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VASCULAR-INTERVENTIONAL

Safety and efficiency of femoral artery access closure with a novel biodegradable closure device: a prospective single-centre pilot study

Karla M. Treitl[1] · **Alma Ali**[1] · **Marcus Treitl**[1]

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Abstract

Objectives Vascular closure devices can accelerate haemostasis after arteriotomy, but induce scarring. The aim of the study was to prospectively analyse the feasibility of a novel biodegradable arterial closure device (CD).

Methods Two hundred fifty-five patients (183 male; age 36–98 years) with an access vessel diameter >3 mm received the biodegradable CD after endovascular therapy. Technical success rate, time-to-haemostasis (TTH) and time-to-ambulation (TTA) were measured. Puncture site complications were categorized as minor (local hematoma, minor bleeding) or major (pseudoaneurysm, embolization, dissection, thrombotic occlusion, hematoma/major bleeding requiring surgery, access site infection).

Results Technical success was achieved in 98.8 % (252 cases); device failure occurred in three cases (1.2 %). The average TTH and TTA were 11.3±26.9 s and 73.0±126.3 min. The major complication rate was 1.6 %, with three pseudoaneurysms and one retroperitoneal bleeding. The minor complication rate was 2.0 %, with five small hematomas. Neither cardiovascular risk factors nor access vessel characteristics had statistically significant influence on adverse events. Re-puncture was uncomplicated in 32 cases after 155.0±128.8 days.

Conclusions Handling of the new biodegradable CD is safe. The complication rates are tolerably low and comparable to other CDs. Post-procedural sonography showed no significant palpable subcutaneous changes in the access site.

Key Points

- *VCDs can increase time efficiency and patient comfort after intervention.*
- *In this prospective single-centre-study, biodegradable CD was safe and easily applicable.*
- *Its major and minor complication rates are comparable to other CDs.*
- *Its mean time-to-haemostasis and time-to-ambulation were 11.3±26.9 s and 73.0±126.3 min.*
- *Post-procedural sonography showed no significant palpable subcutaneous changes at the access site.*

Keywords Vascular closure device · Biodegradable implants · Time-to-haemostasis · Time-to-ambulation · Endovascular techniques

Abbreviations

BMI	Body mass index
CFA	Common femoral artery
CHD	Coronary heart disease
FISH	Femoral introducer sheath & stasis
PAOD	Peripheral arterial occlusive disease
SFA	Superficial femoral artery
TTA	Time to ambulation
TTH	Time to haemostasis
VAS	Visual analogue scale
VCD	Vascular closure device

Introduction

As the indications for endovascular treatments of oncologic and occlusive artery disease have evolved over recent decades, the number of interventions and arterial punctures has

✉ Karla M. Treitl
karlamaria.treitl@med.uni-muenchen.de

[1] Institute for Clinical Radiology, Hospitals of the Ludwig-Maximilian-University of Munich, Nussbaumstr. 20, D-80336 Munich, Germany

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risen. Consequently, access-related complications are associated with higher rates of morbidity and mortality, and have an increasing impact on treatment expense and length of in-hospital stay [1, 2]. The common femoral artery (CFA) is most often used as the access site, and conservative strategies for achieving haemostasis involve time-consuming manual compression, uncomfortable compression bandages and bed rest, depending on sheath size [3].

In light of the increasing complexity of endovascular procedures, new medications for anticoagulation, and the growing economic factors in public health care, the market for vascular closure devices (VCDs) is growing. Three categories of VCDs with corresponding characteristics and limitations can be distinguished: compression assist devices, topical haemostasis devices and active closure devices [2, 4]. The last include suture-based devices, collagen-based plug devices that accelerate the clotting cascade and mechanically seal the artery, and non-collagen-based plug devices that close the arteriotomy with a bioabsorbable plug. Angio-Seal (St. Jude Medical, Inc., St. Paul, MN, USA), ExoSeal (Cordis Corporation, Fremont, CA, USA) and Perclose ProGlide (Abbot Vascular, Abbott Park, IL, USA) have been on the market long enough to have been investigated in two randomized controlled trials [5–7]. The more recently developed mechanical plug devices have been evaluated in non-randomized or retrospective studies with similar endpoints [2].

Several study centres have observed that repeat use of collagen-based devices or devices employing artificial materials can cause scarring, which limits or even prohibits future punctures, although this experience has not been not proven in clinical studies thus far. Animal studies have demonstrated that collagen-based VCDs induce a stronger vessel narrowing and peri-adventitial inflammation than suture-based devices [8]. Consequently, there is a demand for active closure devices with better biocompatibility. The Femoral Introducer Sheath and Hemostasis (FISH) ControlClose^{TM} device (Morris Innovative, Inc., Bloomington, IN, USA) uses porcine small intestinal submucosa (SIS^{TM}; Cook Biotech Inc., West Lafayette, IN, USA) as an active part of its plug-based closure device. SIS has been in use for decades in medicine; it is used as a wound drape for burn wounds, and induces little or no scarring of the wound [9]. The aim of this study was to prospectively assess the feasibility, limitations and complication rates of the novel biodegradable FISH mechanical plug closure device.

