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Development of a model system for *in vitro* simulated application testing of neurovascular stent systems

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Abstract: *In vitro* test setups for simulated application testing are necessary for physician training as well as for development and benchmarking of various devices in interventional neuroradiology. Within the current study, we implemented a test setup for *in vitro* simulated application testing. Trackability in the distal catheter area, which was positioned inside a complex 3D vascular model was analyzed for two neurovascular stent systems (Neuroform EZ 4.0x20 mm and Enterprise VRD 4.5x14 mm) combined with different microcatheters (Excelsior XT-27 Flex, PX Slim Delivery Microcatheter and Prowler Select Plus Infusion Catheter). The described test setup allows for a diffentiation of neurovascular stent systems with regard to the trackability force as a major procedure related indicator for device handling. Therefore, the simulated application system presented within the current work represents an indispensable tool for safely and efficiently developing and evaluating new technologies for interventional neuroradiology prior to clinical implementation.

Keywords: Interventional neuroradiology, simulated use, trackability, 3D printed vessel model

1 Introduction

The use of *in vitro* test setups for simulated application testing is of critical importance for physician training as well as for development and benchmarking of various devices in interventional neuroradiology, such as microcatheters, coil embolization devices, flow diverters or intracranial stents.

Training systems allow physicians to practice and improve their skills in device handling in a realistic clinical setup before using them on patients [1,2]. In addition to standardized vascular models, complex patient-specific anatomies manufactured by 3D printing can also be used for procedure planning, in this regard [3].

During the development phase of innovative products, simulated application test systems allow for an identification of strengths and weaknesses as well as for systematic comparison and benchmarking of commercial devices without the ethical concerns as well as the costs associated with pre-clinical or clinical studies. Previously, our group developed a test setup for simulated use analyses of cardiovascular stents, including models of critical coronary artery anatomies, and used it for benchmarking of various devices [4,5].

As part of our work on the development of a bioresorbable self-expanding microstent for stent-assisted coiling of intracranial aneurysms, it has been shown that the complex neurovascular curvature represents a major challenge [6]. The literature describes numerical as well as experimental approaches for trackability analysis of catheter systems [7,8]. Within the current study, we focused on implementation of a test setup for *in vitro* simulated application testing of stent and catheter systems for interventional neuroradiology. Particular attention was paid to trackability in the distal catheter area, which was positioned inside a complex 3D vascular model.

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2 Materials and methods

2.1 Simulated application test setup

The custom made simulated application test setup (see Figure 1) is based on a linear motor drive equipped with a 5 N load cell (model 8432, measurement uncertainty ± 0.015 N, Burster Präzisionsmesstechnik, Germany) [4].

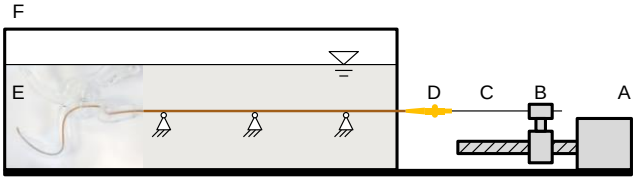

Figure 1: Schematic representation of the simulated application test setup: linear motor drive (A), linear drive unit with force sensor (B), pusher wire (C), microcatheter (D), 3D neurovascular model (E, see detail in Figure 2) and tempered water bath (F) [4].

A 3D neurovascular model is positioned inside a water bath, tempered at 37°C ± 2°C. The neurovascular model was manufactured using the 3D printer Form 2 and Clear Resin (Formlabs Inc., USA) as described elsewhere [3,6]. The distal end of the microcatheter is placed in the desired neurovascular path inside the vascular model (see Figure 2). For prevention of kinking, the microcatheter shaft is stabilized along the entire length using fixation clamps alongside the test bench. The neurovascular stent is loaded into the proximal end of the microcatheter and moved inside the vascular model using a pusher wire, also being stabilized along the entire length.

