Cardiovasc Intervent Radiol (2014) 37:1041–1046
DOI 10.1007/s00270-014-0918-x

LABORATORY INVESTIGATION

Safety and Efficacy of Target Vessel Catheterization with the New Steerable Microcatheter Direxion Compared with a Standard Microcatheter: A Prospective, Preclinical Trial

Oliver Dudeck

Received: 6 March 2014 / Accepted: 9 April 2014 / Published online: 22 May 2014

Abstract
Purpose To assess the potential of a steerable microcatheter in a comparative preclinical trial.
Methods A total of 100 small target vessels of the lower limbs with a maximum diameter of 3 mm were prospectively randomized to catheterize with either the preshaped torqueable Direxion™ (J tip shape; Boston Scientific, Natick, MA) or a similarly steam-shaped Renegade™ microcatheter (Boston Scientific) in a porcine model. Catheterization was first performed in combination with a microguidewire and afterwards without.
Results No significant differences were found for the mean vessel diameter in the Direxion (1.53 ± 0.44 mm; $n = 50$) or Renegade (1.62 ± 0.43 mm; $n = 50$; $p = 0.35$) group. Guidewire-assisted catheterization was successful in all target vessels, whereas access was achieved in most cases with the guidewire alone. However, when it became necessary to steer the Direxion actively, this was regarded as key to obtain vessel access in three of four target vessels (75 %). Vessel catheterization without guidewire was significantly more successful with the Direxion (88 %; $n = 44$) compared with the Renegade (32 %; $n = 16$; $p < 0.0001$). In addition, this catheterization technique was also significantly faster with the Direxion compared with guidewire-assisted vessel catheterization with the Renegade (16.1 ± 14.4 sec compared with 27.1 ± 24.7 sec; $p = 0.011$).
Conclusions The Direxion microcatheter demonstrated unique steerability characteristics, which makes it a promising new tool especially for complex coaxial endovascular procedures.

Keywords Direxion · Preclinical trial · Steerable microcatheter · Vessel catheterization

O. Dudeck
Department of Radiology and Nuclear Medicine, University of Magdeburg, Magdeburg, Germany

O. Dudeck (✉)
German Academy for Microtherapy, Leipziger Strasse 44, 39120 Magdeburg, Germany
e-mail: oliver.dudeck@med.ovgu.de

Introduction

Recent years have seen a gradual increase in the number of catheter-based endovascular procedures. In particular, novel transarterial locoregional anticancer treatments that require advanced skills in microcatheter embolization techniques, such as gastrointestinal bleeding embolization, bland, and chemoembolization, as well as radioembolization (RE) are increasingly being used [1–5].

A large variety of different guidewire directed microcatheters are commercially available today for such embolizations. The choice of which microcatheter to utilize for catheterization of a particular target vessel depends on distal trackability, support, and pushability, as well as individual preference. In theory, all microcatheters can be shaped or reshaped with steam. In certain challenging endovascular procedures, steam shaping of the catheter tip may facilitate successful target vessel catheterization or provide the needed support to achieve a stable tip position for embolization [6]. However, steam shaping is a rarely utilized technique in clinical practice, because it is time-consuming and there is a considerable tendency of spontaneous recovery of the initially steamed shape [7, 8].

Currently, a number of microcatheters with preshaped tips are available, which are mostly used for neuroendovascular procedures to enhance vessel selectivity for

arteries originating at acute angles and to help maintain position within an aneurysm during coil embolization [9]. Such preshaped microcatheters come with 45° or 90° angled tips, J-, S-, or C-shaped curves, range in distal diameter from 1.7 to 2.3 Fr, and generally have two radiopaque distal markers. Selection of a particular shape, as with adding curves to microguidewires, is largely dictated by the angle a targeted vessel (or aneurysm) takes off from its parent artery. Examples of different preshaped microcatheters used in clinical practice include the Prowler™ (Cordis Corp., Miami, FL), the Echelon™ (Covidien, Irvine, CA), and the Excelsior™ (Stryker, Kalamazoo, MI) microcatheter. The level of steerability of these microcatheters as defined by the ability to turn or rotate the distal end of the catheter with a one-to-one movement of the catheter tip is rather low. The Enzo™ microcatheter (Micrus Endovascular Corp., San Jose, CA), which has a dual lumen with an inner wire that can be torqued allowing for deflection of the tip 90° in either direction, thus addressing variations in vessel morphology [10]. However, this microcatheter has similar limitations in terms of catheter steerability.

