagra *et al*, 2010) and saliva composition factors (Grases *et al*, 2003). These, in combination with other physiologic and physical factors, shape salivary calculi into fairly round micronuclei surrounded by concentric circled layers consisting of mucin and various other protein and mineral constituents, especially apatites (Sabot *et al*, 2012).

Sialoliths exhibit morphologic diversity (round, oval, and irregular) during the development of sialolithiasis and the concurrent obstructive sialadenitis, which reflects the mechanisms of lithogenesis. Along with size, location, and orientation, the different shapes of the stones result in various clinical manifestations and treatment options of sialolithiasis (Yu *et al*, 2010). For example, noticeable pain and swelling is elicited upon stimulation at an 80–90% blockage ratio (BR) in the main excretory duct (Xu *et al*, 2012). Calculi of irregular shape are reported to have relatively high recurrence rate and poor prognosis following sialoendoscopic extraction (Luers *et al*, 2011). Moreover, the variety in the shape of stones is known to be determined by the pattern of particle deposition (Schulz, 1987), which in turn is influenced by the salivary flow field.

In recent years, sialoendoscopy has been increasingly applied to the management of sialolithiasis due to its minimally invasive approach that allows endoscopic intraluminal visualization while creating a channel that may be exploited to treat diseases of the ductal system; ultimately, this procedure can eliminate, or at least reduce, the need for sialadenectomy and its related surgical risks (Walvekar *et al*, 2008; Luers *et al*, 2011; Strychowsky *et al*, 2012). Although this procedure has been validated as a safe and effective clinical management option, the rates and mechanisms of sialolith recurrence after endoscopic extraction remain to be definitively determined. Many intraductal tools, such as wire baskets, forceps, drills, and laser lithotripsy, have increased the rates of successful sialolith removal and have thereby improved the overall prognosis since their introduction and widespread application. Suitability of the different techniques for a particular case depends on the size, shape, site, and quality of the sialolith in the duct (Geisthoff, 2007). Although several studies (Marchal and Dulguerov, 2003; Walvekar *et al*, 2009) have reported an association between stone shape and treatment option, most have based their conclusions on empirical research that did not uncover the explicit mechanism and lacked mention of an appropriate treatment program.

In the current study, the change in fluid flow field around stones of different shapes was investigated by a computational fluid dynamic (CFD) method combined with three-dimensional (3D) reconstruction of the ductal system. These data allowed us to construct a reasonable mechanism underlying the evolution of stone shape and recommend treatment schemes corresponding to the various shapes of the sialoliths.

Materials and methods

Study patients and data

The study was designed as a retrospective review of 15 patients with parotid sialoliths who were diagnosed and treated by sialendoscopy (Karl Storz, Tuttlingen, Germany) in the Department of Oral and Maxillofacial Surgery at the Hospital of Stomatology, Sun Yat-Sen University, from January 2009 to May 2011. One of these patients received bilateral sialoendoscopy. The epidemiologic and clinical data, including age, sex, and duration of the symptoms, were collected. Stone numbers, location, size, and shape were evaluated and assessed using occlusal films, panoramic radiographs, axial computed tomography (CT) scans, and sialendoscopies. Informed consent was obtained from all patients prior to the study. The experiments were approved by the Ethical Review Committee of the Hospital of Stomatology at Sun Yat-Sen University (Approval No. ERC-2013-4).

Literature reports

A literature search of the Ovid Medline (1966 to October 2012) and the Web of Science databases (1980 to October 2012) was conducted by two independent reviewers (Yi Lin and Ping Zhu). The electronic search combined intervention- specific terms (sialendoscopy, sialoendoscopy, sialoscopy, endoscopy) with disease-specific terms (salivary gland, sialolithiasis, submandibular, parotid, calculus, stone, sialadenitis) and type-specific terms (shape, configuration, morphology, form) for the following study designs and publication types: meta-analyses, systematic reviews, reviews, and retrospective studies. To ensure that all relevant published articles were captured, the literature search was not limited by study design or publication date. Relevant articles and abstracts were selected and reviewed, and the reference lists from these sources and recent review articles were manually searched for additional publications. The following criteria were set to screen the candidate literature:

1. The stones must reside in Stensen's duct or Wharton's duct.
2. The stones should be located inside the ductal system (main duct, hilum area, or intraglandular).
3. The number of reported cases should be larger than or equal to 2.
4. The description about the shape of stones should be unambiguous (round, oval, etc.).
5. The obstructions should be caused by salivary gland stones, and not a mucous plug or tumor.

