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First in Human Clinical Feasibility Study of Endovascular Navigation with Fiber Optic RealShape (FORS) Technology

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WHAT THIS PAPER ADDS

Fiber Optic RealShape (FORS) technology is a new method to visualise endovascular guidewires and catheters inside the body in 3D, in real time. FORS functions as an add on to conventional fluoroscopy and uses integrated multicore optical fibres to track and visualise the entire devices based on light rather than X-ray. This paper contains the first in human use of FORS technology in (regular and complex) endovascular aortic repair and peripheral lesion repair. This exploratory study demonstrates the feasibility and potential of this technology in clinical practice and forms a foundation for future clinical research.

Objective: Endovascular procedures are conventionally conducted using two dimensional fluoroscopy. A new technology platform, Fiber Optic RealShape (FORS), has recently been introduced allowing real time, three dimensional visualisation of endovascular devices using fiberoptic technology. It functions as an add on to conventional fluoroscopy and may facilitate endovascular procedures. This first in human study assessed the feasibility of FORS in clinical practice.

Methods: A prospective cohort feasibility study was performed between July and December 2018. Patients undergoing (regular or complex) endovascular aortic repair (EVAR) or endovascular peripheral lesion repair (EVPLR) were recruited. FORS guidance was used exclusively during navigational tasks such as target vessel catheterisation or crossing of stenotic lesions. Three types of FORS enabled devices were available: a flexible guidewire, a Cobra-2 catheter, and a Berenstein catheter. Devices were chosen at the physician's discretion and could comprise any combination of FORS and non-FORS devices. The primary study endpoint was technical success of the navigational tasks using FORS enabled devices. Secondary study endpoints were user experience and fluoroscopy time.

Results: The study enrolled 22 patients: 14 EVAR and eight EVPLR patients. Owing to a technical issue during start up, the FORS system could not be used in one EVAR. The remaining 21 procedures proceeded without device or technology related complications and involved 66 navigational tasks. In 60 tasks (90.9%), technical success was achieved using at least one FORS enabled device. Users rated FORS based image guidance "better than standard guidance" in 16 of 21 and "equal to standard guidance" in five of 21 procedures. Fluoroscopy time ranged from 0.0 to 52.2 min. Several tasks were completed without or with only minimal X-ray use.

Conclusion: Real time navigation using FORS technology is safe and feasible in abdominal and peripheral endovascular procedures. FORS has the potential to improve intra-operative image guidance. Comparative studies are needed to assess these benefits and potential radiation reduction.

Keywords: Endovascular surgery, Endovascular navigation, Fiber optic technology, Imaging, Radiation, Three dimensional
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INTRODUCTION

In recent decades, an enormous shift has occurred from open operations to fluoroscopically guided endovascular interventions. However, fluoroscopically guided navigation has several important limitations. While guidewires and catheters are being manipulated in a 3D space, these movements are presented to the physician in a 2D projection. This limits the ability to estimate the spatial

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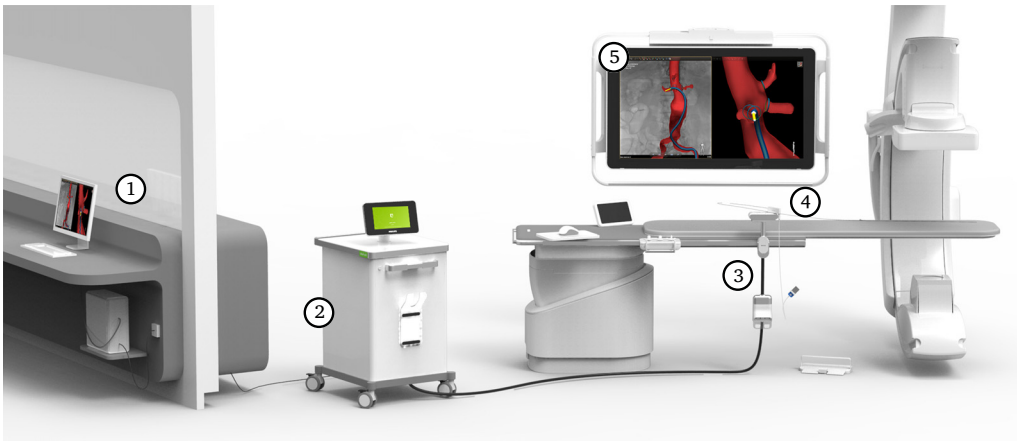

Figure 1. The Fiber Optic RealShape (FORS) system with workstation (1), trolley (2), docking base (3), docking top that connects to the FORS enabled devices (4). The FORS enhanced devices are visualised in context of an anatomical roadmap on the screen (5). Copyright © (2020) Koninklijke Philips N.V. All rights reserved.

relationship between the endovascular device and the vascular anatomy or to identify the shape and pointing direction of the device. These factors complicate conceptually basic tasks such as navigation through tortuous arteries and target vessel catheterisation. Further, fluoroscopy projections are shown as grayscale images. This reduces the ability to differentiate between visible structures on the image, especially if these have similar radiopaque characteristics.