Materials and methods

Patient cohort

Patients with symptomatic peripheral or visceral artery occlusive disease, who were hospitalized at our centre between March 2013 and February 2015 were included, according to the following criteria: 1) indication for endovascular treatment of peripheral or visceral arteries determined in an interdisciplinary consensus conference according to the current national guidelines of the German Society for Angiology and Vascular medicine [10]; 2) at least 24-h prior written informed consent; 3) access vessel≥3 mm in diameter; application of an access sheath with 6 F or 7 F; and 4) agreement to the use of a VCD instead of manual compression.

Predefined exclusion criteria included skin infection or implantation of any other VCD within the last 30 days, and denial of study participation. Of a total of 850 patients screened, 255 were included in the study. Case history and cardiovascular risk factors were collected from patient records (Table 1). The study protocol followed the tenets of the Declaration of Helsinki.

Arterial access

Pre-existing anticoagulation treatment with a vitamin K antagonist was changed to subcutaneous injections of low-molecular heparin and medication with factor Xa inhibitors, which was paused 24 h prior to the intervention. After disinfection of the site and local anaesthesia (20 ml of 1 % mepivacaine), an interventional radiologist with more than 10 years of experience (M.T.) accessed the CFA or superficial femoral artery (SFA) using an antegrade or retrograde approach (18G puncture needle; Peter Pflugbeil GmbH, Zorneding, Germany). All patients received 5000 I.U. of heparin after the insertion of a braided 6 F (Glidesheath®; Terumo Medical Corporation, Somerset, NJ, USA) or 7 F sheath (BriteTip®; Cordis Corporation, Fremont, CA, USA) under fluoroscopic guidance. An additional 2500 I.U. was administered if the procedure lasted longer than 2 h. Angiographic images were obtained in a single projection by uniplanar digital subtraction angiography (DSA; Polystar T.O.P.®, Siemens Healthcare, Erlangen, Germany) with non-ionic water-soluble contrast agent (Solutrast® 300, iopamidol 300 mg/ml; Bracco Imaging Deutschland GmbH, Konstanz, Germany). The degree of calcification of the access vessel was rated post-procedurally from fluoroscopic images on a four-point scale: 0=none; 1=discrete; 2=moderate; 3=severe. In cases of re-puncture after FISH, the level of scarring of the access site was clinically evaluated on a three-point scale: 0= none; 1=palpable resistance, but no resistance during puncture; 2=palpable resistance and resistance during puncture. Procedural data such as the duration of the endovascular treatment, the puncture site, the sheath size and its intra-arterial dwell time were recorded.

Application of FISH

An experienced interventional radiologist (M.T.) performed all FISH implantation procedures. The initial ten procedures

Table 1 Demographics, cardiovascular risk factors and anticoagulation among the study cohort (n=255)

			Number	Percentage or range
Demographics	Total patients		255	
		Male	183	71.8 %
		Female	72	28.2 %
	Age (years)		71.4±10.9	36–98
Risk factors	Diabetes		103	40.4 %
		Insulin-dependent	52	20.4 %
	Arterial hypertension		237	92.9 %
	Hyperlipidemia		205	80.4 %
	Renal failure (stage)	1–2	135	52.9 %
		3	85	33.3 %
		4	15	5.9 %
		5	20	7.8 %
	PAOD		238	93.3 %
	Smoking history		145	56.9 %
		Pack-years	45.1±24.7	10–120
	BMI (kg/m^2)		26.5±4.3	20.3–33.1
		<18.5	9	3.5 %
		18.5–24.9	88	34.5 %
		25–29.9	119	46.7 %
		30–34.9	31	12.2 %
		35–39.9	6	2.4 %
		>40	2	0.8 %
	Systolic blood pressure (mmHg)		143±19	120–240
Blood testing	INR		1.5±6.5	0.9–103
	PTT (s)		34±12	23–120
	Thrombocytes (G/l)		236±97	34–799
	Creatinine (mg/dl)		1.6±1.6	0.4–8.8
Medication	Single antiplatelet therapy		185	72.5 %
	Double antiplatelet therapy		32	12.5 %
	Oral anticoagulant		50	19.6 %
		Coumarin	37	14.5 %
		Rivaroxaban	13	5.1 %
	Heparin		25	9.8 %

PAOD peripheral arterial occlusive disease, *BMI* body mass index, *INR* international normalized ratio, *PTT* partial thromboplastin time

were excluded from the analysis to avoid the effects of a learning curve.

