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Crossing Total Occlusions using a hydraulic pressure wave: A feasibility study

Aimée Sakes^{1*}, Tjibbe Nicolai¹, Jordan Karapanagiotis², Paul Breedveld¹, and Jo W. Spronck²

¹Department of BioMechanical Engineering, Faculty of Mechanical, Maritime, and Materials Engineering, Delft University of Technology, Delft, the Netherlands.

²Department of Precision and Microsystems Engineering, Faculty of Mechanical, Maritime, and Materials Engineering, Delft University of Technology, Delft, the Netherlands.

* Corresponding author

E-mail: a.sakes@tudelft.nl

Abstract

Crossing highly calcified occlusions is technically challenging mainly due to guidewire buckling. In an effort to prevent buckling, a catheter that uses a dynamic impulse load is proposed. The proposed *Wave* catheter consists of an input plunger to generate an impulse at the handle, a hydraulic pressure wave confined within a Ø2 mm catheter to transfer the impulse towards the tip, and an output plunger to transfer the impulse to the occlusion. To determine the feasibility of this catheter, an experiment was performed in which the input and output impulses were recorded as a function of the catheter type, curvature, and plunger travel distance. Additionally, the system was tested on artificial CTO models to determine the clinical validity. The catheter has illustrated the ability to safely transfer high-force impulses of up to 43N (1.5 N required) with only minimum catheter type and no curvature dependency, allowing for delivering high-force impulses through tortuous vasculature and under any angle. Furthermore, the catheter was able to penetrate the artificial CTO models within 1 strike.

Introduction

With continued development of smaller and more advanced instruments, such as advanced catheters and stiffer and more responsive guidewires, invasive open heart surgeries are slowly being replaced by minimally invasive “nonsurgical” cardiovascular interventions [1-3]. One of the last frontiers of cardiovascular interventions is the Percutaneous Coronary Intervention (PCI) of Chronic Total Occlusion (CTO), defined as heavily calcified total occlusions of an artery of at least three months old. CTOs are characterized as the most technically challenging lesions interventionist face, evidenced by a significant lower success rate in between 50–90% in comparison to acute lesions where success rates of over 95% are achieved [4]. The main failure mode in the percutaneous treatment of CTO is the inability to cross the occlusion, accounting for approximately 60% of the failure cases [5], mainly due to guidewire buckling (Fig 1). Guidewire buckling occurs if the force needed to puncture the CTO, which is usually around 1.5 N [6], exceeds the critical buckling load ($F_{critical}$) of the guidewire, which is around 0.008–0.26 N depending on the type of guidewire[7]. Buckling is unwanted as the bifurcations can damage the blood vessel wall and it lowers the force the guidewire or catheter can deliver onto the target tissue area, which can eventually result in procedural failure and transfer to the much more invasive Coronary Artery Bypass Grafting (CABG) open heart surgery if the occlusion cannot be crossed.

Buckling of slender, flexible, cylindrical instruments, such as catheters and guidewires, can be prevented by decreasing their slenderness λ – defined as the length L [mm] divided by the diameter $\varnothing$ [mm] of the instrument –, by increasing the Young’s Modulus E [GPa] of their material, or by increasing the second moment of area I [mm⁴] by changing the shape of the instrument [8, 9]. However, as the anatomy of the vasculature restricts the instrument diameter, a certain flexibility is required to travel safely through the vasculature, and a