Besides these qualitative limitations, exposure to X-ray radiation poses health risks for both patients and medical staff who are exposed to radiation throughout their career.[1–3] The growing number of endovascular procedures and their increasing complexity raises concerns about long term risks. Therefore, the development of new endovascular guidance technologies, without these drawbacks, is of utmost importance.

Fiber Optic RealShape (FORS) technology offers 3D visualisation of specially designed endovascular devices comprising guidewires and catheters by means of light instead of X-ray. The research group recently reported the preclinical feasibility and safety of FORS technology in phantom and porcine models.[4] The potential of FORS technology was demonstrated by yielding positive results in technical success rates, user experience, accuracy, and safety. In the present first in human clinical study, the primary objective was to evaluate feasibility of endovascular navigation with FORS enabled catheters and guidewires in a clinical environment, thereby using FORS based guidance as an add on to standard Xray guidance.

MATERIALS AND METHODS

Study design

This was a prospective, single arm feasibility study at a single centre. The University Medical Center Utrecht Medical Ethics Committee approved the study protocol (METC 18/422), and all patients signed an informed consent prior to enrolment.

The Fiber Optic RealShape system

The FORS equipment sends laser light through a multicore optical fiber, the FORS fiber optic sensor, and then receives and analyses the returning light that runs through this optic sensor. Twists and bends in the optical fiber influence the wavelength spectrum of the light. By analysing the wavelength spectra of the returned light, it is possible to reconstruct the 3D shape of the full length of the multicore optical fiber. Because these optical fibers are integrated in guidewires and catheters, FORS allows radiation free visualisation of the endovascular devices in real time and in 3D. The clinical set up of the FORS system is shown in Figs. 1 and 2.

For easy differentiation between the devices, the wire is shown in a bright yellow colour and catheters in distinctive blue, and for optimisation of visibility, the devices are shown 50% thicker than their actual size. The devices are tethered. Guidewires are only front loadable, while catheters are both front and back loadable. All FORS enabled devices are radiopaque like regular guidewires and

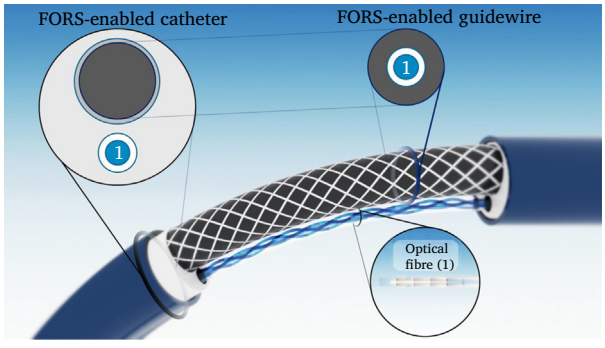

Figure 2. Fiber Optic RealShape (FORS) enhanced guidewire and catheter. These devices have a secluded sensor lumen with an integrated multicore optical fiber (1), through which laser light is transmitted. Copyright © (2020) Koninklijke Philips N.V. All rights reserved.

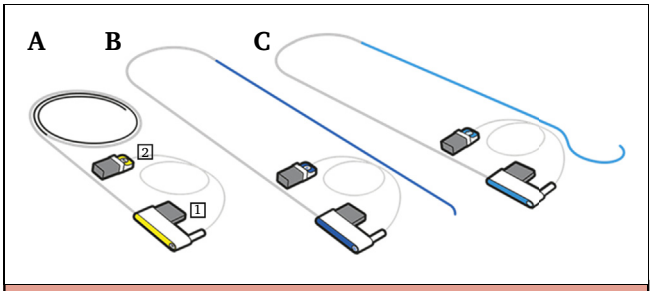

Figure 3. The three available Fiber Optic RealShape (FORS) enabled devices. The floppy guidewire (A), Berenstein catheter (B), and Cobra 2 catheter (C). The docking fin (1) of the devices is connected to the docking top, and the optical connector (2) is connected to the docking base. Copyright © (2020) Koninklijke Philips N.V. All rights reserved.

angiography catheters and are also fully compatible with conventional guidewires and catheters.

Three endovascular devices equipped with FORS technology were used in this study (Fig. 3):

- A 0.035 inch angled, hydrophilic angiographic guidewire with a flexible nitinol core and a floppy tip, and an in body working length of 120 cm.
- A 5.5F Cobra C2 angiographic catheter with an in body working length of 80 cm.
- A 5.5F Berenstein angiographic catheter with an in body working length of 80 cm.

FORS works in conjunction with a fluoroscopy system to create anatomical overlays of the arterial vessels from regular digital subtraction angiograms (DSA) or X-ray images. Also, pre-operative imaging data, like a CT scan, can be used to create a 3D overlay of the patient anatomy.

Patients

The target population of this study consisted of patients with abdominal aortic aneurysms (AAA) or iliac aneurysms (IA), or both, who were planned for endovascular repair (EVAR), and patients with peripheral arterial disease with haemodynamically significant stenotic lesions in the common iliac artery (CIA), superficial femoral artery (SFA) or popliteal artery (PA), or with a popliteal aneurysm planned for endovascular peripheral lesion repair (EVPLR). Inclusion and exclusion criteria are listed in Table 1.

