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Percutaneous Thrombin Injection Based on Computational Fluid Dynamics of Femoral Artery Pseudoaneurysms

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Objective: To analyze the computational fluid dynamics (CFD) of femoral artery pseudoaneurysm (FAP), identify a suitable location and timing for percutaneous thrombin injection (PTI) based on this analysis, and report our clinical experience with the procedure.
Materials and Methods: CFD can be used to analyze the hemodynamics of the human body. An analysis using CFD recommended that the suitable location of the needle tip for PTI is at the center of the aneurysm sac and the optimal timing for starting PTI is during the early inflow phase of blood into the sac. Since 2011, seven patients (three male and four female; median age, 60 years [range, 43–75 years]) with FAP were treated with PTI based on the devised suitable location and time. Prior to the procedure, color Doppler ultrasonography was performed to determine the location and timing of the thrombin injection.
Results: The technical success rate of the PTI was 100%. The amount of thrombin used for the procedure ranged from 200 IU to 1000 IU (median, 500 IU). None of the patients experienced any symptoms or signs of embolic complications during the procedure. Follow-up CT images did not reveal any embolism in the lower extremities and showed complete thrombosis of the pseudoaneurysm.
Conclusion: Based on our study of CFD, PTI administered centrally in the FAP during early inflow, as seen on color Doppler, can be an effective technique.
Keywords: *Femoral artery; False aneurysm; Thrombin; Injections*

INTRODUCTION

Femoral artery pseudoaneurysm (FAP) usually occurs after obtaining femoral artery access for vascular intervention, including cardiac, neurological, and visceral artery interventions [1,2]. After the intervention, hemostasis is achieved by manual compression, use of a vascular closure device, or by surgical closure. However, incomplete hemostasis can cause hematoma around the puncture site and continued arterial flow can occur from the feeding artery (femoral artery) to the hematoma. Although surgical removal was the treatment of choice in the past, percutaneous thrombin injection (PTI) under ultrasonography guidance is commonly used currently because it is less invasive, enables rapid management, and has high cost-effectiveness [3-8] even in obese or pediatric patients [9,10]. However, there are constant concerns regarding embolism in peripheral arteries during the procedure, which is related to the thrombin injection and is one of the major complications [1,11-14].

During the thrombin injection, the needle tip is positioned centrally or far from the neck of the aneurysm [1,15], and the optimal timing for the injection has not been investigated. The position of the needle tip and timing of the injection can be determined to prevent or

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minimize embolism in the peripheral arteries when the blood flow pattern in the FAP is considered (in- and out-flow between the feeding artery and the aneurysm). In a previous study [16], we developed models of FAP and used computational fluid dynamics (CFD) to understand the blood flow pattern in the aneurysm. Based on the analysis, we have devised a method to determine the location and timing of thrombin injection, and we perform the procedure accordingly. Herein, we report our clinical experience with FAP.

MATERIALS AND METHODS

This retrospective study was approved by the Institutional Review Board of Boramae Medical Center and was conducted in accordance with the Declaration of Helsinki. The need for informed consent from the patients was waived (IRB No. 10-2018-98).

Development of the PTI Method Based on a CFD Study

CFD was developed to analyze flow phenomena using governing equations with numerical techniques. It is widely used in engineering fields such as hydrodynamics [17,18]. Recently, CFD has also been used in the medical field for flow analysis [19-24]. We used CFD to understand the blood flow patterns in FAPs to obtain helpful information or clues for performing the PTI procedure [16]. For the numerical analysis, a three-dimensional (3D) model of a round FAP (sac size, 20 mm; neck length, 3 mm; neck width, 3 mm) was constructed using ANSYS Design Modeler software (Ansys Inc.). To analyze the flow characteristics in the model, an inlet and outlet boundary condition was applied with Doppler waveforms that were measured in the proximal and distal femoral arteries. In addition, the pressure boundary condition was set to 0 as the reference pressure value at the outlet point. To investigate the flow pattern in the FAP, the selected times for the flow cycle were set at peak velocity, lowest velocity, the same velocity in the acceleration and deceleration phases, and a velocity of 0 m/s in the Doppler waveform.