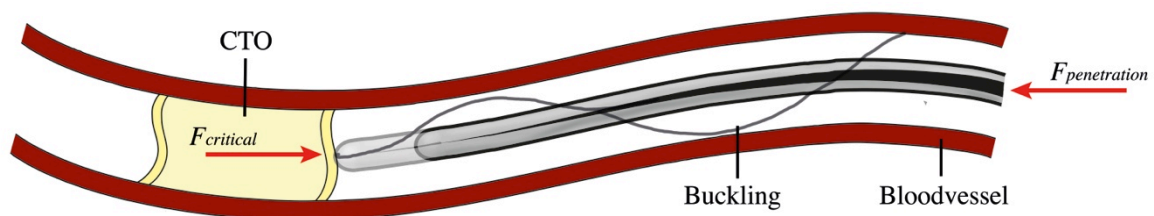


Fig 1. Buckling of the guidewire during the endovascular treatment of CTOs. The guidewire is pushed from outside the body against the CTO (yellow) using a penetration force ($F_{penetration}$). The CTO exerts an opposite compressive force onto the guidewire until puncture is achieved at approximately 1.5 N according to Thind *et al.*[6]. If the compressive force exerted by the CTO exceeds the critical buckling load ($F_{critical}$) of in between 0.008–0.26 N depending on the guidewire, buckling of the guidewire tip, indicated by the dark grey line, will occur.

certain length is required to reach the occlusion site, these variables cannot be altered significantly. Therefore, in order to improve the buckling resistance of the endovascular instruments and improve the procedural success rates of PCIs of CTOs, we propose to use a mechanical impulse J [Ns], defined as the integral of a force F [N] over the time interval dt [s] for which it acts, during the crossing procedure. Using an impulse to dynamically load the guidewire and CTO can prevent buckling in two main ways: (1) the critical load of the guidewire increases with a decrease in the time interval [10] and (2) dynamic loading of the CTO can lower the required penetration load, as illustrated in the studies of Heverly and Jelínek *et al.* [11, 12], as the environmental damping and the inertia of the target tissue can act as a reaction force to the impulse force.

In order to apply an impulse J onto the CTO, translational momentum p , defined as the product of mass m [kg] and velocity v [m/s], should be generated inside the guidewire or crossing tool. Translational momentum can be generated using many different methods, either locally in the distal tip of the crossing tool or proximally in the handle. In this study, we propose to use a hydraulic pressure wave to transfer translational momentum through the catheter (Fig 2). A hydraulic pressure wave is characterized as a longitudinal wave with regions of increased density, known as compressions, and regions of reduced density, known as rarefactions, through a fluid (Appendix A). In order to initiate a hydraulic pressure wave, a sudden change in velocity of the fluid is needed. In our proposed tool, an input impulse J_{input} [Ns] is applied on an input plunger proximally inserted into the lumen of a flexible tube or catheter. The applied input impulse is subsequently converted into translational momentum p of the fluid in the form of a hydraulic pressure wave. Finally, the translational momentum p of the fluid is converted into an output impulse J_{output} [Ns] during the distal impact on the CTO.

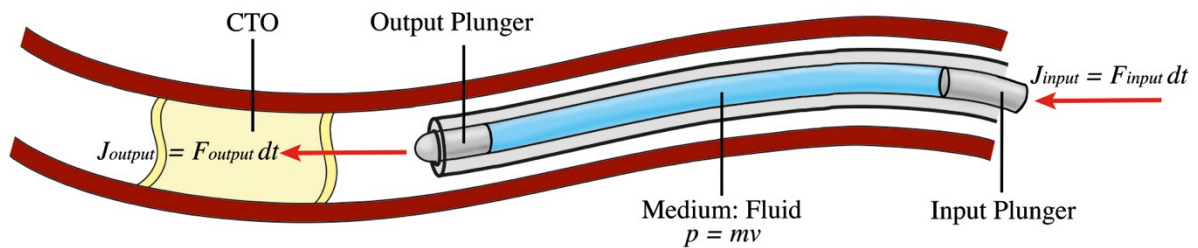


Fig 2. Hydraulic pressure wave concept for crossing CTOs. In this concept, a dynamic input impulse J_{input} [Ns] is exerted on the input plunger of the device. J_{input} is converted into translational momentum p [kgm/s] of the plungers and fluid (blue). Finally, p is converted into an output impulse J_{output} [Ns] during the collision of the CTO with the output plunger. In the clinical situation, the plunger may be in direct contact with the CTO and a preload may be applied.