Study procedures

Procedures were performed by an experienced vascular surgeon (J.H. or C.H.) or an experienced interventional radiologist (E.V.) as the first operator. These clinicians were familiar with the FORS system as they have not only been involved in the development process of the FORS technology and devices but also used the FORS system in an animal study and in several procedures on phantoms.[4] Before patients were enrolled into the study, the whole staff underwent hands on training to optimise and standardise the workflow with the FORS system.

Table 1. **Inclusion and exclusion criteria of patients for a feasibility study of endovascular navigation with Fiber Optic RealShape (FORS) technology**

Inclusion criteria	Exclusion criteria
Age >18 years	Subjects unable to understand verbal and/or written informed consent
Signed informed consent	Emergency procedure
Scheduled for elective endovascular procedure for stenotic or aneurysm pathology	Subjects unwilling or unable to comply with the protocol
Anatomy suitable for the investigational medical devices (5.5 F 80 cm Cobra C2 catheter, and/or 5.5 F 80 cm Berenstein catheter, and a 0.035 inch 120 cm guidewire	Intolerance of contrast media
	Current participation in a concurrent trial that may confound study results

Procedures were done in a hybrid operating room with a ceiling mounted C arm (Allura FD20 Flexmove with ClarityIQ; Philips Medical Systems Nederland B.V., Best, The Netherlands). After regular patient preparation and vascular access, the operator performed 2D—3D registration of X-ray to a pre-operative computed tomography angiogram (if available) to create the arterial anatomical overlay. Then, the operator acquired two X-ray images at $> 30^{\circ}$ different angles of the FORS enabled catheter and guidewire for registration of these devices. Subsequently, FORS enabled devices were ready to use. Endovascular tasks were started with FORS enabled guidewire and/or FORS enabled catheter, but during the task the operator could switch to any available catheter and guidewire, as in regular practice. However, the use of FORS enabled catheters and guidewires was encouraged.

The FORS system was intended to be used during the navigational part of the procedures only, whereas therapeutic tasks, such as stent graft deployment and balloon angioplasty, were performed with conventional X-ray guidance, as in standard practice. The intended endovascular tasks with the FORS enabled devices are summarised in Table 2, examples include catheterisation of the contralateral limb, catheterisation of a target vessel, or crossing of a stenotic lesion.

Study end points

The primary study end point was the technical success of the intended endovascular tasks during aortic and peripheral endovascular procedures. A task was considered a technical success if the target vessel or contralateral stent graft limb were catheterised using a FORS enabled catheter and/or guidewire with the catheter and guidewire in a stable position. Technical success was confirmed by fluoroscopy or DSA, or both.

Table 2. Intended tasks with Fiber Optic RealShape (FORS) technology enabled devices

Intended task with FORS enabled devices during procedure
Endovascular aortic repair (EVAR)
Catheterisation of the aorta above the aneurysm
Catheterisation of the contralateral limb of the stent graft
Catheterisation of the target aortic side branches for fenestrated or branched EVAR
Catheterisation of internal iliac artery for iliac branched EVAR
Endovascular peripheral lesion repair
Catheterisation of the target vessel (iliac, femoral or popliteal artery)
Aortic crossover manoeuvre
Crossing of the stenotic lesion

As secondary study end point, qualitative scores were collected from the first operator on performance parameters of FORS based image guidance. The scored parameters are listed in Table 3. An additional secondary study end point was fluoroscopy time.

Statistical methods

There are no studies available which report on the navigation success rate when limiting the devices to a guidewire, a Berenstein, and a Cobra 2 catheter. Reported success rates for comparable navigations without this limitation are between 90.5% and 100%.[4,5] For this exploratory study, a reference rate of 92% was assumed. Sample size calculation with an 80% power, and a Wald one sided 95% confidence interval resulted in a sample size of at least 60 endovascular tasks. After reaching these, enrolment in the study was considered complete. Qualitative scores by the operators were pooled for the complete data set as well as for the EVAR and EVPLR groups individually.

For secondary end points, the mean and standard deviation were calculated for the overall cohort as well as for the patients in the EVAR and EVPLR groups. Statistical analysis was performed with SAS (Version 9.4, SAS institute Inc., Cary, NC, USA).

RESULTS

The study enrolled 22 patients who met the inclusion/exclusion criteria. Procedures were performed between 31 July 2018 and 11 December 2018. In one patient (patient 11), the FORS system had a technical start up issue and could not be used. The patient was treated with conventional devices only and was therefore excluded from analysis.

The 21 patients, five women (24%) and 16 men (76%), had a mean age of 68 years (range, 48–89 years). The mean body mass index was 27.6 kg/m^2 (range, 21–34 kg/m^2). The planned intervention was EVAR in 13 patients and EVPLR in eight patients. Baseline characteristics and comorbidities are specified in Tables S1 and S2, respectively. There were 67 endovascular tasks performed with at least one attempt with a FORS enabled guidewire and/or a FORS enabled catheter. Detailed information about the type of intervention is given in Table S3.