The FISH device is constructed like a standard access sheath (Fig. 1), but carries an L-shaped piece of SIS consisting of a longer and a shorter part. The shorter part is wrapped around the body of the sheath and kept in place by a sliding tube called a "cuff stabilizer". The longer portion is located inside the sheath body and fixed by a suture that can be withdrawn to fold it against the inner vessel wall (Fig. 2a/b). The SIS therefore seals the puncture defect at the inner and outer surfaces of the vessel wall. Since it is made from one piece, the risk of an intravascular loss is minimized. Figure 2 illustrates the preparation for the FISH procedure. The side-port of FISH was flushed with heparinized saline and left open as a bleeding indicator. The dilator was advanced into the device, and the extravascular part of the L-shaped SIS-fragment, which is wrapped around the outer surface, was wetted with heparinized saline to reduce resistance during implantation. With the use of a standard 0.035-inch guide wire, the introducer sheath was replaced with the FISH device, which was advanced until bleeding through the open side-port indicated its correct placement. Acting as a support, the cuff stabilizer kept the SIS-fragment in the correct position until the deployment was complete (Fig. 2a). To activate FISH, a release wire, which was connected to a violet knob next to the hub of the device, was withdrawn. The sheath hub was advanced into the vessel

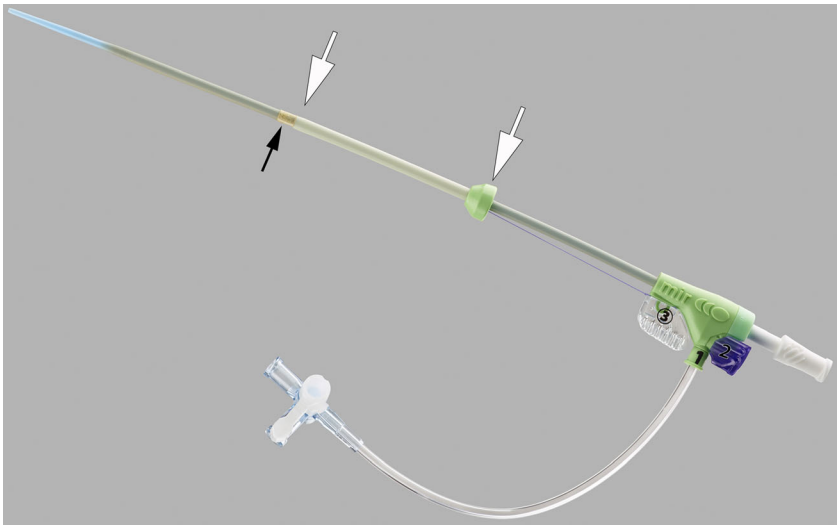

Fig. 1 The FISH™ ControlClose™ device has the look and configuration of a standard access sheath. The sliding tube on the body of the sheath acts as a "cuff stabilizer" (*white arrows*) to stabilize the position of the extravascular part of the L-shaped piece of SIS™ (*black arrow*) that acts as the active component. The side port (#1) is initially left open, as bleeding through the side port indicates correct positioning of the SIS. The violet knob next to the *hub* (#2) activates FISH, because it is connected to the release wire that releases the suture tab (#3) when it is withdrawn. The suture tab (#3) interfolds and presses the intravascular, long part of SIS against the vessel intima. After removal of the sheath and guide wire, hemostasis can be obtained by slightly pressing the cuff stabilizer against the outer vessel wall and simultaneously pulling back the suture tab

until it gained contact with the cuff stabilizer. In order to interfold the intravascular part of the SIS-fragment against the vessel wall, the suture tab was withdrawn until the suture straightened completely and was felt as resistance (Fig. 2b/c). In this step, is advisable to pull gently to avoid withdrawal of the entire SIS-fragment. With the cuff stabilizer kept in position, the sheath and the guide wire were removed. Residual trickling blood flow was stopped by slightly pressing the