Even though several shockwave catheters are described in the patent literature in which the translational momentum or shockwave is created inside the distal catheter tip using a shockwave generator, specifically an electric arc [13-15], there are three main advantages of generating the translational momentum proximally. (1) The tip remains flexible, whereas the tip of distally generated momentum catheters incorporate a generator with connector, making the tip rigid and less suited for motion through curved vasculature. (2) The complexity of the catheters in which the pressure wave is generated distally is relatively high in comparison to the complexity of our proposed proximally generated momentum catheter. (3) The output characteristic of the proposed proximally generated momentum catheter can be easily altered by changing the input characteristic, whereas the output characteristic in distally generated momentum catheters is limited mainly due to the size restrictions of the generator.

The goal of this study was to determine the feasibility of a hydraulic pressure wave to transport translational momentum p through a catheter that in turn can be transformed into an impulse J_{output} that can be used to puncture and cross CTOs. In order to answer this question, a proof-of-principle experiment has been carried out. In this experiment, the effect of the magnitude of the input impulse, the elastic behavior of the catheter, and the curvature of the catheter, on the efficiency of the system by dividing the output peak force through the input peak force was determined. We hypothesized that the efficiency of the system is negatively influenced by the elasticity of the catheter, but remains unchanged by curvatures of the catheter shaft. Additionally, the effectiveness of the catheter in puncturing artificial CTO models was tested. Finally, based on the proof-of-principle experiment outcomes, a conceptual design of a hydraulic pressure wave catheter is proposed.

Methods

Mechanical Feasibility

Experimental Goal

The main goal of the experiment was twofold: (1) evaluate the performance of the hydraulic pressure wave catheter in terms of delivered peak force and (2) determine the feasibility of using the hydraulic pressure wave catheter for crossing CTOs. For this purpose, an experimental facility was developed.

Research Variables

Dependent Variables

1. **Output peak force (F_{output}).** In order to determine the feasibility of using a hydraulic pressure wave to puncture a CTO, the output peak force F_{output} was measured. In order to puncture a CTO, the output peak force should be at least 1.5 N according to a study of Thind *et al.* [6].
2. **Pressure wave velocity (v).** The velocity of the hydraulic pressure wave was calculated to test two assumptions: (1) decreased catheter elasticity increases the velocity (Korteweg *et al.* [16]) and (2) the magnitude of the pressure wave, or in other words, the input impulse, does not affect the velocity (Marey *et al.* [17]). In order to determine the velocity of the hydraulic pressure wave, the time between the input (F_{input}) and output peak force F_{output} was measured.

Independent Variables

1. **Input peak force (F_{input}).** Together with F_{output} , the input peak force F_{input} was measured and altered to determine the peak force efficiency η of the *Wave* catheter. Three input peak forces were set: 8 N, 13 N, and 20 N. The associated input impulses were approximately 0.025, 0.0375, and 0.050 Ns, respectively. The time interval of the input impulse was approximately 0.3 ms.
2. **Catheter curvature [diameter and angle].** In order to reach the CTO in the Right Coronary Artery (RCA) [18] or Superficial Femoral Artery (SFA) [19], it is necessary to cross several intersections and curves in the vascular system. In order to determine the effect of curvature on energy losses, and in turn the output peak force, different curvatures have been tested.

The geometry, in terms of radius, angle, and diameter, of endovascular routes to reach the RCA or SFA has been analyzed in Appendix B. All curves were modeled as circles. The curve radii of these stylized single-radius curves ranged between 20 mm in the aortic arch and 100 mm in the Common Femoral Artery (CFA). Based on this analysis, a curve radius of 25 mm was selected, which is close to the minimum radius encountered in the endovascular approaches. When adding the encountered curves and their curve angles from incision point to occlusion site, the accumulated curve angle may be as high as 1080°. Therefore, it was chosen to loop the catheter 3 times; 3x360° or 1080°, in order to simulate an extremely tortuous environment.