The CFD study demonstrated flow phenomena in the pseudoaneurysm sac and neck in six phases (acceleration, peak velocity, deceleration, zero velocity, lowest velocity, and zero velocity) of a cycle. As shown in Figure 1, in the

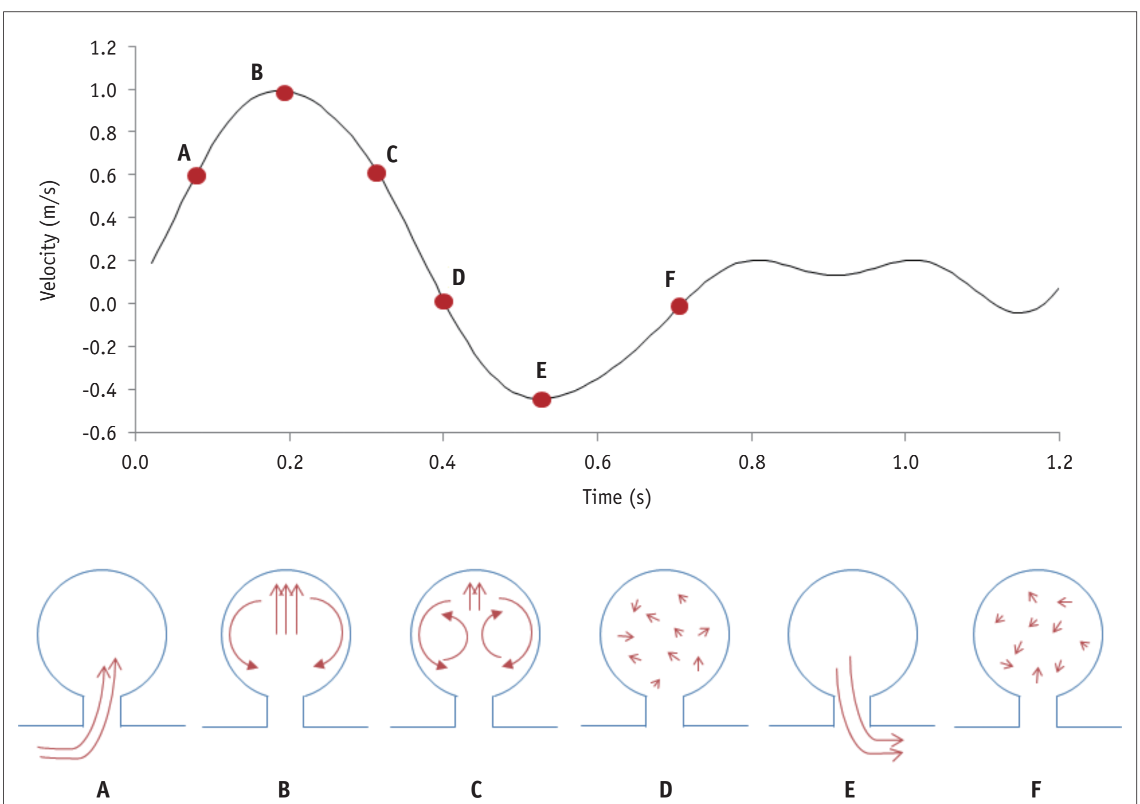

Fig. 1. Flow pattern in a pseudoaneurysm. The velocity waveform seen in the figure was obtained from the femoral artery just proximal to the pseudoaneurysm. **A** to **F** are the six points of the cycle and the six figures at the bottom demonstrate the flow field in the sac at each phase.

acceleration phase (A), the blood in the femoral artery is found to enter the pseudoaneurysm sac through its neck. At peak velocity (B), the flow bumps into the pseudoaneurysm roof and moves outward in the sac. In the deceleration phase (C), a vortex flow forms in the periphery of the sac. During the two zero-velocity phases (D, F), the flow stagnates in the sac with irregular flow velocity vectors. At the lowest velocity (E), the blood in the sac exits into the femoral artery through the neck of the pseudoaneurysm.