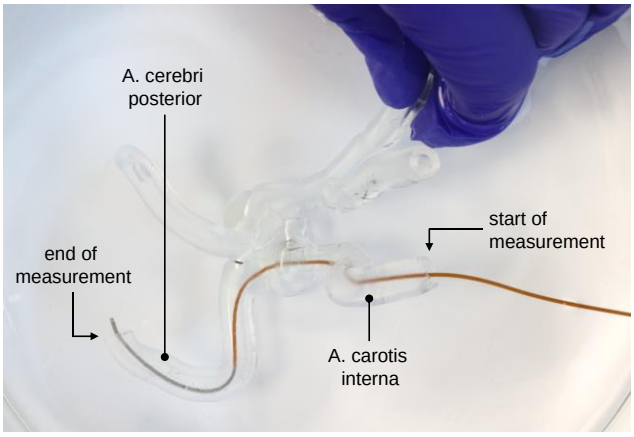

Figure 2: Detail of the distal end of the microcatheter placed in a neurovascular path inside the vascular model. Start and end of force and distance recording are marked, respectively.

Using the path through the vascular model shown in Figure 2, a relevant length for force and distance recordings of approximately 110 mm results. A test speed of 7.5 mm s^{-1} was used to advance the stents.

2.2 Analyzed devices

Within the current feasibility study, two neurovascular stent systems combined with the corresponding pusher wires were used: (i) Neuroform EZ 4.0x20 mm (Stryker Neurovascular Corp., USA) and (ii) Enterprise VRD 4.5x14 mm (Codman, Johnson & Johnson Corp., USA). Due to availability, three different microcatheters were used: (i) Excelsior XT-27 Flex (ID 0.027", Stryker Neurovascular Corp., USA), (ii) PX Slim Delivery Microcatheter (ID 0.025", Penumbra Inc., USA) and (iii) Prowler Select Plus Infusion Catheter (ID 0.021", Codman, Johnson & Johnson Corp., USA).

3 Results

The positioning of all three microcatheters within the 3D neurovascular vessel model was successfully implemented in the simulated application test setup (see Figure 3).

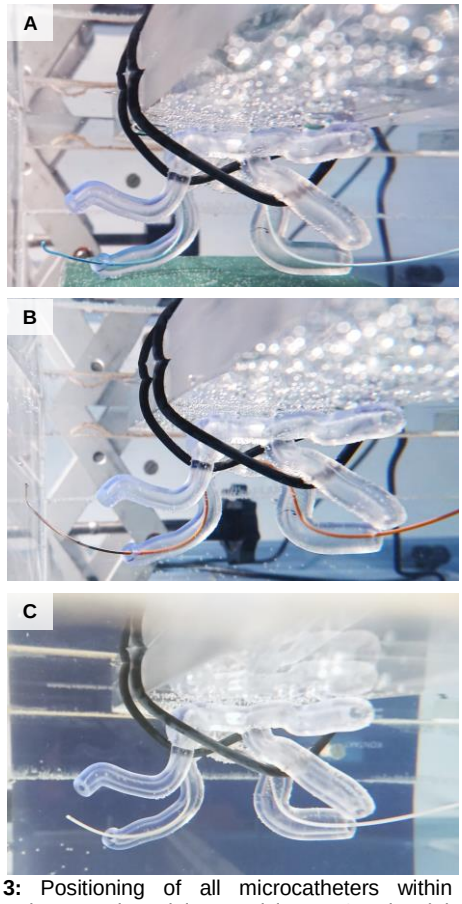

Figure 3: Positioning of all microcatheters within the 3D neurovascular vessel model: Excelsior XT-27 Flex (A), PX Slim Delivery Microcatheter (B) and Prowler Select Plus Infusion Catheter (C)

The recordings of the proximal track force as a function of the distance are shown in Figure 4 for different combinations of neurovascular stents and microcatheters, respectively.

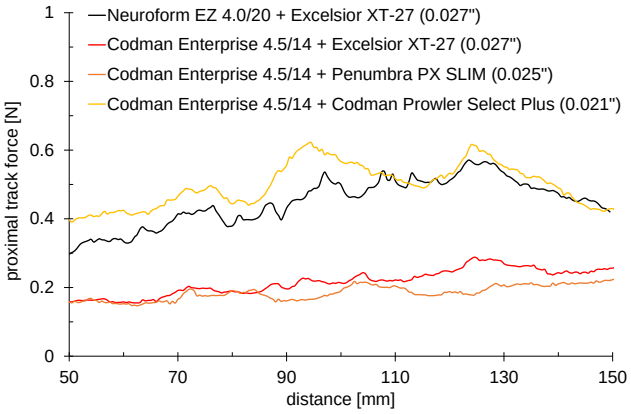

Figure 4: Proximal track force as a function of the distance for different combinations of neurovascular stents and microcatheters. Averaged curves based on *n* = 3 single recordings, respectively.