3. **Catheter type.** Catheters come in different shapes, sizes (most commonly between Ø0.6–3.0 mm), constructions, and materials. Depending on the type of intervention, the stage of the intervention, and the

interventionist's preference, different catheters are used; from very stiff ones that provide support during the procedure, to floppy ones allowing for atraumatic navigating through the vasculature. The support catheters usually consist of several braided structures encased in a polymer, whereas the floppy catheters are usually made out of a single polymer [20]. During PCI of CTOs, floppy catheters are not used; instead support catheters are used to provide additional strength to the guidewire. In order to determine the effect of catheter morphology, and thus stiffness, on its ability to transfer and confine the hydraulic pressure wave through the catheter, we used two different 6F ($\varnothing 2$ mm, $L = 1$ m) cardiac support catheters of varying stiffness: the more elastic single-braided *Mach1 6F CLS4* guide catheter (Boston Scientific, Marlborough, MA) and the stiffer double-braided *Impulse 6F AL3* angiographic catheter (Boston Scientific, Marlborough, MA).

4. **Output plunger travel distance (d).** This parameter describes the travel distance of the output plunger before it hits the CTO. The main reason this parameter was included was to test the difference in efficiency and impact peak force between an “in-contact” situation ($d = 0$ mm) and a “no-contact” situation ($d = 2$ mm or $d = 4$ mm) as in the clinical situation it might be challenging to determine whether the device is in direct contact with the CTO.

Experimental Facility

The experimental facility is illustrated in Figures 3 and 4. The input impulse was generated by a compression spring ($\varnothing 8.63$ mm, spring constant $k = 0.37$ N/mm) vertically suspended in a construction rail using 2 L-shaped brackets. The input impulse was altered by manually varying the spring compression distance from 10, 15, to 25 mm, and validating these settings using an input load cell (*LSB210*, *QSH00519*, FUTEK Advanced Sensor Technology Inc., Irvine, CA) connected to the load mechanism, resulting in an input peak force of 8, 13, and 20 N. For data acquisition and analysis, an analogue signal conditioner (*CPJ RAIL*, SCAIME, Annemasse, France) and a data acquisition system (*NI USB-6211*, National Instruments Corporation, Austin, TX) with a sampling rate set to 10 kHz were connected to the input load cell. The input load cell was controlled through *LabVIEW 2014* (National Instruments Corporation, Austin, TX).

The input impulse was delivered upon a stainless steel input plunger ($\varnothing 2$ mm shaft, $\varnothing 5$ mm cap), placed within an input cylinder. This input plunger converts and transfers the generated impulse of the mass-spring system into translational momentum of a column of saline fluid of 9g salt/L inside the catheter. The tight fit between the input plunger and the input cylinder strongly reduced fluid leakage. The input cylinder was connected to the aluminum connection block, which was vertically suspended in the 25 mm connection rail.

In order to confine the fluid, the two 6F cardiac catheters were used as previously discussed. Each catheter was attached to the input cylinder using an epoxy resin and guided along a breadboard (*MB3090/M*, Thorlabs Inc., Newton, NJ; Figs 3 and 4). It was chosen not to confine the catheter entirely along its length to closely resemble the clinical situations in which the catheter is also able to move inside the vasculature.

The output of the catheter consisted of an output plunger with cylinder (identical to the input plunger with cylinder) fitted in an aluminum connection block connected to a second connection rail (identical to the input). The output peak force was measured using an output load cell (*LSB200, FSH00103*, FUTEK Advanced Sensor Technology Inc., Irvine, CA), connected to an analogue signal conditioner (*CPJ RAIL*, SCAIME, Annemasse, France) and a data acquisition system (*NI USB-6211*, National Instruments Corporation, Austin, TX) with a sampling rate set to 10 kHz, and controlled through *LabVIEW 2014* (National Instruments Corporation, Austin, TX). The output load cell was placed into direct contact with, or slightly above to test the effect of the plunger travel distance d , the output plunger using a right-angle bracket connected to the connection rail.