Based on the results of the CFD study, we developed a method to determine the location and timing of the PTI: placement of the needle tip at the center of the aneurysm sac and the start of the thrombin injection in the acceleration phase, which refers to the early inflow phase.

Patients

From May 2011 through March 2018, seven consecutive patients (three male and four female; median age, 60 years [range, 43–75 years]) with FAP were treated with PTI according to the method developed by us. The pseudoaneurysm developed in all patients after a common femoral artery (right = 5, left = 2) puncture was performed for vascular diagnostic or interventional angiography procedures namely, cerebral angiography (n = 2), coronary artery angiography (n = 1), superficial femoral artery angioplasty and stenting (n = 1), bronchial artery embolization (n = 1), superior gluteal artery embolization (n = 1), and hybrid thoracic endovascular aortic repair (n = 1). The caliber of the femoral sheaths used for the angiography or intervention was 5 Fr (n = 5), 7 Fr (n = 1), and 18 Fr (n = 1). Hemostasis was achieved by manual compression (n = 6) or purse-string sutures (n = 1). Pseudoaneurysm was confirmed based on the presence of a sac and neck with blood inflow and outflow using color Doppler ultrasonography (n = 7). CT was performed in six patients before the consultation for PTI at other departments in the hospital.

Percutaneous Thrombin Injection

Before draping, we evaluated the pseudoaneurysm using ultrasonography to determine the timing and point of the injection in the aneurysm based on our previous research results. After reviewing the flow of blood in the aneurysm in several cardiac cycles, the decision was made to start the thrombin injection in the systolic phase equivalent to the early inflow phase. A 1 cc syringe with a 22G needle (length, 9 cm) was used for the thrombin injection, which contained 1000 IU of thrombin (Reyon Thrombin Lyophilized Powder, Reyon Pharmaceutical Co., Ltd.). After draping, the needle was inserted into the aneurysm under ultrasonography guidance, and we attempted to advance the needle tip as far into the center of the aneurysm as possible (Fig. 2). Two patients had a FAP with two chambers. In these cases, the needle tip was placed at the center of the proximal chamber adjacent to the femoral artery.

Color Doppler ultrasonography was performed to enable the injection of thrombin at the appropriate time. As mentioned previously, thrombin was injected when the early inflow from the femoral artery to the aneurysm was visualized. The endpoint of thrombin injection was when the flow signal disappeared, and the thrombus filled the aneurysm completely.

After the injection, complete isolation of the aneurysm from the femoral artery was evaluated using ultrasonography. A physical examination prior to and following the injection, including palpation of the dorsalis pedis and posterior tibial arteries and assessment of toe color and pain, was performed to rule out the occurrence of embolism during the procedure.

Ultrasonography (n = 2) or lower extremity CT angiography (n = 5) was performed to confirm the status of the aneurysm 1 week to 1 month after the procedure. The patients were evaluated in an outpatient clinic to identify any problems related to the FAP.

RESULTS

The neck of the FAP was not wide (> 1.0 cm) [25] in any of the patients treated with PTI in this study. There were no significant difficulties in inserting the needle tip at the center of the aneurysm and injecting thrombin at the appropriate time. The amount of thrombin injected during the procedure ranged from 200 IU to 1000 IU (median, 500 IU; interquartile range, 300 IU) (Table 1).

In one of the two complex pseudoaneurysms, only 200 IU of thrombin was injected into the proximal chamber, which resulted in complete thrombosis of the two chambers. However, the other patient required an additional thrombin injection in the distal chamber after injection in the proximal chamber.