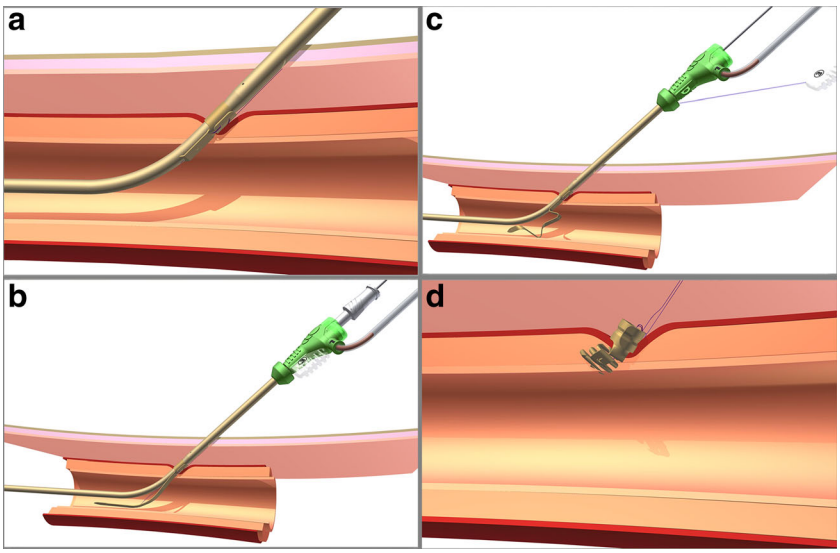

Fig. 2 Steps for implantation of FISH™ ControlClose™ device. The FISH device replaces the access sheath, and is advanced into the vessel until blood flows though the side port, which then can be closed. (**a**) The cuff (smaller outer part of the L-shaped SIS™) is held against the outer surface of the vessel wall by the cuff stabilizer. Withdrawal of the violet knob next to the hub, which is connected to the release wire, releases the suture tab and activates FISH. (**b**) Advancing the sheath hub into the vessel until it gains contact with the cuff stabilizer releases the intravascular part of SIS. (**c**) Pulling back the suture tab until the suture straightens completely and until a resistance is felt, will interfold the intravascular, long part of SIS and press it against the inner vessel wall. With the cuff stabilizer kept in position, the sheath and guide wire can be removed. Residual blood flow can be stopped by slightly pressing the cuff stabilizer against the outer vessel wall and simultaneously pulling back the suture, sealing the puncture defect in an intravascular and extravascular manner. (**d**) When hemostasis is achieved, the cuff stabilizer can be removed, and the suture is cut below skin level. Reprinted with permission of Morris Innovative, Inc., Bloomington, IN, USA

cuff stabilizer against the vessel wall, and by pulling back the suture again and holding that position for a few more seconds until complete hemostasis was achieved. Finally, the cuff stabilizer was removed and the suture was cut below skin level (Fig. 2d). A sterile wound dressing was applied, and the patient was required to remain immobile for 1 h, after which time they were allowed to get up and were asked to walk 10 m under observation to observe whether they could do so without assistance. In cases of VCD failure, the access site was manually compressed for at least 15 min, and a compression bandage was applied for 24 h. These patients were required to remain immobile for 6 h.

Study endpoints and follow-up

The primary feasibility endpoints were as follows: technical success (deployment of the plug at the puncture site and achieving haemostasis with no complications), time to haemostasis (TTH, defined as the time from sheath removal until the stopping of arterial bleeding, recorded in seconds), and time to ambulation (TTA, defined as the time from sheath removal until the patient was able to comfortably walk a distance of 10 m, recorded in hours.). The secondary feasibility endpoint was procedure-related comfort ascertained by the level of pain during implantation using a ten-point visual analogue scale (VAS). The safety endpoints distinguished major from minor complications according to current quality improvement guidelines of the Society of Interventional Radiology [2]. According to their definitions, a major complication (pseudoaneurysm, device embolization, dissection, thrombotic occlusion, access site infection, major bleeding requiring surgery) results in admission to a hospital or an unplanned increase in the level of care, prolonged hospitalization, permanent adverse sequelae, or death. Minor complications (local hematoma, minor bleeding not requiring surgery or transfusion) should not lead to permanent restraints and require only nominal therapy or a short hospital stay for observation.

The follow-up examination on the first post-procedural day assessed the safety endpoints and included inspection of the access area, palpation of the pulses, duplex ultrasound of the puncture site, and measurement of the ankle brachial index. Follow-up medication included lifelong aspirin (100 mg/day). After stent implantation or the use of drug-eluting devices, the patients received an oral loading dose of 300 mg clopidogrel on the first post-procedural day, which was continued at 75 mg/day for 1 or 3 months. In patients who were receiving vitamin K antagonists or factor Xa inhibitors prior to the intervention, tissues were resaturated.

Statistical analysis

IBM SPSS statistical software, version 22.0 (IBM Corp., Armonk, NY, USA) was used for calculation. A p value of <0.05 was considered statistically significant. Technical success, TTH and TTA, minor and major complications, cardiovascular risk factors and medication were reported in absolute values and percentages. Fisher's exact test and the chi-square test were applied to evaluate the association between categorical variables and post-interventional access complications. The association between interval-scaled variables and post-interventional access complications was evaluated using bivariate correlation analysis.