Based on the recordings, mean and maximum values for proximal track force were calculated (see Figure 5).

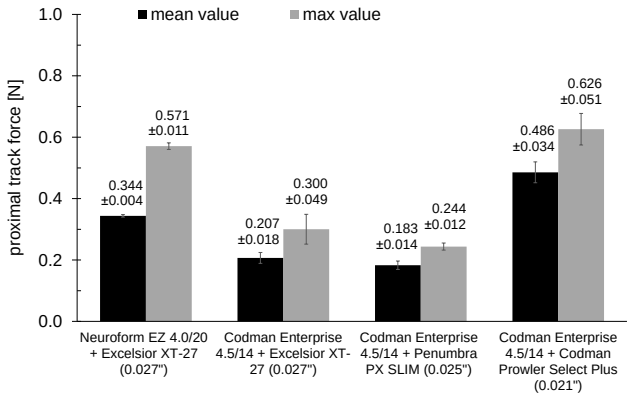

Figure 5: Mean and maximum values for proximal track force for different combinations of neurovascular stents and microcatheters, (*n* = 3) respectively.

4 Conclusion

As part of the current work, a test setup for *in vitro* simulated application testing of neurovascular stent systems within any 3D printed vessel models was successfully implemented.

The described test setup allows for a diffentiation of neurovascular stent systems with regard to the trackability force as a major procedure related indicator for device handling. Using the stent Enterprise VRD 4.5x14mm as an example, we were able to show that particularly the microcatheter used has a decisive influence on the trackability force (maximum force of 0.300 N or 0.244 N in microcatheters with 0.027" or 0.025" inner diameter vs. 0.626 N in a microcatheter with 0.021" inner diameter). In addition, it was shown that the system is also sensitive enough to detect differences in trackability forces between different neurovascular stents when using the same microcatheter (maximum force of 0.571 N vs. 0.300 N for the Neuroform EZ 4.0/20 and the Enterprise VRD 4.5x14mm in an Excelsior XT-27 Flex microcatheter).

Jun et al. measured trackability forces of different neurovascular flow diverter systems in a 2D silicone vessel model from femoral access to intracranial vessels. A spatially resolved measurement of the track force within a complex three-dimensional neurovascular anatomy was not carried out here [8]. Nevertheless, Jun et al. found track forces in the same order of magnitude as measured in our current work [8]. All in all, the absolute force values are highly dependent on the vessel model used. A direct comparison of absolute values for trackability between different works only makes sense if the same vessel model is used in addition to the same microcatheter or implant. Force measurement is therefore crucial for benchmarking tests of different products. In the context of training, however, force measurement plays a subordinate role. To the authors' knowledge, there is no specific threshold value for trackability forces.

It should be noted that the combinations of neurovascular stent and microcatheter tested here have only limited clinical relevance. In reality, it is clearly defined which microcatheter is suitable for which stent. Since the present study was primarily about a proof of concept of the *in vitro* test setup for trackability measurement and less about a benchmark of different products, this was neglected.

Our group previously developed a novel bioresorbable self-expanding microstent for stent-assisted coiling of intracranial aneurysms [6]. Due to the inferior material properties of the bioresorbable polymer used, larger cross sections of stent structures are necessary compared with commercially available devices, which are basically made of nickel titanium alloys (NiTi). As a result of the larger cross sections the radial force of the bioresorbable stent increases disproportional for very small crimping diameters, as necessary for loading the device into small lumen neurovascular microcatheters [6]. Therefore, the simulated application system presented within the current work represents an indispensable tool for safely and efficiently developing and evaluating new technologies for interventional neuroradiology prior to clinical implementation.

Author Statement

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