Complete thrombosis and isolation from the femoral artery was achieved in all cases, which were confirmed by ultrasonography performed immediately after the thrombin injection and by ultrasonography or CT angiography

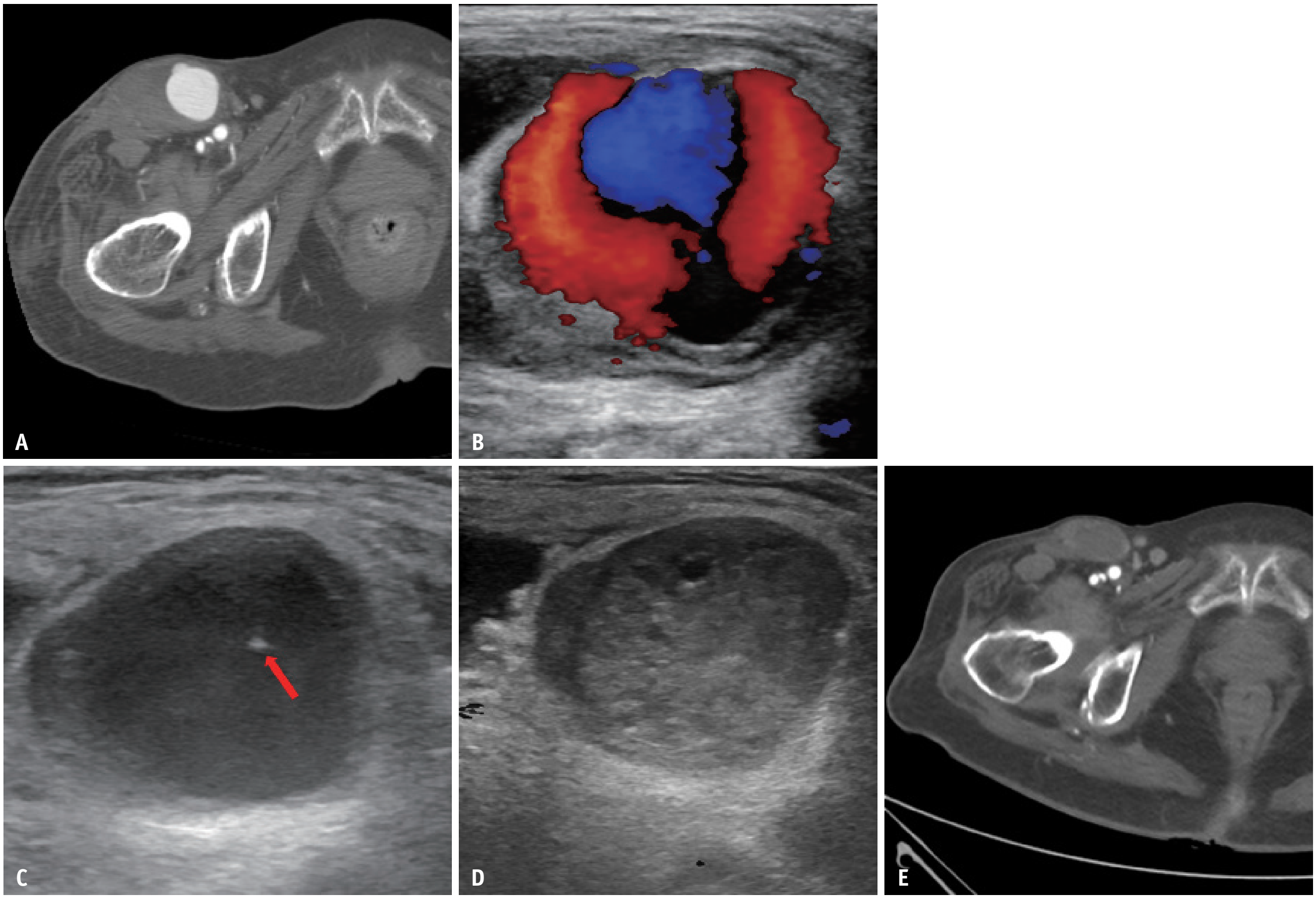

Fig. 2. CT scan and ultrasonography images of a 75-year-old female undergoing percutaneous thrombin injection.
A. CT scan image depicting a pseudoaneurysm in the right femoral artery. **B.** Color Doppler ultrasonography image showing the pattern of the blood flow in the sac (peak velocity flow phase). **C.** A 22G needle (arrow) inserted percutaneously under ultrasonography guidance and the tip is placed at the center of the sac. **D.** Color Doppler ultrasonography image showing no flow in the sac and complete thrombosis after thrombin injection. **E.** CT scan image after percutaneous thrombin injection demonstrates complete thrombosis of the femoral artery pseudoaneurysm.

performed later. None of the seven cases showed arterial embolism. There were no cases of any other complications, such as allergic reactions or infections.