The Direxion™ (Boston Scientific Corp., Natick, MA) is a new microcatheter comes with various tip shapes and contains a proprietary nitinol hypotube design to allow steerability.

The purpose of this prospective trial was to assess safety and efficacy of this microcatheter in catheterization of small target vessels and explore the boundaries of steerability in the exception scenario without guidewire assistance compared with a similarly preshaped standard microcatheter (Renegade™, Boston Scientific Corp.), which has a continuous fiber braid design for kink resistance and trackability as well as improved visibility and a lubricious coating designed to be abrasion resistant for improved trackability.

Materials and Methods

This trial was planned and executed by the German Academy for Microtherapy with no influence on the study design by Boston Scientific. The animal experiment was performed with permission from the Animal Experimentation Ethical Committee and according to the Animal Care Guidelines of the Committee. Two male swine were used in this study, which were 2 months old, weighted 28 and 30 kg, and were maintained on a standard laboratory diet. After an overnight fast, the swine were premedicated with intramuscular ketamine (20 mg/kg). After endotracheal intubation general anesthesia was maintained with mechanical ventilation and inhalation of 0.5 to 1.5 % halothane. Fentanyl (0.025 mg/kg/h) was administered for analgesia.

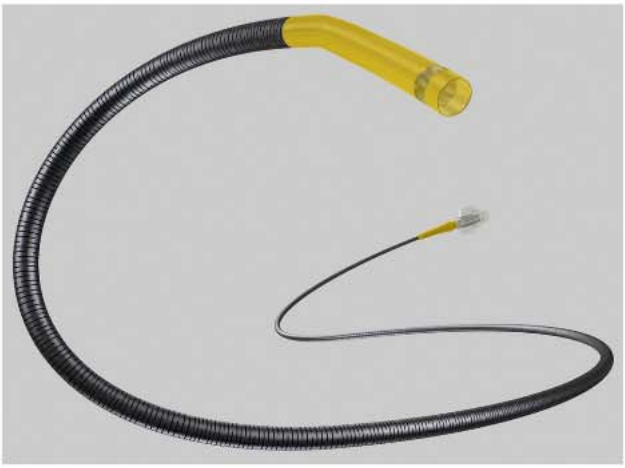

Fig. 1 Drawing to illustrate the unique design of the Direxion (Boston Scientific Corp.) microcatheter. The slotted nitinol design allows for excellent torqueability of the catheter shaft while retaining a similar pushability, trackability, and flexibility compared with other microcatheters. This results in precise steerability in combination with an angled-tip shape

All endovascular procedures (Artis zee, SIEMENS, Erlangen, Germany) were performed by the same physician with 12 years experience in interventional radiology. First a 5-French (F) sheath was placed sonographically guided in the left common carotid artery and attached to pressurized saline infusion to which 5,000 IU of heparin had been given. A 5-F multipurpose catheter (Cordis, Warren, USA) was used for catheterization of the lower limb vessels. A total of 100 target vessels were identified that resembled side branches from both hypogastric arteries as well as the profound or superficial femoral arteries bilaterally. This trial was designed to identify small target vessels, which had to have at maximum diameter of 3 mm. The diameters of the parent vessels as well as the take-off angle from the parent artery were recorded. Randomization was performed to vessel catheterization with either a 0.027″ Direxion HIFLO (Boston Scientific; Group B) with a preshaped j tip or a similarly steam shaped 0.027″ Renegade HIFLO (Boston Scientific; Group A). The slotted nitinol design of the Direxion is accomplished by laser cutting micro cuts along the length of the shaft giving the catheter the desired pushability, trackability, and flexibility while still transmitting torque along the entire length of the catheter. This torqueability in combination with an angled tip resulted in the ability to steer this new microcatheter (Fig. 1).

For the documentation of the interventional procedure, the following parameters were recorded: catheterization success, fluoroscopy time for catheterization, catheterization time, as well as any complications such as vasospasm, thrombosis, or dissection. The start of the catheterization procedure was defined with the tip of the microcatheter positioned at the end of the guiding catheter. The procedure

was completed with the angiographic proof of successful vessel access. This angiographic run then also was used to assess for catheterization-related complications. In both groups, catheterization of the same vessel was first performed with a microguidewire (Fathom™, Boston Scientific) and afterwards without wire. Whenever guidewireless vessel catheterization was regarded impossible or after after a maximum time interval of 2 min a microguidewire was used to complete the procedure.