CT imaging protocol

A 46-year-old healthy Chinese woman was enrolled in this study as a control. The volunteer had no history of salivary gland diseases. The study was approved by the Ethical Review Committee of the Hospital of Stomatology, Sun Yat-Sen University (Approval No. ERC-2013-4). The volunteer was informed of the details of the study and provided informed consent. A total of 1.5 ml 60% meglumine diatrizoate (contrast agent) was administered intraductally to the right parotid gland with a plastic intravenous catheter introduced through

the orifice of the Stensen's duct. The maxillofacial region was scanned transversely and sagittally using a 64-section CT scanner (Somatom Sensation; Siemens, Munich, Germany). The following imaging parameters were used: 300 mA; 120 kV; section thickness, 0.2 mm; and field of vision, 512×512 .

Numerical procedure

The main portion of the volunteer's Stensen's duct was reconstructed and modeled by Mimics 14.11 (Materialise Technologies, Leuven, Belgium). The reconstruction covered the main duct and the three-first-generation branches of the right parotid gland. The parotid stone was placed at 23 mm from the orifice. The geometric configurations of obstacles were set as round, oval, and streamlined shape, with approximately 80% BR ($BR = d^2/D^2$, where d is obstructive diameter and D is duct diameter) and 1.20 mm, 2.00 mm, and 2.76 mm in the length along the duct, respectively. As described in our previous study (Xu *et al*, 2012), the proximal duct system in front of the sialolith was defined as upstream (48–25 mm), whereas the distal duct system behind the obstacle was defined as downstream (21–0 mm). The peripheral zone of the sialolith was defined as the obstructive area (21–25 mm). The calculation model was meshed by Gambit 2.1.30 (Fluent Inc., New York, NY, USA). Tetrahedral grid cells were used to mesh the models, and the total mesh number was approximately 950 000; the meshes near the obstruction were improved and refined. The finite volume technique was employed based on a computational fluid dynamics package, Fluent 6.1 (Fluent Inc.), to conduct the simulation and fluid dynamics analysis. All the numerical methods and parameter settings are in accordance with our previous report (Xu *et al*, 2012).

Statistical analysis

The statistical analysis was performed using SPSS software, version 15.01 (SPSS, Inc., Chicago, IL, USA). Repeated-measure ANOVA was used to test for differences between groups. If a significant difference was indicated by Wilks' lambda, the groups were subjected to further pairwise comparison using the Bonferroni method. Paired-samples *t*-test was used to compare the difference of the same group in two states. Differences were considered statistically significant at the *P*-level of 0.05.

Results

Fifteen sialolithiasis patients with manifestation of ductal obstruction who subsequently underwent sialoendoscopy, and one who received bilateral sialoendoscopic surgery, were included in our retrospective study. The mean age at presentation was 51 years (range: 27–77 years) with a male-to-female ratio of 8:7 (Table 1). Among the salivary calculus extracted by endoscopy, five were round (31.3%), eight were oval (50.0%), and three were streamlined (18.7%). Most (83.3%) sialoliths resided in the Stensen's duct system, nearly 20 mm away from the orifice, whereas only four of the stones (16.7%) were located in the hilum area. A review of the reports on the shape of sialoliths in the literature is shown in Table 2, indicating that the most common shape is oval.

Using the CT data of the volunteer subject, we established 3D models of parotid sialolith that included a duct of 48 mm with three different contours (round, oval, and streamlined) (Figure 1). We also obtained the fluid flow in the reconstructed Stensen's duct in unstimulated and stimulated states. By analyzing the fluid flow trajectories, we determined that saliva moves closely along the surface of calculi and has abrupt changes in velocity upon encountering different contours. The three types of sialoliths analyzed resulted in significantly different salivary flow rates in the obstructive area, as demonstrated by multivariate tests ($P = 0.019$ both during unstimulated and stimulated states). With regard to the difference between groups, pairwise comparisons indicated that the salivary velocity of the streamlined type was significantly higher than that of the other two types; however, there was no difference between the round and oval types (Table 3).

Areas with flow rates <0.1 mm/s were defined as low-velocity zones and were found only during the unstimulated state beneath the ends of the stones (Figure 2). The area around the oval stone was the largest (0.202 mm^2), followed by those around the round and streamlined stones, respectively (Table 4). However, under stimulated conditions, the salivary flow rate increased significantly ($P = 0.001$), 58-fold compared with that in the unstimulated conditions (Figure 3a, b). In addition, low-velocity areas were not found in the stimulated state, and local vortexes were found in places that corresponded to the downstream-side low-velocity areas under rest conditions (Figure 4). Vortexes were observed around the round (0.092 mm^2) and oval (0.087 mm^2) stones, but not around the streamlined stone (Table 4).