DISCUSSION

Embolism is a complication that can occur after PTI administered to treat FAP. Although microembolization is relatively common (15–38%), significant peripheral arterial embolism is rare [1,11,12]. However, embolism causes limb ischemia or necrosis, leading to a fatal event and requires vascular intervention, such as aspiration embolectomy, intra-arterial thrombolysis, or surgical removal of the emboli in the event of complications [13,14]. For this reason, interventional radiologists are concerned about preventing embolism while administering PTI to treat FAP. Here, we have suggested a suitable timing and location for PTI based on our previous basic research [16].

Hanson et al. [15] recommended that thrombin should be administered as far from the aneurysm neck as possible to reduce the risk of arterial embolism. Ahmad et al. [1] stated that the needle tip should lie centrally in the aneurysm; however, they did not provide any reasons for doing so. As in the other studies, we have also recommended the center of the pseudoaneurysm as the point of injection. The inflow from the femoral artery to the pseudoaneurysm passes through the its neck, runs into its center, bumps into its roof, and creates a vortex flow in its peripheral portion. The outflow from the aneurysm to the femoral artery runs through the bottom of the aneurysm and passes through the neck of the pseudoaneurysm. The center of the aneurysm was considered the thrombin injection point because a relatively long course of blood flow was guaranteed at this location.

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Table 1. Patient, Femoral Artery Pseudoaneurysm, and Percutaneous Thrombin Injection Characteristics

Age/Sex	Caliber of Access Used (Fr)	Type of Closure Attempt	Sac Size (mm)	Neck (mm)			Thrombin Amount (IU)	Tecnhical Success	Complications
				Length	Width	Shape			
43/Male	5	Manual compression	12 x 13 x 15	12	6	Tortuous	500	Yes	No
73/Female	5	Manual compression	Bilobar, 11 x 12 x 11, 19 x 14 x 15	5	3	Straight	200	Yes	No
75/Female	5	Manual compression	29 x 25 x 28	6	3	Jagged	400	Yes	No
56/Female	7	Manual compression	15 x 12 x 14	19	7	Beaded	200	Yes	No
74/Male	18	Double purse string sutures	Bilobar, 23 x 21 x 22, 17 x 14 x 19	25	4	Curved	1000	Yes	No
54/Female	5	Manual compression	22 x 42 x 31	18	5	Curved	500	Yes	No
60/Male	5	Manual compression	14 x 10 x 24	8	3	Straight	700	Yes	No

Grewe et al. [26] performed injection testing with echo contrast to determine the appropriate spot before thrombin injection. Small amounts of contrast were injected repeatedly during needle advancement and retraction, which demonstrated the flow pattern in the aneurysm. They avoided the spot where the contrast flowed into the femoral artery and selected the one where the contrast remained in the aneurysm without any flow into the femoral artery. In our study, the spot selected as the thrombin injection point matched the space with the vortex flow. Our CFD study demonstrated that blood drains centrally into an aneurysm from the femoral artery, flowing upward and outward, creating a vortex flow in the peripheral space. Wojtarowicz et al. [27] reported that the use of ultrasonographic contrast along with the enhancement of a color Doppler signal helped to confirm the correct position of the needle.

In this study, thrombin was injected under color Doppler ultrasonography guidance to ensure that the start of injection was during the early systolic forward flow. However, Hanson et al. [15] performed the procedure under real-time grey-scale ultrasonography guidance to quantify the amount of thrombin necessary for complete thrombosis of the aneurysm. It was possible to visualize the progression of the thrombosis and determine the end point of the thrombin injection under color Doppler ultrasonography guidance.