Table 2 Procedural data of the study cohort (n=225)

		Number	Percentage or range
Type of procedure	Diagnostic	8	3.1 %
	Intervention	247	96.9 %
Kind of intervention	PTA	223	87.5 %
	Embolisation	10	3.9 %
	Thrombectomy	2	0.8 %
	Thrombolysis	8	3.1 %
	TACE	1	0.4 %
	Renal denervation	1	0.4 %
	Removal of foreign bodies	1	0.4 %
Puncture direction	Antegrade	142	55.7 %
	Retrograde	113	44.3 %
Duration of procedure (min)		61.1±189	4–2400
Sheath in place (min)		71.3±221.7	7–2405
Heparin i.a.	5000	248	97.3 %
	7500	3	1.2 %
	10,000	2	0.8 %

PTA percutaneous transluminal angioplasty, *TACE* transcatheter arterial chemoembolization, *i.a.* intra-arterial

Results

Patient cohort

Two hundred fifty-five patients (183 men), with an average age of 71.4±10.9 years (range 36–98), were enrolled. The baseline characteristics are presented in Table 1. The distribution of cardiovascular risk factors was high, with 103 (40.4 %), 237 (92.9 %) and 205 (80.4 %) patients suffering from diabetes, arterial hypertension and hyperlipidemia, respectively. The average thrombocyte volume (236±97 G/l) and partial thromboplastin time (PTT; 34±12 s) were within normal range, but the international normalized ratio (INR; 1.5 ±6.5) was slightly elevated. Prior to the intervention, 185 (72.5 %) and 32 (12.5 %) patients were taking single and double antiplatelet medications, respectively. Body mass index (BMI) above 25 kg/m^2 was observed in 157 (61.6 %) patients.

Procedural data

The number of endovascular interventions was significantly higher than the number of diagnostic procedures (247/96.9 % vs. 8/3.1 %; $p<0.001$). Percutaneous transluminal angioplasty (PTA) was the most frequent intervention (223/87.5 % vs. 23/12.5 %; $p<0.001$; Table 2). The CFA was the most frequent access vessel (CFA: 237/92.9 %; SFA: 15/5.9 %; bypass: 2/0.8 %; shunt: 1/0.4 %; Table 3), and neither access site was significantly preferred (left: 123/48.2 %; right: 132/51.8 %; $p<0.738$). There was no significant difference in puncture direction (antegrade: 142/55.7 %; retrograde: 113/44.3 %). All retrograde punctures occurred at the CFA. The most frequently used sheath and FISH device size was 6 F (237/92.9 %) at an average access vessel diameter of 6.5±1.7 mm. A 7 F sheath and a 7 F FISH were used in 18 cases (7.1 %). The average duration of the entire endovascular procedure was 61.1±189 min, ranging from 4 to 2400 min (long-term thrombolysis overnight), while the time for sheath localization in situ was longer, at 71.3±221.7 min, ranging from 7 to 2405 min.

Technical results

Successful deployment of FISH was achieved in 252 of 255 patients (98.8 %; Table 4). Primary device failure occurred in three cases (1.2 %), but haemostasis was achieved by manual compression. The average TTH was 11.3±26.9 s, and average TTA was 73.0±126.3 min. Only 12 patients (4.7 %) experienced pain during the implantation of FISH, in a range of 1.4–4.8 on the VAS and an average of 3.1±1.7, but implantation was successful in all of these.

The overall complication rate was 3.6 %, and it comprised four cases (1.6 %) with major complications and five (2.0 %) with minor complications, which were all small local hematomas, with an average size of 3.4±1.5 cm. The most frequent major complication was a pseudoaneurysm (3/1.2 %), but these patients did not obey immobilization instructions and left the bed immediately after they were back in the ward.

Table 3 Characteristics of the access vessel and of FISH^{TM} ControlClose^{TM} (n=255)

		Number	Percentage or range
Access vessel	CFA	237	92.9 %
	SFA	15	5.9 %
	Bypass or shunt	3	1.2 %
Side	Left / right	123 / 132	48.2 % / 51.8 %
	Both	7	2.7 %
Sheath size	6 F	237	92.9 %
	7 F	18	7.1 %
FISH^{TM} ControlClose^{TM} size	6 F	237	92.9 %
	7 F	18	7.1 %
Vessel diameter (mm)		6.5±1.7	2.7–14.5
Calcification	None	63	24.7 %
	Discrete	61	23.9 %
	Moderate	79	31 %
	Severe	52	20.4 %
Plaque		63	24.7 %
Patch		20	7.8 %
Tortuosity		69	27.1 %
Arteriotomy (without closure device) within last 30 days		11	4.3 %

CFA common femoral artery, *SFA* superficial femoral artery, *F* French

Table 4 Technical results, minor and major complication rates of FISH™ ControlClose™ (n=255)

		Number	Percentage or range
Technical success		252	98.8 %
	Compression bandage in case of failure	3	1.2 %
Time to hemostasis (s)		11.3±26.9	3 - 300
Time to ambulation (min)		73.0±126.3	60 – 1440
Pain during implantation		12	4.7 %
	Severity (VAS 10 steps)	3.1±1.7	1.4–4.8
Bed rest (hours)		1.21±2.1	1 - 24
Major complications		4	1.6 %
	Bleeding requiring surgery or transfusion	1	0.4 %
	Pseudoaneurysm	3	1.2 %
Minor complications		5	2.0 %
	Small hematomas	5	2.0 %

VAS visual analogue scale

However, none of these required surgery; all were treated by sonographic compression and/or thrombin injection. One patient required surgery due to retroperitoneal bleeding that affected the haemoglobin level (1/0.4 %).