Statistical analysis was performed with SPSS suite (version 19.0; SPSS, Chicago, IL). Binary regression analysis was used to compare nominal values like catheterization success rates and incidences of vasospasm in the two catheter groups, whereas the Mann–Whitney test was used to compare ratio parameters for vessel catheterization for differences. A p value of 0.05 was set to be the level of statistical significance.

Results

Guidewire-assisted catheterization was successful in all target vessels ($n = 100$), which consisted of side branches of the hypogastric, superficial, as well as deep femoral arteries bilaterally. There were no significant differences in the mean diameter of vessels catheterized with either the Direxion microcatheter (1.53 ± 0.44 mm; $n = 50$; $p = 0.126$) or the Renegade (1.63 ± 0.30 mm; $n = 50$). The mean parent artery diameter was quite similar in both groups (3.43 ± 0.40 mm and 3.24 ± 0.91 mm; $p = 0.433$), and no significant differences were found for the mean angle of the parent to the target vessel between groups (Table 1). Results for guidewire-assisted vessel catheterization were similar for both microcatheters (Table 2). In both groups, access to all target vessels was achieved, which in most cases vessel was accomplished by the guidewire only. In the Renegade group, reshaping of the guidewire was needed four times for successful vessel catheterization, whereas this was necessary only once in the Direxion group. This difference was due to the fact that once needed the physician used the ability to actively steer the Direxion to gain vessel access when it was not possible with the wire only before reshaping the guidewire. This technique was successful in three of four target vessels (75 %). The mean guidewire-assisted vessel catheterization time with the Direxion microcatheter was with 25.9 ± 38.2 sec similar to 27.1 ± 24.7 sec when the Renegade was used ($p = 0.859$; Table 2). In three incidences, it was difficult to advance the Direxion at the level of the orifice deeper over the wire into the target vessel, a situation that happened only once in the Renegade group. No complication other than mild vasospasm in two cases in the Direxion group and in three cases in the Renegade group was noted.

Table 1 Characteristics of target vessels

	Renegade group ($n = 50$)	Direxion group ($n = 50$)	p value
Target vessel diameter (mm)	1.63 ± 0.3	1.53 ± 0.44	0.126
Parent artery diameter (mm)	3.43 ± 0.4	3.24 ± 0.61	0.433
Take-off angle from parent artery (°)	74.4 ± 20.6	73.0 ± 22.4	0.795

MC microcatheter

Table 2 Parameters for guidewire-assisted target vessel catheterization

	Renegade group ($n = 50$)	Direxion group ($n = 50$)	p value
Success in vessel cannulation (%)	100 (50/50)	100 (50/50)	
Fluoroscopy time for catheterization (sec)	22.3 ± 17.7	21.9 ± 31.2	0.95
Catheterization time (sec)	27.1 ± 24.7	25.9 ± 38.2	0.859

MC microcatheter

Subsequently, vessel catheterization was attempted without a guidewire to better assess the inherent steerability of the microcatheters. For that, contrast media was injected through a 1-cc syringe whenever needed to improve visual control and to separate the tip of the catheter from the vessel wall to reduce the risk of vessel wall injury. Due to the improved steerability of the Direxion, vessel access was achieved in 44 of 50 cases (88 %), whereas vessel catheterization was successful in only 16 of 50 cases (32 %) with the Renegade ($p < 0.0001$; Fig. 2). In two vessels, only the orifice could be catheterized with the Direxion (Fig. 3). Mild vasospasm was noted in two target vessels in the Renegade group and three vessels in the Direxion group. No other catheter-related complications were found.

Catheterization was achieved in significantly less time with the Direxion microcatheter with mean fluoroscopy time in the Direxion group of 14.6 ± 14.7 sec compared with 110.6 ± 62.8 sec for the Renegade group ($p < 0.0001$; Table 3). Similarly, a significantly reduced mean catheterization time in the Direxion group was observed 16.1 ± 14.4 sec compared with 122.4 ± 59.0 sec for the Renegade group ($p < 0.0001$; Table 3). Moreover, guidewireless catheterization time with the Direxion was also significantly shorter compared with guidewire-assisted target vessel catheterization in the Renegade group ($p = 0.011$; compare Tables 2, 3).