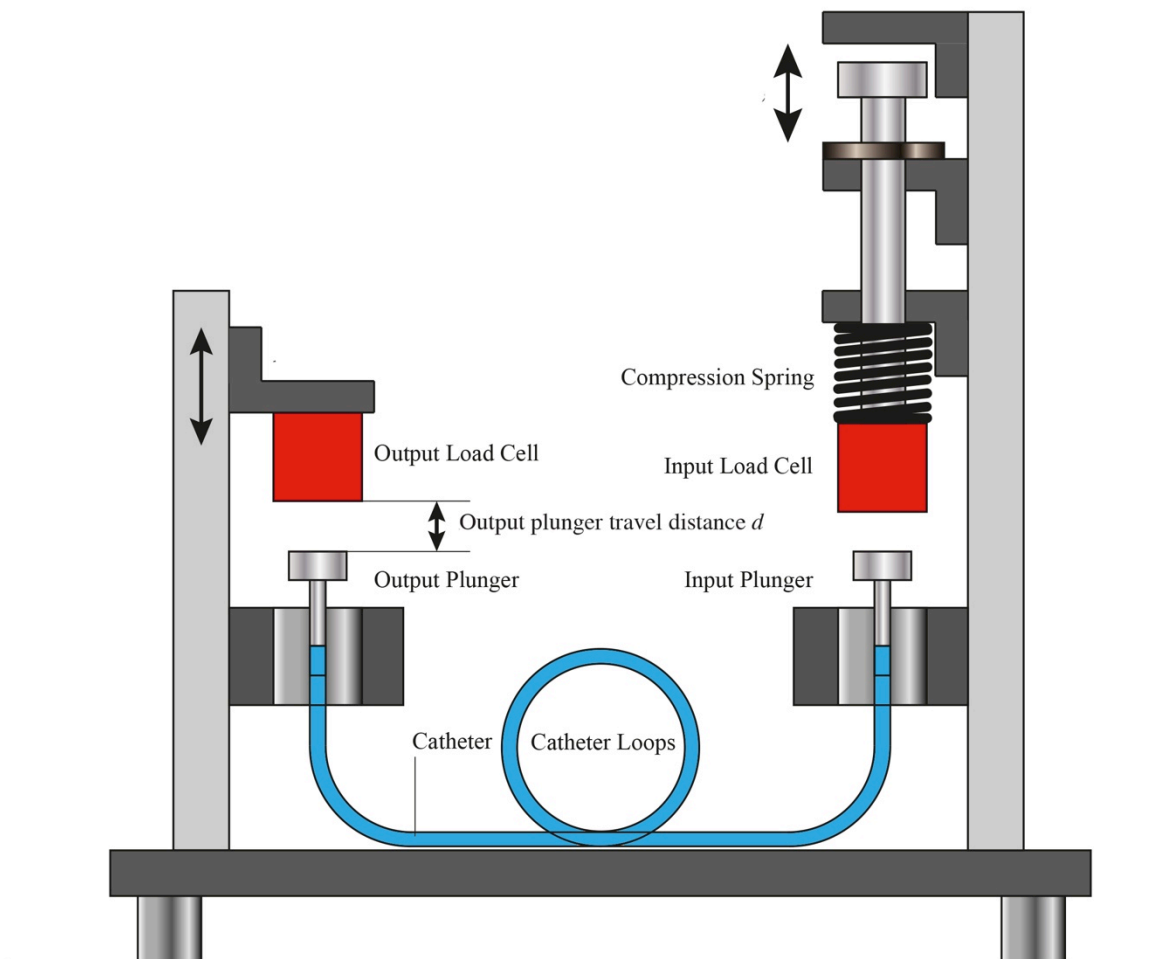


Fig 3. Schematic Representation of the Measurement Facility and the Research Variables. For explanation see text.