The present study did not include a large number of patients, which could negatively affect the validity of the suggestion based on our basic research and experience with PTI. However, this limitation may be overcome in upcoming studies that follow the method described in the present study. Another limitation could be the diversity in the shape of the FAP. We constructed 3D models of FAP for the CFD study; however, it might not accurately represent various FAPs.

Our current clinical study based on CFD may provide theoretical grounds for the aforementioned studies regarding the optimal injection spot. The current study suggests the early inflow phase as the optimal timing for the injection and the center of the pseudoaneurysm sac as the injection spot for successful PTI. Therefore, PTI can be administered based on this method to treat FAP. This method may be helpful for interventionalists to determine the location and timing of thrombin injection, especially for those with limited experience.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: all authors. Data curation: Young Ho Choi. Formal analysis: Kyung-Wuk Kim, Hyoung-Ho Kim, Changje Lee, Min Uk Kim. Methodology: Changje Lee,

Yasutaka Baba. Supervision: Young Ho Choi. Validation: Yasutaka Baba. Writing—original draft: Kyung-Wuk Kim, Hyoung-Ho Kim, Young Ho Choi. Writing—review & editing: Changje Lee, Min Uk Kim, Yasutaka Baba.

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REFERENCES

1. Ahmad F, Turner SA, Torrie P, Gibson M. Iatrogenic femoral artery pseudoaneurysms--a review of current methods of diagnosis and treatment. *Clin Radiol* 2008;63:1310-1316
2. Kacila M, Vranic H, Hadzimehmedagic A, Sehovic S, Granov N. The frequency of complications of pseudoaneurysms after cardiac interventional diagnostic and therapeutic interventions. *Med Arh* 2011;65:78-81
3. Mishra A, Rao A, Pimpalwar Y. Ultrasound guided percutaneous injection of thrombin: effective technique for treatment of iatrogenic femoral pseudoaneurysms. *J Clin Diagn Res* 2017;11:TC04-TC06
4. Kleczynski P, Rakowski T, Dziewierz A, Jakala J, Dudek D. Ultrasound-guided thrombin injection in the treatment of iatrogenic arterial pseudoaneurysms: single-center experience. *J Clin Ultrasound* 2014;42:24-26
5. Gürel K, Gür S, Özkan U, Tekbaş G, Önder H, Oğuzkurt L. US-guided percutaneous thrombin injection of postcatheterization pseudoaneurysms. *Diagn Interv Radiol* 2012;18:319-325
6. Vlachou PA, Karkos CD, Bains S, McCarthy MJ, Fishwick G, Bolia A. Percutaneous ultrasound-guided thrombin injection for the treatment of iatrogenic femoral artery pseudoaneurysms. *Eur J Radiol* 2011;77:172-174
7. Krueger K, Zaehringer M, Strohe D, Stuetzer H, Boecker J, Lackner K. Postcatheterization pseudoaneurysm: results of US-guided percutaneous thrombin injection in 240 patients. *Radiology* 2005;236:1104-1110
8. Lönn L, Olmarker A, Geterud K, Risberg B. Prospective randomized study comparing ultrasound-guided thrombin injection to compression in the treatment of femoral pseudoaneurysms. *J Endovasc Ther* 2004;11:570-576
9. Yoo T, Starr JE, Go MR, Vaccaro PS, Satiani B, Haurani MJ. Ultrasound-guided thrombin injection is a safe and effective treatment for femoral artery pseudoaneurysm in the morbidly obese. *Vasc Endovascular Surg* 2017;51:368-372