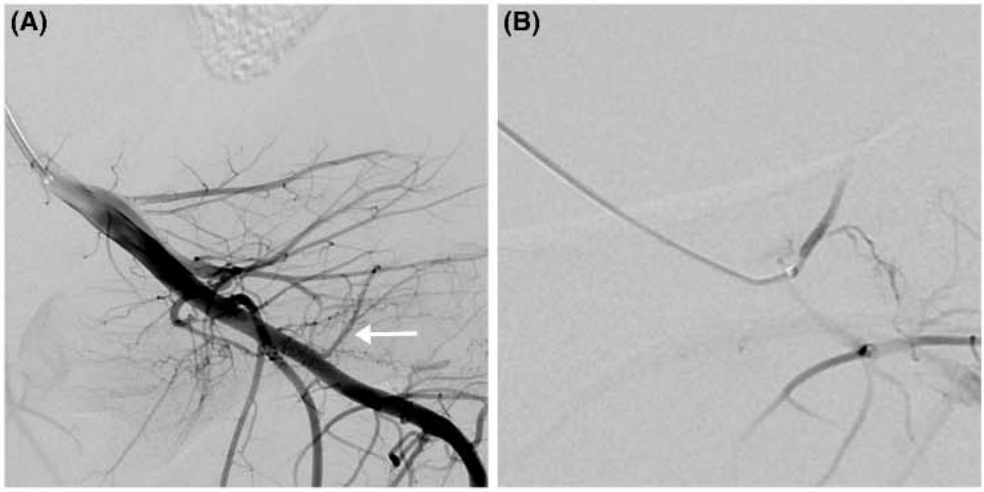

Fig. 2 **A** Angiogram of the left porcine superficial femoral artery displays numerous small side branches as potential target vessels for microcatheter catheterization. The *arrow* indicates the target vessel selected, which has a diameter of 1.6 mm originating with an acute angle of 40°. **B** Selective angiogram confirms successful guidewireless catheterization

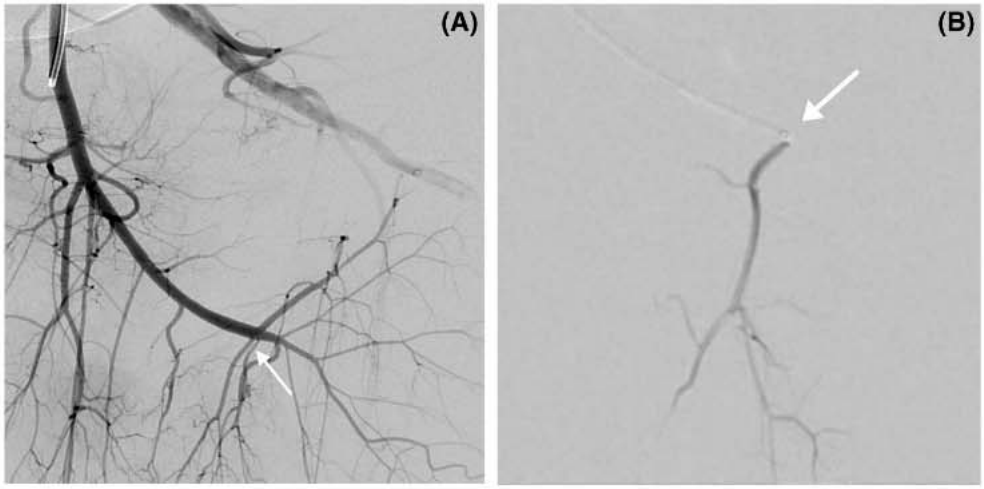

Fig. 3 **A** Angiogram of the left porcine deep femoral artery also displays various small side branches as potential target vessels for microcatheter catheterization. The *arrow* indicates the target vessel selected, which has a diameter of 1.4 mm originating with an acute angle of 85°. **B** Selective angiogram confirms successful guidewireless catheterization with the steerable microcatheter Direxion without complications, although only vessel access at its orifice could be achieved (*arrow* indicates tip of microcatheter)

Table 3 Parameters for guidewireless target vessel catheterization

	Renegade group ($n = 50$)	Direxion wireless group ($n = 50$)	p value
Success in vessel cannulation (%)	16 (32 %)	44 (88 %)	<0.0001
Vasospasm (%)	2 (4 %)	3 (6 %)	0.19
Fluoroscopy time for catheterization (sec)	110.6 ± 62.8	14.6 ± 14.7	<0.0001
Catheterization time (sec)	122.4 ± 59.0	16.1 ± 14.4	<0.0001

Discussion

Liver-directed therapies for unresectable cancer in the liver are evolving [1, 11–15]. These treatments resemble complex endovascular procedures for which microcatheters are generally needed. Particularly in RE, successful catheterization and subsequent prophylactic embolization of such tiny and angled vessels as the right gastric artery is

crucial to prevent radiation-induced gastritis afterwards [16, 17].