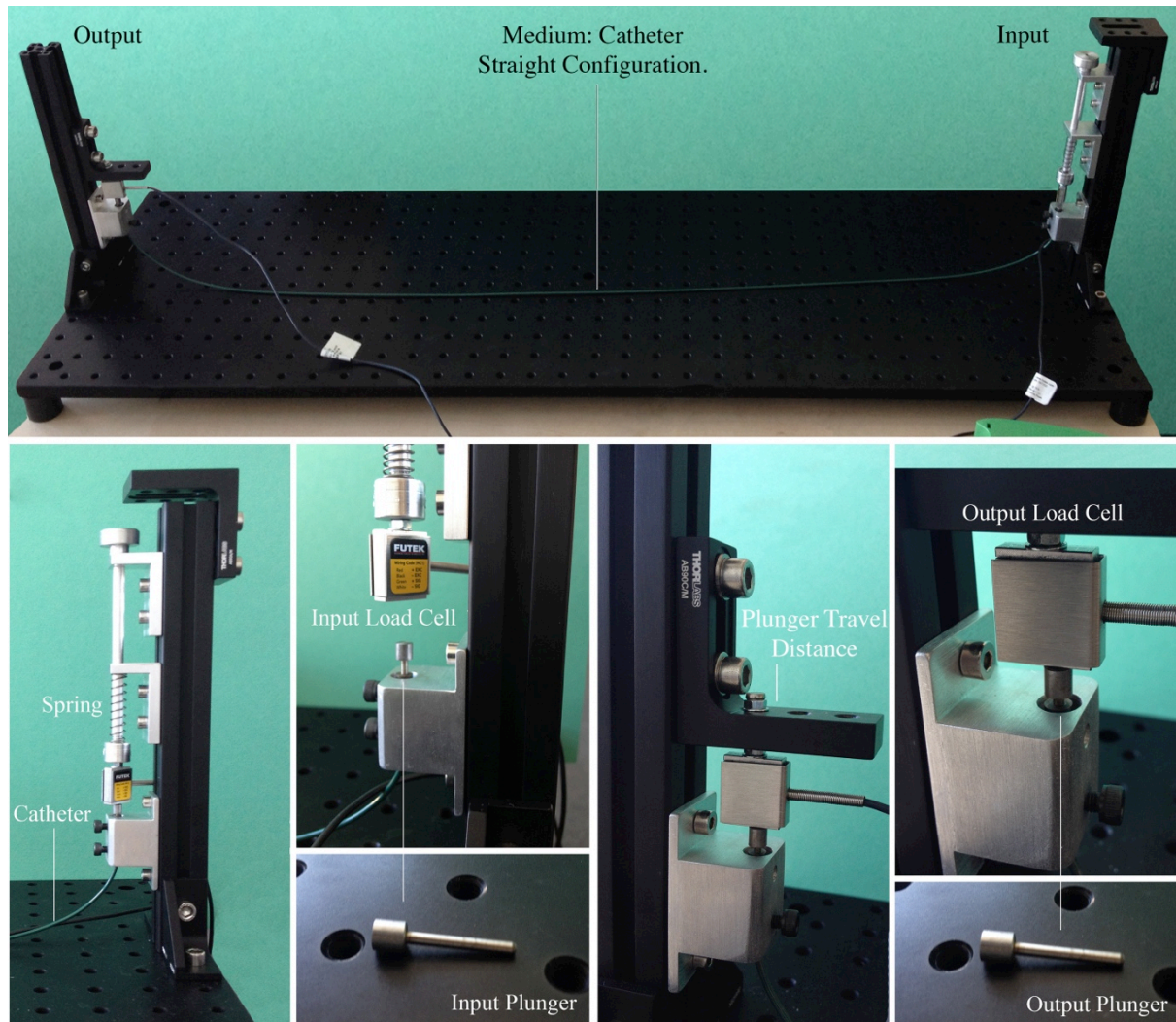


Fig 4. Final Measurement Facility. For explanation see text.