Table 3. Qualitative scoring of performance of Fiber Optic RealShape (FORS) technology parameters in endovascular tasks during endovascular aortic (EVAR) or peripheral lesion repair (EVPLR) in 21 patients

Performance of FORS parameter	Scoring in EVAR patients (n = 13)	Scoring in EVPLR patients (n = 8)
The usefulness of the FORS based image guidance during navigation		
1: Better: More useful compared with standard practice	10/13	6/8
2: At par: moderately useful, compared with standard practice	3/13	2/8
3: Worse: not useful compared with standard practice	0/13	0/8
The quality of the visualisation and registration of the FORS based device image with Xray		
1: Accurate	4/13	7/8
2: Slightly off but acceptable	8/13	1/8
3: Not accurate and not acceptable	1/13	0/8
The responsiveness of the FORS based device visualisation		
1: Responsive enough for device manipulation	13/13	8/8
2: Not responsive enough for device manipulation	0/13	0/8
The ability to steer the FORS based device during navigation (torquability, pushability, trackability)		
1: Better than devices in current practice	0/13	0/8
2: At par with devices in current practice	13/13	8/8
3: Worse than devices in current practice	0/13	0/8
The compatibility of the FORS device when used in combination with ancillary devices		
1: Good	13/13	8/8
2: Moderate	0/13	0/8
3: Poor	0/13	0/8
The ability to inject contrast agent manually through the FORS catheter compared with your current practice		
1: Good	12/12	5/5
2: Moderate	0/12	0/5
3: Poor	0/12	0/5

One of these 67 tasks was retrospectively excluded from analysis, because one of the inclusion criteria was violated. Recanalisation of the SFA in this patient was performed from the contralateral groin, which required a working length of >80 cm.

Of the remaining 66 tasks, 53 (80%) were performed during EVAR procedures, and 13 (20%) during the EVPLR procedures. Seven tasks (10.6%) were performed from left brachial access, and the others from right or left femoral access. The specification of the tasks is reported in Table 4.

Table 4. Technical success rate with Fiber Optic RealShape (FORS) technology enabled devices in endovascular tasks during endovascular aorto-iliac or peripheral lesion repair in total 21 patients

Procedure and endovascular task	Tasks − *n*	Technical success − *n*	Proportion (90% CI)
Endovascular aorto-iliac repair			
Catheterisation of thoracic aorta from groin	21	21	1.00 (1.000–1.000)
Catheterisation of abdominal aortal from left arm	1	1	1.00 (1.000–1.000)
Catheterisation of coeliac trunk	3	2	0.67 (0.219–1.000)
Catheterisation of superior mesenteric artery	5	5	1.00 (1.000–1.000)
Catheterisation of right renal artery	5	4	0.80 (0.506–1.000)
Catheterisation of left renal artery	5	5	1.00 (1.000–1.000)
Catheterisation of fenestrated cuff (after partial deployment)	1	1	1.00 (1.000–1.000)
Cross over aortic bifurcation	1	1	1.00 (1.000–1.000)
Catheterisation of contralateral limb stent graft	9	7	0.78 (0.550–1.000)
Catheterisation of internal iliac artery	2	2	1.00 (1.000–1.000)
All	53	49	0.92 (0.865–0.984)
Endovascular peripheral lesion repair			
Cross over aortic bifurcation	2	1	0.50 (0–1.000)
Catheterisation of abdominal aorta from groin	2	2	1.00 (1.000–1.000)
Recanalisation occluded (stent) in common iliac artery	1	1	1.00 (1.000–1.000)
Crossing common iliac artery stenosis	3	3	1.00 (1.000–1.000)
Recanalisation occluded internal iliac artery	1	0	0.00 (0–0)
Crossing superficial femoral artery stenosis	2	2	1.00 (1.000–1.000)
Crossing popliteal artery stenosis	1	1	1.00 (1.000–1.000)
Crossing popliteal aneurysm	1	1	1.00 (1.000–1.000)
All	13	11	0.85 (0.682–1.000)
Total	66	60	0.91 (0.851–0.967)

CI = confidence interval.

Primary end point

Sixty of the 66 tasks (90.9%) were successfully performed with at least a FORS enabled catheter or FORS enabled guidewire. Forty-four tasks (66.7%) were successfully completed with both a FORS enabled catheter and FORS enabled guidewire.

In 16 tasks (24.2%) successful catheterisation was achieved with a FORS enabled guidewire in combination with a regular non-FORS enabled catheter. In five of these 16 tasks, the targeted vessels were anatomically incompatible with the available shapes of FORS enabled catheters. Non-FORS SOS catheters (Soft-Vu, Angiodynamics, Inc. Queensbury) were successfully used. In one of these tasks, a SOS catheter was used with FORS enabled guidewire for embolisation of the hypogastric artery. To avoid extra procedure steps, these devices were also used for the next task (catheterisation of the thoracic aorta).