The major and the overall complication rates correlated positively with the PTT (PR=0.187, p=0.003; PR=0.215, p=0.001). There was no difference in overall complication rates based on puncture direction (p=0.732), sheath size (p=0.982) or any other characteristic of the access vessel (e.g., level of calcification: p=0.602; plaque: p=0.963; tortuosity: p=0.738, patch: p=0.613), nor was there any association with age (p=0.453), BMI (p=0.994), dwell time of the sheath (p=0.699), medication, or any cardiovascular risk factor (diabetes: p=0.813; hypertension: p=0.646; hyperlipidemia: p=0.132; smoking: p=0.128; renal insufficiency; p=0.770). The distribution of all complications and device failures was homogenous throughout the study period.

Subgroup analysis of re-punctures

After a period of 155±128.8 days, 32 (12.5 %) patients of the initial study cohort underwent re-puncture (Table 5). All re-punctures were uncomplicated, and no defacing resistance or luminal narrowing was observed (Fig. 3). Division of this subgroup according to the time at which FISH was completely resolved (90 days) revealed four patients (12.5 %) who had a manual palpable resistance at the access vessel, but no defacing resistance of the vessel during re-puncture (0–90 days/>90 days: 2.0/0.8 %). Re-puncture was performed in two of these on the first post-procedural day. The remaining 28 patients (87.5 %) showed no resistance whatsoever (0–90 days: 8/3.1 %; >90 days: 20/7.8 %). There was no observance of device displacement or peripheral embolization.

Table 5 Re-punctures after implantation of FISH™ ControlClose™ (n=255)

		Number	Percentage or range
Re-punctures		32	12.5 %
	After interval	155±128.8	1–500
	0–1 days	2	0.8 %
	2–90 days	8	3.1 %
	>90 days	22	8.6 %
Access site scarring			
0–90 days	None	8	3.1 %
	Palpable resistance, no resistance during puncture	2	0.8 %
	Palpable resistance, resistance during puncture	0	0.0 %
>90 days	None	20	7.8 %
	Palpable resistance, no resistance during puncture	2	0.8 %
	Palpable resistance, resistance during puncture	0	0.0 %
Device displacement/embolization caused by re-puncture		0	0.0 %

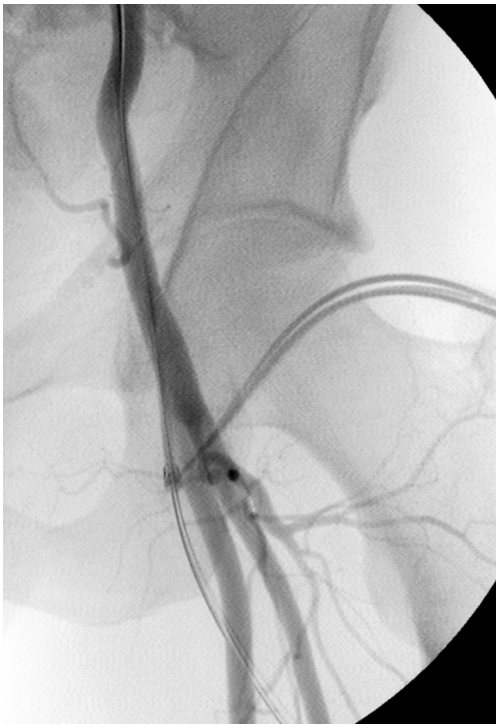

Fig. 3 Angiographic image of the left CFA on the first day after the implantation of the FISH™ ControlClose™. No intravascular foreign body or irregularity of the vessel lumen can be seen. No device displacement occurred in this early re-puncture

Discussion

VCDs were designed and developed in order to achieve satisfactory bleeding control and to reduce access-related complications, patient discomfort and post-procedural monitoring time after arteriotomy [11]. The quality improvement guidelines for vascular access and closure devices released by the Society of Interventional Radiology state that most of the currently available data derive from cardiovascular interventions and low-risk procedures among patients with low to moderate mortality risk, but data regarding interventional radiologic procedures are limited [2]. VCD complication rates do not significantly exceed those associated with manual compression, but they have introduced new VCD-related complications, including device failure, infection, and embolization of device components or acute thromboembolic occlusion. However, the advantages of VCDs, especially the fast ambulation, accelerated workflow, and shorter periods of patient immobilization, are important in an outpatient setting, and spur the growth of VCDs. In addition, patients are increasingly undertaking multi-agent anticoagulation and antiplatelet regimens, which raises the demand for a safe and stable closure of vascular access [12].