Experimental Protocol

At the start of the experiment, a validation test was executed in order to verify that the catheter shaft itself did not transfer the impulse. Subsequently, the catheter was filled with saline by removing both plungers and injecting saline into the lumen using a syringe until the catheter was fully filled and saline started to spill from the distal end.

The output peak force was measured for all measurements defined by the four independent variables (3 input peak forces, 2 curvatures, 2 catheter types, and 3 output plunger travel distances). The output peak force was derived from the load cell data. The effect of the input impulse and the associated peak force value on the peak force efficiency was measured in the straight configuration for the *Impulse 6F AL3* angiographic catheter (Boston Scientific, Marlborough, MA) with the output plunger in direct contact with the output load cell. The

effect of the curvature was measured for an input peak force of 20 N, the output plunger in direct contact with the output load cell, and the *Impulse 6F AL3* angiographic catheter. The effect of the catheter types was measured using an input peak force of 20 N with both catheters in the straight configuration with the output plunger in direct contact with the output load cell. Finally, the effect of the output plunger travel distance was measured for the *Impulse 6F AL3* angiographic catheter in the straight configuration with an input peak force of 20 N. The velocity of the pressure wave was measured for the 3 input impulses, 2 curvatures, and 2 catheter types, similarly as described for the output impulse.

A Power analysis was conducted to calculate the required minimum number of repetitions to detect an effect of the independent variables on the efficiency of the system. The required number of repetitions was calculated using G*Power software [21] to be a minimum of 15 repetitions using a significance level p of 0.05 and an effect size of 0.4. We decided to test each condition 17 times to minimize the effect of outliers; resulting in a total of 612 tests.

Data Analysis

Per test, the data from the load cells were processed with *MATLAB 2015b* (The Mathworks, Inc., Natick, MA) to identify the input peak force and output peak force for each measurement. Per condition, the mean input peak force and mean output peak force, with their accompanying standard deviations, were determined across the 17 repetitions. Furthermore, per condition the peak force efficiency η was calculated. The velocity of the pressure wave was derived using the time interval between input peak force and output peak force. The distance over which the pressure wave travelled was known since the two catheters used were cut to a length of 1 m; allowing us to calculate the velocity from the plotted data.

Clinical Validity

In order to evaluate the clinical validity of the hydraulic pressure wave catheter, an artificial CTO model was built. In this model, calcium sulfate (CaS) was used to mimic the calcium content and gelatin, the product of degradation of collagen, to mimic the collagen content of the CTO. The model consisted of a proximal cap, representing the hardest, most calcified region, placed on top of a core model, surrounded by an environmental model (Fig 5). The proximal cap model consisted of 55 wt% CaS powder and 45 wt% liquid gelatin mixture, which represented the mean value of the failed PCI of CTO procedures in a study of Cho *et al.* [22]. The models had a diameter of Ø5 mm and were approximately 0.5 mm of thick; equal to the mean CTO proximal cap

thickness [23]. The core of the CTO was mimicked using a mixture of 35 wt% CaS and 65 wt% gelatin, representing the overall average percentage of calcium in CTOs found in the study of Cho *et al.* [22]. The core model had a diameter of Ø5 mm and length of 20 mm, which equals the cut-off value above which PCI of CTOs becomes progressively difficult [24]. The environment model consisted of 25 wt% gelatin and 75 wt% water, which results in an estimated Young's modulus between 100 kPa and 130 kPa, resembling the Young's modulus of cardiac muscle tissue [25]. Finally, the model was submerged into Blood Mimicking Fluid (BMF) to mimic the viscosity of the blood in the coronary arteries, which is in between 2.8 and 3.8 mPas. The BMF was made out of 30 wt% glycerine and 70 wt% clear water of 20°C, resulting in a viscosity of approximately 3.0 mPas [26].

Each model was tested 5 times. The input peak force was set to 36 N and the indenter was placed in direct contact with the plunger. The number of punctures was evaluated by eye. In order to resemble the clinical situation more closely the catheter was allowed to translate freely.