Discussion

Sialolithiasis is a common disease of salivary glands characterized by obstructive symptoms caused by the presence of intraductal stones. The formation of stones in the salivary extraglandular system has been predominantly attributed to slow salivary flow, salivary stagnation, and intricate metabolic events (Waseem and Forte, 2005). Various studies (Kinoshita *et al*, 2008; Su *et al*, 2010; Ribeiro *et al*, 2011) have demonstrated the microstructure of sialoliths and features of electrolyte alteration in saliva during pathologic states; however, less attention has been paid to the macroscopic effects of changes in salivary flow. Using CFD, we explored the changes in the salivary flow field of Stensen's duct, which we believe may affect the symptoms and prognosis of this pathologic condition. These data were used to construct a possible dynamic mechanism of calculi formation and development, correlating with the stone morphology.

From the results of the retrospective analysis and literature review, we found that the reported sialoliths embrace round, oval, or irregular shape, with the majority being oval (59/98), followed by irregular (24/98, including the streamlined stones) and round (15/98). It has been reported that round stones often occur during the early phase of sialolithiasis, are generally small in size and shape, and are composed of a fairly round mineralized core surrounded by few concentric layers (Sabot *et al*, 2012). Owing to their high tendency for rolling and low strength of fixation to the ductal wall, round sialoliths are considered easily removable by surgical procedures (Yu *et al*, 2005; Luers *et al*, 2011). Moreover, our previous study has shown that small stones with BR $< 80\%$ are often asymptomatic, even

under stimulation conditions (Xu *et al*, 2012); hence, conservative treatments, such as sialagogues and massage, are the preferable choices for clinical management. Moreover, these features may also explain why small round stones are less frequently found by sialoendoscopy, compared with the oval and irregular ones.

In our numerical model of fluid dynamics, the sialoliths were fixed to the epithelial wall. We observed a dramatic decrease in the speed of saliva flow beneath both ends of the calculi (Figure 2), whereas the salivary flow speed between the ductal wall and the stone's surface was increased, with significant differences noted between the streamlined stones and the two other shapes ($P = 0.013$ and $P = 0.025$ compared with round and oval stones, respectively). During the process of lithogenesis, degenerative substances are provided by saliva, which is followed by calcification around these substances (Kinoshita *et al*, 2008), leading to various shapes of calculi being formed gradually. The area of low velocity around the fixed round stone, often formed during the early phase of sialolithiasis, is 0.168 mm^2 , which is double the size observed around the streamlined stone (0.079 mm^2). Consequently, saliva particles tend to deposit in these low-velocity zones, resulting in streamline-shaped stones. On the other hand, if the small round stone is not fixed to the epithelial wall, it will roll within the duct, following the salivary flow. Conceivably, the high-velocity zone would then be located between the ductal wall and stone's surface, which would represent the maximal BR section, while the low-velocity zone would shift to the space around the rotation center of the stone. Under these circumstances, long oval (also described as elongated in the literature) stones are formed. These preliminary theories may explain the prevalence of streamlined and oval stones found in the present study that includes both case retrospective analysis and literature review.

Under stimulated conditions, saliva flow velocity is 57-fold higher than that under unstimulated conditions ($P = 0.01$), thus eliminating low-velocity zones. Instead, local vortices were formed at the places corresponding to the downstream-side low-velocity zones during the unstimulated condition, both around the round and oval stones (Figure 4). This swirling action is expected to facilitate the prolonged stay of particles and contribute to the development of concentric structures within the calculi. Specifically, the salivary flow field around the streamlined stone was found to be free of vortex, indicating that it may be the static and final state of sialolith evolution. Due to the effect of vortex, other concentric structures, starting from the additional core, can be observed beneath both ends of the calculi stone. These collective results reveal an important role of salivary flow field in the formation of multicentric sialoliths.

Most reported stones are located in the extraglandular ducts and hilum region and can be reached by intraductal techniques under endoscopic control. The shape of the stone plays an important role in the clinical decision of endoscopic stone removal. The basket technique might be a worthwhile option for round stones ($< 3\text{--}7 \text{ mm}$) (Geisthoff, 2007) that are loosely fixed to the duct wall. The swaying and rotating movements of the basket help to entrap and remove the stone. Elongated stones are often reported in patients presenting with giant calculus ($> 5 \text{ mm}$) (Bodner, 2002) for prolonged duration. Fragmentation with a drill may be needed in such cases, to produce a 'Swiss cheese' aspect, with forceps used to grasp the resultant fragments (Geisthoff, 2007). For a streamlined calculus, both the peripheral stable

saliva flow field and large integrated area within the ductal wall contribute to its poor removal rate. Laser systems have been used to fragment this kind of sialolith (Marchal and Dulguerov, 2003), wherein irrigation and suction are essential to improve surgical visibility by washing away floating particles and making it easier for the remaining large fragments to be removed using forceps or graspers.