10. Boubalos JJ, Connolly BL, Amaral JG, Temple MJ, Parra DA. Ultrasound-guided thrombin injection for the treatment of femoral pseudoaneurysm in pediatric patients. *J Vasc Interv Radiol* 2016;27:519-523
11. Kurzawski J, Sadowski M, Janion-Sadowska A. Complications of percutaneous thrombin injection in patients with postcatheterization femoral pseudoaneurysm. *J Clin Ultrasound* 2016;44:188-195
12. Lewandowski P, Maciejewski P, Wąsek W, Pasierski T, Budaj A. Efficacy and safety of closing postcatheterisation pseudoaneurysms with ultrasound-guided thrombin injections using two approaches: bolus versus slow injection. A prospective randomised trial. *Kardiol Pol* 2011;69:898-905
13. Gabrielli R, Rosati MS, Vitale S, Millarelli M, Chiappa R, Siani A, et al. Fatal complication after thrombin injection for post-catheterization femoral pseudoaneurysm. *Thorac Cardiovasc Surg* 2011;59:372-375
14. Ohlow MA, Secknus MA, von Korn H, Weiss R, Lauer B. Percutaneous thrombin injection for treatment of iatrogenic femoral artery pseudoaneurysms: a case for caution. *Angiology* 2008;59:372-375
15. Hanson JM, Atri M, Power N. Ultrasound-guided thrombin injection of iatrogenic groin pseudoaneurysm: Doppler features and technical tips. *Br J Radiol* 2008;81:154-163
16. Suh SH, Kim HH, Choi YH, Lee JS. Computational fluid dynamic modeling of femoral artery pseudoaneurysm. *J Mech Sci Technol* 2012;26:3865-3872
17. Goto A, Nohmi M, Sakurai T, Sogawa Y. Hydrodynamic design system for pumps based on 3-D CAD, CFD, and inverse design method. *J Fluids Eng* 2002;124:329-335
18. Zhang ZR, Liu H, Zhu SP, Zhao F. Application of CFD in ship engineering design practice and ship hydrodynamics. *J Hydrodyn* 2006;18:315-322
19. Dazeo N, Dottori J, Boroni G, Larrabide I. A comparative study of porous medium CFD models for flow diverter stents: advantages and shortcomings. *Int J Numer Method Biomed Eng* 2018;e3145
20. Burgos MA, Sanmiguel-Rojas E, Rodríguez R, Esteban-Ortega F. A CFD approach to understand nasoseptal perforations. *Eur Arch Otorhinolaryngol* 2018;275:2265-2272
21. Wang M, Zhou H, Huang Y, Gong P, Peng B, Zhou S. Hydrodynamics analysis and CFD simulation of portal venous system by TIPS and LS. *Hepatogastroenterology* 2015;62:1016-1022
22. Goubergrits L, Riesenkampff E, Yevtushenko P, Schaller J, Kertzscher U, Berger F, et al. Is MRI-based CFD able to improve clinical treatment of coarctations of aorta? *Ann Biomed Eng* 2015;43:168-176
23. Kim HH, Choi YH, Lee SB, Baba Y, Kim KW, Suh SH. Numerical analysis of the urine flow in a stented ureter with no

peristalsis. *Biomed Mater Eng* 2015;26 Suppl 1:S215-S223
24. Sacco F, Paun B, Lehmkuhl O, Iles TL, Iaizzo PA, Houzeaux G, et al. Evaluating the roles of detailed endocardial structures on right ventricular haemodynamics by means of CFD simulations. *Int J Numer Method Biomed Eng* 2018;34:e3115
25. Sizemore G, Ayubi F, Clark B, Kellicut D. Ultrasound-guided percutaneous thrombin injection following iatrogenic femoral artery pseudoaneurysm: patient selection and perspectives. *J Vasc Diagn Interv* 2018;6:1-5
26. Grewe PH, Mügge A, Germing A, Harrer E, Baberg H, Hanefeld C, et al. Occlusion of pseudoaneurysms using human or bovine thrombin using contrast-enhanced ultrasound guidance. *Am J Cardiol* 2004;93:1540-1542
27. Wojtarowicz A, Lewandowski M, Płońska E. Ultrasonographic contrast injection enhances safety of thrombin - induced obliteration of femoral artery pseudoaneurysm. *Kardiol Pol* 2005;63:649-650; discussion 651