In five other tasks that were performed with a FORS enabled guidewire with a non-FORS catheter, a non-FORS pigtail catheter was needed in the aorta to perform angiography. In these tasks, the pigtail catheters were successfully navigated over the FORS wire. In the remaining five tasks (in two patients) technical issues were the reason for using a non-FORS enabled catheter.

Five catheterisation tasks (7.6%) were started with FORS enabled devices but were switched to non-FORS catheters and non-FORS guidewires. Four of these tasks were successfully performed with SOS-0 and SOS-2 catheters. Because the operators knew in advance that these catheters would need to be changed over the wire when the targets were cannulated, they decided to combine the catheters with regular guidewires, which are back loadable, in contrast to the FORS enabled guidewires.

In the fifth task, the contralateral limb of a stent graft was cannulated with FORS enabled devices; however, the FORS enabled Berenstein catheter did not follow over the wire into the stent graft. Because the wire was not back loadable, the wire also had to be removed from the contralateral limb. The devices were changed for a regular non-FORS enabled guidewire (Radifocus, Terumo Medical, Tokyo, Japan) and comparably shaped regular catheter (Impress, Merit Medical Systems, South Jordan, USA). Catheterisation of the contralateral limb was then performed successfully.

One task, recanalisation of an occluded internal iliac artery (IIA), failed. The FORS enabled guidewire and catheter passed the occlusion, but re-entry into the lumen of the distal IIA was not achieved with either the FORS catheter or after changing to a non-FORS catheter and wire.

Table S4 reports the final catheter and guidewire combinations that were used for the endovascular tasks, and Table 4 reports the technical success rate with FORS enabled devices for the different endovascular tasks.

Secondary end points

Qualitative assessment of the performance of the FORS system. The detailed scorings of the qualitative assessment of the FORS system are provided in Table 3. The usefulness of the FORS based image guidance during navigation was scored as “better than standard guidance” in 16 of 21 procedures (76%) and was never scored as “worse than

Table 5. Fluoroscopy time, task duration and radiation dose for different types of task using Fiber Optic RealShape (FORS) technology in endovascular aorto-iliac or peripheral lesion repair in 21 patients

Navigation task	*n*	Fluoroscopy time – min		Task duration – min		Dose Area Product – Gy cm^2	
		Mean ± SD	Median (range)	Mean ± SD	Median (range)	Mean ± SD	Median (range)
Total	66	3.15 ± 8.26	0.34 (0.00–52.24)	13.3 ± 18.1	6.3 (1.0–108.0)	7.14 ± 15.25	0.73 (0.00–95.96)
Catheterisation of							
Thoracic aorta from groin	21	0.15 ± 0.23	0.05 (0.00–0.68)	4.0 ± 2.4	4.0 (1.0–10.0)	0.37 ± 0.75	0.08 (0.00–3.31)
Partially deployed fenestrated cuff	1	5.08		19.0		8.95	
Contralateral stent graft limb	9	2.14 ± 4.32	0.60 (0.00–13.48)	15.2 ± 10.2	16.0 (2.5–27.0)	3.93 ± 4.75	3.54 (0.00–15.15)
Superior mesenteric artery	5	4.89 ± 4.49	4.38 (0.96–11.84)	13.0 ± 6.2	14.0 (4.0–20.0)	16.70 ± 12.45	19.91 (0.49–32.78)
Coeliac trunk	3	2.99 ± 2.32	2.17 (1.18–5.60)	15.3 ± 1.5	15.0 (14.0–17.0)	17.03 ± 16.16	14.71 (2.15–34.22)
Right renal artery	5	13.48 ± 21.93	5.35 (0.27–52.23)	32.8 ± 33.1	31.0 (4.0–87.0)	24.56 ± 40.41	8.43 (0.45–95.96)
Left renal artery	5	10.29 ± 16.94	1.26 (0.82–40.03)	33.6 ± 44.7	8.0 (3.0–43.3)	16.61 ± 22.89	8.31 (0.61–56.26)
Internal iliac artery	2	5.10 ± 2.55	0.00 (0.00–6.90)	24.5 ± 24.8	(2.5–42.0)	18.07 ± 20.84	(3.34–32.81)
Abdominal aortic stent from left arm	1	0.43		6.0		2.49	
Abdominal aorta from groin	2	0.22 ± 0.19	(0.08–0.35)	3.1 ± 0.1	(3.0–3.2)	0.24 ± 0.20	(0.08–0.35)
Cross over manoeuvre	3	2.81 ± 2.67	2.91 (0.09–5.43)	17.7 ± 11.5	18.0 (6.0–29.0)	7.40 ± 8.14	5.89 (0.13–16.19)
Recanalisation of occluded stent in CIA	1	0.38		15.1		0.43	
Crossing stenosis in CIA	3	0.03 ± 0.06	0.00 (0.00–0.10)	3.6 ± 2.1	2.7 (2.0–6.0)	0.04 ± 0.06	0.00 (0.00–0.11)
Recanalisation of occluded IIA	1	4.34		15.1		0.43	
Crossing SFA stenosis	2	0.23 ± 0.28	(0.03–0.42)	6.8 ± 0.2	(6.7–7.0)	0.16 ± 0.18	(0.03–0.29)
Crossing popliteal artery stenosis	1	0.02		2.0		0.01	
Crossing popliteal aneurysm	1	3.22		20.0		1.37	

CIA = common iliac artery; IIA = internal iliac artery; SFA = superficial femoral artery; SD = standard deviation.

standard guidance". These scores were similar for aorto-iliac and peripheral procedures.