There are several limitations to our study that should be noted. The retrospective nature of the data, small sample size, and lack of extended follow-up limited our ability to reach a strong conclusion. However, by applying CFD, we have clearly expounded the relationship between the shape of sialolith and the salivary flow field, presenting a plausible evolution pattern of sialolith shape concurrently with an explanation about why different shapes of sialolith are more suitable for specific treatment schemes. Further studies and more detailed case reviews are necessary to validate our findings.

In conclusion, salivary dynamics around the sialolith plays an important role in their formation and evolution into mono- or multicentric stones. Analysis of the flow field in the salivary duct during sialolithiasis reveals that differences in the shape of sialoliths lead to the changes in the area of low-velocity zone during unstimulated condition and the vortex zone during stimulation. This may provide a deeper understanding of the prevalence of salivary stones of different shapes and aid in developing successful treatment strategies.

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Figure 1.

Three-dimensional finite-volume model of a parotid sialolith in a parotid duct of 48 mm and with the stone located at 23 mm from the orifice. The salivary flow trajectory around the parotid stone is shown in the right top corner (top view) and left bottom corner (sagittal view).

Figure 2. Velocity profile of different shapes of stones under unstimulated conditions. The red line indicates the low-velocity zone.

Figure 3.

Salivary velocity in obstructive areas (21–25 mm) of parotid stones of different shapes in (a) unstimulated and (b) stimulated conditions. Bar graph (c) of the mean velocities in obstructive areas of different shapes of stones under unstimulated and stimulated conditions. The values for each type of stone were significantly different between the two states: $P = 0.001$ for round and streamlined stones; $P < 0.001$ for oval types.

Figure 4. Fluid flow trajectory of different shapes of stones under stimulated conditions. The red line indicates the vortex zone.

Table 1

Patient data and sialendoscopic findings

	Age	Sex	Duration	Side	Number	Sialolith size, mm	Shape	Sialolith location
1	51	F	6 M	L	1	1	Round	Hilar
2	44	F	1 Y	L	1	1	Round	Ductal
3	59	M	4 M	L	1	5	Streamlined	Ductal
4	40	F	2 W	L	1	10	Streamlined	Ductal
5	70	M	20 D	L	1	2	Oval	Ductal
6	46	F	6 Y	L	1	1	Round	Ductal
7	57	M	6 M	L	1	3	Oval	Ductal
8	77	M	7 Y	L	1	8	Oval	Ductal
9	40	M	2 Y	L	1	5	Oval	Hilar
10	54	F	1.5 M	L	1	2	Round	Hilar
11	57	M	3 Y	R	1	6	Streamlined	Ductal
12	54	M	1 W	R	1	1	Round	Ductal
13	27	F	2 D	L	1	2	Oval	Hilar
14	58	F	15 D	L	1	2	Oval	Ductal
15 ^a	35	M	2 Y	L	1	6	Oval	Ductal
15 ^a	35	M	3 Y	R	1	5	Oval	Ductal

^a Bilateral sialendoscopy during the same procedure.

Sex abbreviation: M, male; F, female. Time abbreviations: D, day; W, week; M, month; Y, year. Side abbreviations: L, left; R, right.

Table 2

Prevalence of different shapes of sialoliths reported in the literature

Investigator (Year)	Round	Oval	Long oval	Irregular
Bodner L (2002)	1	1	1	3
Su Y (2010)	1	1	–	–
Walvekar RR (2009)	4	4	2	–
Luers JC (2011)	4	42	–	18
Total	10	48	3	21

Table 3

Pairwise comparison of salivary velocities in the obstructive area between three different shapes of sialoliths under the unstimulated and stimulated conditions

State	<u>Between-group comparisons</u>		
	R-O	R-S	O-S
Unstimulated	0.084	0.013*	0.025*
Stimulate	0.085	0.013*	0.025*

Stone abbreviations: R, round; O, oval; S, streamlined;

* statistically significant.

Table 4

Areas of low-velocity zones and vortex zones around stones of different shapes

Zone		Sialolith shape, mm ²		
		Round	Oval	Streamlined
Low velocity	Unstimulated	0.168	0.202	0.079
	Stimulated	0	0	0
Vortex	Unstimulated	0	0	0
	Stimulated	0.092	0.087	0