This preclinical trial was performed to assess the value of a steerable microcatheter to aid in catheterization of such demanding vessels. Therefore, only small target vessels with a maximum diameter of 3 mm were included, which resulted in a very small mean target vessel diameter of 1.49 ± 0.44 mm. Vessel catheterization in the Direxion group was achieved with the use of the microguidewire in most incidences ($n = 47$; 94 %) so that the additional advantage of this steerable microcatheter could not be fully appreciated. Certainly, this must be regarded as a limitation of this study, which was performed in healthy animal arteries in which successful catheterization even of small vessels turned out not to be as demanding as in patients in the presence of atherosclerotic disease. The performance of this study in healthy porcine arteries may be seen as a limitation as even small arteries proved to be not as demanding as in patients in the presence of atherosclerotic disease. Only three target vessel could not initially be catheterized with the shape of the microguidewire, so that it became necessary to steer with the angled tip of the microcatheter. This was found to be very helpful and key in order to successfully gain vessel access in two of these cases (66.7 %). Nevertheless, the number of incidences certainly was too small to have an impact on differences in total catheterization and fluoroscopy time. On the other hand, the investigator experienced certain difficulties to advance the Direxion microcatheter deeper at the level of the vessel orifice despite successful microguidewire access in three acute angled target vessels. This seemed to be attributed to the angulated tip as such an incidence was encountered less frequent in the Renegade group and must be regarded as a potential limitation.

Vessel catheterization was also performed without guidewire to assess fully the steerability characteristics of the microcatheters. The design of the Direxion microcatheter resulted in enhanced steerability so that target vessel catheterization was successful in 88 % ($n = 44$) compared with only 32 % ($n = 16$; $p < 0.0001$) with the Renegade and was achieved significantly faster (16.1 ± 14.4 sec. vs. 122.4 ± 59.0 sec; $p < 0.0001$; Table 3). Guidewireless catheterization technique is undoubtedly uncommon in clinical practice, because it bears a certain risk of vessel injury and has potential for catheter kinking within its unsupported length; therefore, this part of our trial was primarily intended to assess the full potential of the handling this new device in a preclinical setting. No complication was observed other than mild vasospasm, which occurred in both groups with similar low frequency. Nevertheless, this trial lacks a histological assessment to assert the absence of vascular trauma by this catheterization technique.

Which clinical fields of application could be interesting for such a steerable microcatheter? The Direxion could provide a stable platform for coil deployment in neuroendovascular procedures to help to maintain position within an aneurysm during coil embolization, but currently this microcatheter is only available for 0.021″ and 0.027″ systems, which are more suitable for abdominal and peripheral interventions. In general, this microcatheter may enhance vessel selectivity in challenging anatomies in which the attempt to gain access with standard microguidewires/-catheters has failed. Whether challenging vessels, such as the right gastric artery, can be catheterized with a higher success rate compared with standard microcatheters needs to be elucidated in clinical trials. The ability to manoeuvre the tip of the Direxion during the procedure could be used to facilitate redirection of coils, allowing for more control over the positioning and packing of coils, which may reduce the risk of coil migration. In case of catheter kick-out during coil embolization, it may also be possible to reposition the microcatheter without guidewire back into the target vessel and finish the coiling procedure, although this is out with its current directions of use. The Direxion technology also appears appealing for liquid embolizations with glue or Onyx in embolizations of vascular malformations or portal vein embolizations. Once the catheter is filled with the liquid embolic, a microguidewire cannot be reinserted precluding the microcatheter to be navigated to another target vessel to continue the embolization. In such procedures, use of the Direxion to reposition the microcatheter without guidewire can save procedure time and even catheter material. The potential to reposition this microcatheter wirelessly could be useful in patients scheduled for RE, in which technetium-99m-MAA during workup angiography as well as yttrium-90 during the treatment itself needs to be administered from different catheter positions to which the physician may be able to navigate without the need of a microguidewire, thus reducing the risk of contamination due to insertion and removal of the guidewire. Interestingly, this catheterization technique proved to be faster than guidewire-assisted vessel catheterization, which may be crucial to identify and eliminate the site of bleeding as fast as possible in hemodynamically unstable patients.

In conclusion, the Direxion microcatheter represents a new device that demonstrated remarkable steerability characteristics. Whether these promising preclinical results allow for higher vessel selectivity in challenging anatomies in patients should be addressed in further trials and clinical evaluation.

Acknowledgment This preclinical trial was supported by a research Grant of Boston Scientific.

Conflict of interest The author has participated in scientific advisory boards for Boston Scientific.

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