Fluoroscopy time, dose area product, and task duration. Fluoroscopy time, dose area product, and task duration of all the different tasks are provided in Table 5. The series of tasks is relatively small, and the tasks are very heterogeneous. Owing to this heterogeneity, it is not possible to draw solid conclusions regarding a potential reduction in X-ray use, despite the fact that several navigational tasks could be completed without or with only minimal X-ray use.

Complications

No device or FORS related complications were noted during the 21 procedures. During the hospital stay, a pulmonary infection occurred in one patient, that was treated with antibiotics. New onset atrial fibrillation developed in a second patient, causing type II myocardial ischaemia. A third patient showed temporary paraparesis of both limbs after fenestrated EVAR. None of these three complications was considered to be related to the FORS enabled devices, and all three complications resolved during the hospital stay.

DISCUSSION

This report describes the first clinical experience of medical use of Fiber Optic RealShape technology, a new technology that shows FORS enabled catheters and guidewires in colour, in real time, in 3D, and using light instead of X-ray.

Sixty-six endovascular navigation tasks were attempted with a FORS enabled guidewire or catheter, or both. Sixty of these were performed successfully, which appears promising, given that only two different catheters (Cobra C2 and Berenstein configuration) were available.

In future releases of the system, more device lengths and catheter shapes are expected to be supported with FORS technology. This will undoubtedly increase the usability of the FORS system in a wider spectrum of anatomical variations.

FORS enabled devices are radiopaque and fully compatible with regular 0.035 inch guidewires and catheters. When

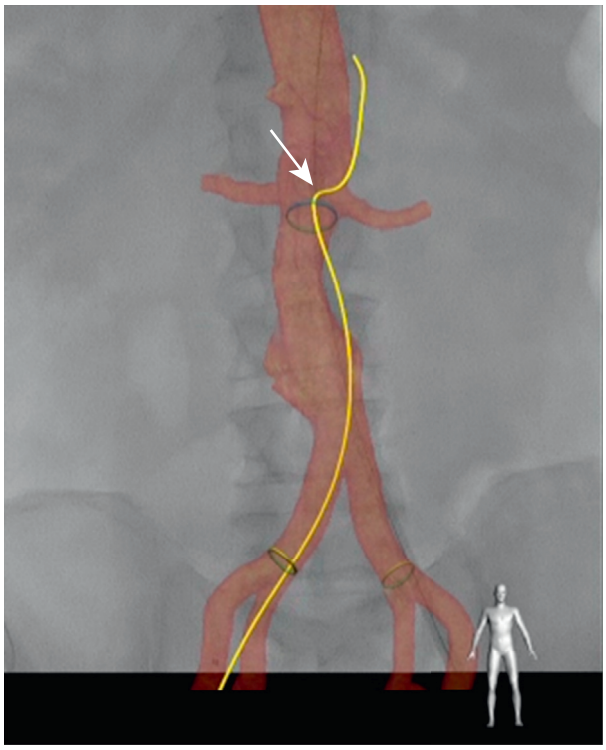

Figure 4. Advance of a conventional pigtail catheter over a Fiber Optic RealShape (FORS) enabled guidewire, which is visible due to the changes in guidewire shape. The white arrow indicates the position of the pigtail catheter.

a FORS enabled guidewire is used in combination with a regular catheter, the wire still provides excellent visibility with FORS, and the shape of the wire in most situations gives an impression of the position of the catheter (Fig. 4).

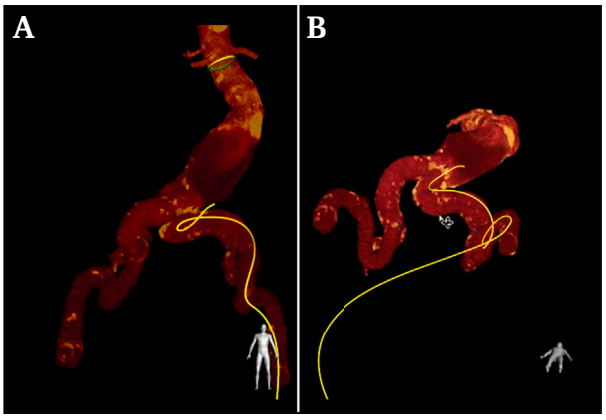

Figure 6. Catheterisation of a tortuous iliac artery using the biplane viewing mode of the Fiber Optic RealShape (FORS) system. The biplane visualisation is composed of (A) an anteroposterior view and (B) caudocranial view of the computed tomography angiogram, and provides useful 3D information to assist device manipulation within a tortuous iliac segment.