The VCDs currently available can be divided into three categories [2–4]. Passive closure devices prevent embolization or arterial occlusion as a result of their explicit extravascular components, but they require additional manual compression and encounter higher failure rates, especially in obese or cachectic patients and in those receiving multi-agent anticoagulation therapy [2, 13]. In contrast, active closure devices involve the implantation of some non-bioabsorbable foreign material, such as a mechanical plug device, suture, or nitinol clip and pro-coagulant material. The bioabsorbable components usually consist of bovine collagen, thrombin, polylactic acid or polyethylene glycol, and resolve within 60–90 days. They pose a potential risk of allergic reaction and a higher risk of infection and peripheral embolization. Some prohibit re-puncture within the first 30 days after implantation to avoid device dislocation and late failure. Collagen-based plugs, in particular, induce not only clot formation, but a local peri-adventitial inflammatory response that results in significant scarring and luminal narrowing, which are palpable for up to 90 days (personal observation; animal studies [8]). Considering the improving long-term survival rates after endovascular interventions, and the progressively greater possibility of re-punctures due to repetitive transarterial chemoembolization or selective internal radiation therapy in oncologic diseases and PTA in peripheral arterial occlusive disease (PAOD), scarring is of concern, as it may limit the future use of this access vessel increase the risk of access-related complications due to reduced vessel conformability, elasticity and luminal diameter.

FISH deploys a plug consisting of bioabsorbable SIS, which is well established for the treatment of burns [9], because it improves the wound-healing process and prevents scarring. Under development since 2000, the premise behind FISH was to be a biocompatible VCD for vessel diameters starting at 3 mm, with a minimal risk of peripheral embolization. The plug acts in an intra- and extraluminal manner to achieve haemostasis quickly and safely. In contrast to other VCDs, whose intra- and extraluminal sealants are divided into separate parts, the FISH plug consists of only one piece, reducing the risk of intravascular dislodgement. Because FISH sought to combine the function of a sheath and a VCD, there are two models available: FISH ControlClose, which incorporates a cuff stabilizer and provides arterial closure over the wire, and FISH CombiClose™, which additionally maintains access during the endovascular procedure.

FISH ControlClose works like an access sheath, which is used to implant a small L-shaped piece of SIS to seal the puncture defect. SIS contains extracellular matrix and growth factors that induce healing rather than inflammation. Aside from the initial registration trial of the US Food and Drug Administration from 2004 to 2006, there are no available data available yet on FISH. This first prospective study including 255 patients with transfemoral access shows that FISH is an efficient and safe biodegradable mechanical plug device with a high technical success rate (98.8 %) and tolerably low minor and major complication rates (2.0 % and 1.6 %, respectively), based on current recommendations [2].

The overall failure rate was as low as or lower than those reported in meta-analyses of other VCDs, and met the criteria of the Society of Interventional Radiology [2, 14, 15]. The three cases with primary device failure had a very steep puncture channel in common, which caused a rectangular entry of FISH into the vessel and impaired its release. There was no device embolization and no infection of the device or of the puncture site. The only minor complication was a small local hematoma, which did not affect the length of in-hospital stay. One patient with a major complication required surgery, but achieving haemostasis in this case was complicated by additional risk factors: the patient was receiving triple-antiplatelet therapy due to a severe PAOD and coronary heart disease (CHD), and had already undergone a dozen interventions with access over the left CFA. Three other patients developed a pseudoaneurysm that was successfully treated by ultrasound-assisted compression combined with thrombin injection. Reconstruction of the post-procedural course of these patients revealed that the period of immobilization was too short in all cases, as they had left the bed when unobserved, due to inconvenience and/or non-compliance. All complications and device failures were homogenously distributed across the study period. In order to avoid the effects of a learning curve, one experienced interventionalist performed all arterial punctures and FISH deployments. Moreover, the initial ten implant procedures were excluded, although no device failure or complication occurred.

Prior studies have reported that the average TTH and TTA (11.3±26.9 s; 73.0±126.3 min) were reduced compared to the institutional standard of manual compression (678±252 s; 360±150 min) [11, 16]. FISH was well accepted in all patients, and no allergic reaction was observed. Only 12 patients (4.7 %) experienced pain during implantation, and the average level of pain never exceeded the median of the visual analogue scale, and was fairly low, at 3.1±1.7. Neither the type of access vessel nor the puncture direction had an impact on complication rates, as FISH is multifunctional, independent of the type and length of sheath, and available in 6 F and 7 F, adapting to a broader range of vessel diameters and able to seal defects of 5 F–7 F sheath systems. In contrast to other VCDs, morphological impairment of the access vessel such as calcifications or obesity did not affect the complication rate. Only the PTT correlated positively with the rate of complications, which is reasonable given that a high PTT promotes bleeding complications. No other predictor for complications or device failure was observed, although the average age of the study cohort was high, and a high incidence of cardiovascular risk factors were encountered.