When the FORS enabled catheter is combined with a regular non-FORS guidewire, the catheter remains visible in 3D. Depending on the stiffness of the wire, an impression of the position of the wire is visible, without using X-ray, as long as the wire is positioned in the catheter.

An important part of this feasibility study was the qualitative assessment of the performance of the FORS system. The technical characteristics of the FORS enabled guidewire and catheters were rated as “at par” with regular devices. Also, the compatibility with ancillary devices and the responsiveness of the FORS based visualisation was scored positive in all cases.

The usefulness of the FORS based image guidance during navigation was scored as “better than standard guidance” in

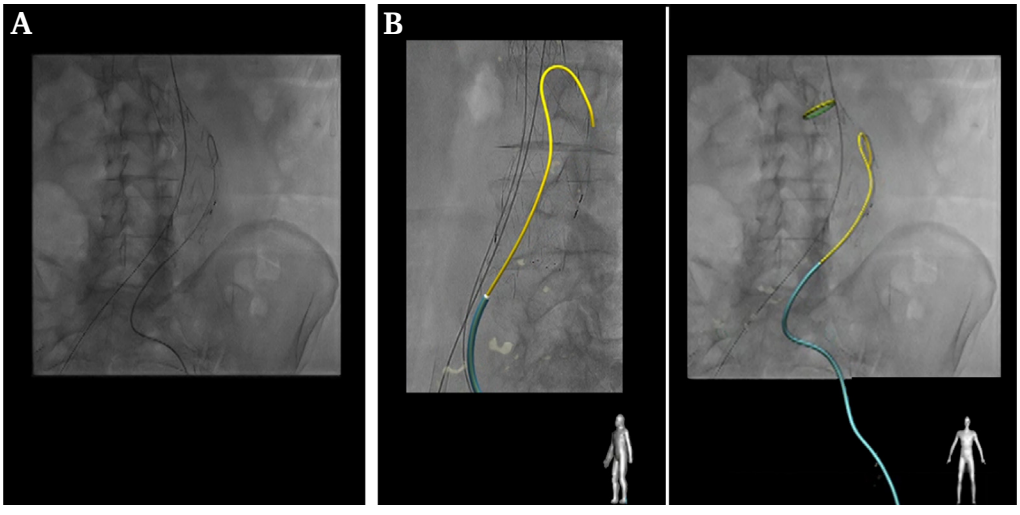

Figure 5. Comparison of (A) Xray visualisation and (B) Fiber Optic RealShape (FORS) based biplane visualisation of Cobra 2 catheter and guidewire. Shading, and the distal tip marker emphasise the shape and facing direction of the devices.

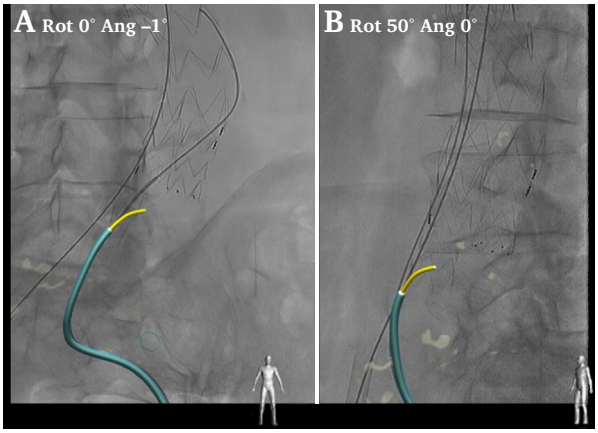

Figure 7. Catheterisation of a contralateral limb during endovascular aortic repair (EVAR), using the biplane viewing mode of the Fiber Optic RealShape (FORS) system. The biplane visualisation is composed of (A) an anteroposterior X-ray projection and (B) a 50° left anterior oblique (LAO) X-ray projection of the EVAR stent, and provides 3D information to assist catheterisation of the contralateral limb within the aneurysm sac.

16 of 21 procedures (76%) and "equal to standard guidance" in five procedures. "Standard guidance" for complex EVAR means the use of a 3D overlay of an intra-operatively acquired cone beam computed tomography angiography, which is the best available X-ray based guidance so far. For EVPLR "standard guidance" consists of fluoroscopy with use of an overlay of 2D DSA.

The reason why the usefulness of FORS based guidance was scored as "better", or "equal" compared with standard guidance, was not registered in the report forms. The operators were, however, positive about the ability to see the direction in which the devices pointed and moved in 3D. For comparison, an example of an Xray image *vs.* a FORS based image is shown in Fig. 5.

Furthermore, the fact that viewing angles with FORS are unrestricted, was experienced as a major advantage. Fig. 6 shows a patient with tortuous iliac arteries. In the anteroposterior view it appeared difficult to pass a severe kink. When the image was rotated to an extreme caudocranial view, the direction of the kink became clear, which facilitated navigation. This view would have been impossible with fluoroscopy because the C-arm would have needed to be rotated through the patient to achieve this.

In addition, the operators found it beneficial to have a biplane view. For cannulation of a contralateral limb from a bifurcated stent graft, for instance, two X-ray images from different angles were acquired from the deployed stent graft. These X-ray images could be used as an overlay in the biplane mode, that, in combination with the 3D view of the guidewire and catheter, was reported as helpful by the operators (Fig. 7).

Besides improved visualisation, FORS has also been developed to reduce X-ray exposure. This first feasibility study, however, was not designed to prove radiation reduction with FORS. In this study several tasks could be performed without or with very limited use of X-ray, including cross over of the aortic bifurcation, stenotic lesion crossing and cannulation of the contralateral limb. Randomised trials with less heterogeneous pathology are needed to objectively quantify X-ray reduction using FORS technology. Similarly, procedure times, technical success and complication rates will have to be analysed to assess the benefit of the adjunctive image guidance provided by FORS technology in more qualitative terms.

In the literature, several other approaches have been proposed to enable X-ray reduction and/or 3D visualisation of endovascular devices inside the body of which ultrasound based systems, electromagnetic (EM) tracking systems and robotic catheter systems have shown particular potential.[5]

Duplex ultrasound or intravascular ultrasound (IVUS) guidance can reduce radiation exposure and contrast volume in endovascular procedures.[6–8] In fact, in patients with contrast allergy and straightforward anatomy, duplex ultrasound was proven to be non-inferior to conventional fluoroscopic guidance in EVPLR.[9] While the use of US or IVUS imaging, has a positive impact on radiation and contrast use, it does not improve device navigation as these techniques lack 3D visualisation and are characterised by a narrow field of view and high image noise.

EM tracking systems enable real time tracking of endovascular devices in 3D space, using a combination of electromagnetic sensors embedded in the tip of the endovascular devices and an electromagnetic field generator.[10,11] Compared with FORS technology, these EM tracking systems have several drawbacks. Firstly, EM tracking quality is negatively affected by electromagnetic interference caused by nearby electronic equipment, such as the C-arm system. Secondly, the trackability of the current EM tracking systems is limited to the tip of the device, whereas FORS technology visualises the entire device. Full length device visualisation provides the physician additional cues on device tension, for instance, the likelihood of dislodgement from its position. Thirdly, the integration of the EM sensors in guidewires and catheters, has been shown to influence their mechanical properties.[10,11] In the current study, all operators rated the FORS enabled guidewire and catheter as "at par" with the non-FORS enabled devices that the operators normally used.

Robotic catheter systems are remotely operated steerable catheters with multiple degrees of freedom and a deformable catheter tip. Robotic device control improves the stability and steerability of the device, resulting in fewer wall hits and less histopathological damage than conventional catheter manipulation.[12] Device visualisation is provided by either fluoroscopic imaging (in 2D), magnetic tracking (in 3D), and/or a visualisation of the commanded catheter position (in 3D). Cochennec *et al.*[13] reported a 81% success rate of the cannulation of visceral and renal arteries during FEVAR/BEVAR with a mean cannulation time of 4:20 min using fluoroscopic guidance. Bismuth *et al.*[14] reported 95% cannulation success rate during EVPLR with mean cannulation time of 21 min using a combination of fluoroscopic guidance and the visualisation of the commanded catheter position. Both systems used in these

single arm feasibility studies are heavily dependent on fluoroscopic guidance, and lack full length device visualisation in 3D.

Limitations

Although the operators had experience with the system in preclinical studies, they went through a learning curve during clinical use. The optimal visualisation settings (regarding viewing angle, magnification, mono- or biplane mode, and optimal overlay) had to be identified for the different types of procedure. Also, workflow improvements, like the optimal positioning of the system, to work from both the groin and the arm, had to be learned during the study. In this first study, the technical success would probably have been higher if more than two differently shaped catheters had been available. Other limitations for clinical use are the limited working length of the catheters and guidewire available for this study and also the inability to backload the guidewires. These issues will be addressed in future releases of the system.

Final limitations during this study were technical issues with the FORS equipment. The technology could not be used in one patient, and using two FORS devices at the same time was impossible in one other patient, which probably affected study results.

Conclusion

Real time 3D navigation using FORS technology is safe and feasible in endovascular procedures. Comparative studies are needed to prove and quantify the benefits and potential radiation reduction for all types of endovascular procedures.

CONFLICTS OF INTEREST

Philips Medical Systems Netherlands B.V. provided a research grant according to fair market value to the Division of Surgical Specialties of the University Medical Center Utrecht to support this study. The Division of Surgical Specialties of the University Medical Center Utrecht has a research and consultancy agreement with Philips. The department of Vascular Surgery is part of the Division of Surgical Specialties. J. van Herwaarden and C. Hazenberg are or have been consultants for Cook Medical, Gore Medical, Medtronic and Terumo Aortic. G. de Borst has been consultant for Gore Medical. R. Bullens is an employee of Philips Medical Systems. The views expressed in this article are those of the authors and do not necessarily reflect those of Philips Medical Systems.

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APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2020.10.016.

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