One disadvantage of mechanical plug devices is the risk of secondary scarring caused by peri-adventitial inflammation. Objective evaluation of scarring is difficult, however, because there is no standard scoring system. The results of this study suggest that the biodegradable FISH device has overcome this limitation: among the 32 patients who underwent re-puncture, there was no evidence of luminal narrowing or relevant scarring deflecting the puncture needle, and patients did not suffer from device displacement or embolization. Only four patients had a manually palpable resistance, which did not deface the puncture needle. Two underwent re-puncture on the day after the initial puncture, and in these two, the resistance was explained by local induration due to slight bleeding and swelling of the vessel wall and residuals of FISH, which resolved after 90 days. The other two underwent re-puncture after 90 days. One was the patient discussed above, who required surgery, which causes more distinctive scarring. The other had suffered a groin infection after coronary PTA 5 years ago.

Finally, certain limitations must be addressed. First, this is a single-arm evaluation of FISH that lacks a randomized comparison to manual compression, although a corresponding trial is under preparation. Second, the follow-up period was rather short, but the study included a subgroup analysis of patients who underwent re-puncture after 155±128.8 days, and no one in this group reported any subjective discomfort. Moreover, re-puncture was uncomplicated in all cases, and 87.5 % showed no resistance of the groin whatsoever. A third limitation is the heterogeneity of the cohort, which may have biased the risk factor analysis. However, this is a feasibility study, and the rather unselective cohort with a high average age, high incidence of cardiovascular risk factors, and various anticoagulation medications represents a realistic patient group, although further evaluations in larger subgroups with specific risk factors are necessary.

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Written informed consent was obtained from all subjects (patients) in this study. Some study subjects or cohorts were reported at the 2014 RSNA meeting. Methodology: prospective, observational, performed at one institution.

References

1. Patel MR, Jneid H, Derdeyn CP et al (2010) Arteriotomy closure devices for cardiovascular procedures: a scientific statement from the American Heart Association. Circulation 122:1882–1893
2. Sheth RA, Walker TG, Saad WE et al (2014) Quality improvement guidelines for vascular access and closure device use. J Vasc Interv Radiol 25:73–84
3. Hon LQ, Ganeshan A, Thomas SM, Warakaulle D, Jagdish J, Uberoi R (2010) An overview of vascular closure devices: what every radiologist should know. Eur J Radiol 73:181–190

4. Treitl M, Eberhardt KM, Maxien D, Behrends B, Reiser MF (2013) Arterial closure devices. What device for which clinical situation? Radiologe 53:230–245
5. Schulz-Schupke S, Helde S, Gewalt S et al (2014) Comparison of vascular closure devices vs manual compression after femoral artery puncture: the ISAR-CLOSURE randomized clinical trial. JAMA 312:1981–1987
6. Nelson PR, Kracjer Z, Kansal N et al (2014) A multicenter, randomized, controlled trial of totally percutaneous access versus open femoral exposure for endovascular aortic aneurysm repair (the PEVAR trial). J Vasc Surg 59:1181–1193
7. Chevalier B, Lancelin B, Koning R et al (2003) Effect of a closure device on complication rates in high-local-risk patients: results of a randomized multicenter trial. Catheter Cardiovasc Interv 58:285–291
8. Gargiulo NJ 3rd, Veith FJ, Ohki T et al (2007) Histologic and duplex comparison of the Perclose and Angio-Seal percutaneous closure devices. Vascular 15:24–29
9. Zhu J, Clark RA (2014) Fibronectin at select sites binds multiple growth factors and enhances their activity: expansion of the collaborative ECM-GF paradigm. J Investig Dermatol 134:895–901
10. Huppert P, Tacke J, Lawall H, Deutschen Gesellschaft fur AG (2010) S3 guidelines for diagnostics and treatment of peripheral arterial occlusive disease. Radiologe 50:7–15
11. Koreny M, Riedmuller E, Nikfardjam M, Siostrzonek P, Mullner M (2004) Arterial puncture closing devices compared with standard manual compression after cardiac catheterization: systematic review and meta-analysis. JAMA 291:350–357
12. Popma JJ, Satler LF, Pichard AD et al (1993) Vascular complications after balloon and new device angioplasty. Circulation 88: 1569–1578
13. Lewis-Carey MB, Kee ST (2003) Complications of arterial closure devices. Tech Vasc Interv Radiol 6:103–106
14. Das R, Ahmed K, Athanasiou T, Morgan RA, Belli AM (2011) Arterial closure devices versus manual compression for femoral haemostasis in interventional radiological procedures: a systematic review and meta-analysis. Cardiovasc Intervent Radiol 34:723–738
15. Reekers JA, Muller-Hulsbeck S, Libicher M et al (2011) CIRSE vascular closure device registry. Cardiovasc Intervent Radiol 34: 50–53
16. Biancari F, D'Andrea V, Di Marco C, Savino G, Tiozzo V, Catania A (2010) Meta-analysis of randomized trials on the efficacy of vascular closure devices after diagnostic angiography and angioplasty. Am Heart J 159:518–531