In order to determine the required force to penetrate the CTO model, a small control experiment was performed. In this control experiment, a static force of approximately 1.2 ± 0.4 N ($n = 8$) was needed to puncture the cap with a Ø2 mm stainless steel rod. This value is similar to the value found in the study of Thind *et al.* [6].

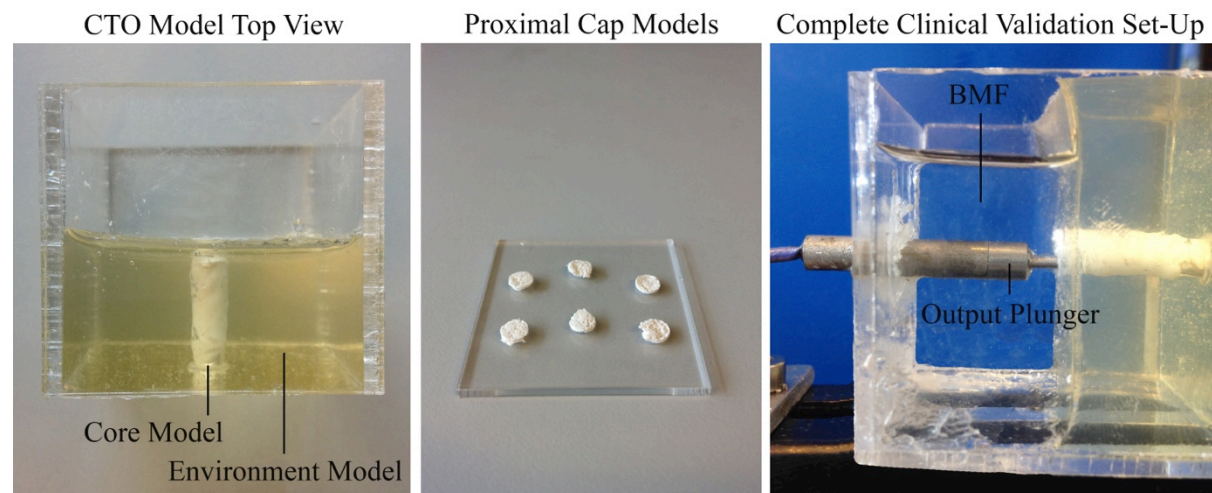


Fig 5. Clinical Validity Experimental Facility. The experimental facility consisted of a rectangular box in which the CTO model was submerged in Blood-Mimicking Fluid (BMF). The CTO model consisted of a proximal cap model (Ø5 mm, 0.5 mm thick), core model (Ø5 mm, 20 mm long), and environment model.

Results

Peak Force Efficiency

In this study we have tested the peak force efficiency of our proposed hydraulic pressure wave catheter using a Ø2 mm 1 m long clinically available catheter. At the proximal and distal end of the catheter a plunger was placed to transfer the impulse to the fluid. The catheter was fixed to the experimental facility at the in- and output. The input impulse was given by a mass-spring system. In order to measure the in- and output peak force, two load cells were placed at the in- and output, respectively. Figure 6 shows an example of the input and output force characteristics of the catheter as a result of an input impulse. From this figure we could deduct the acceleration of the input mass (1 in Fig 6), the input peak force (2 in Fig 6), the velocity of the pressure wave (3 in Fig 6), the output peak force (4 in Fig 6), and the reflections of the pressure wave. The peak force efficiency η was calculated by dividing the output peak force over the input peak force and multiplying this value by 100%. In Table 1 an overview of the experimental results is illustrated. As can be seen from Table 1, the peak force efficiency was negatively, and statistically significantly, affected by the magnitude of the input impulse as determined by a one-way ANOVA ($F(2, 48) = 11.36, p = 9.2 \cdot 10^{-5}$). In other words, the higher the input impulse the lower the peak force efficiency. The mean peak force efficiency was $71.0 \pm 11.2\%$ (mean $\pm$ standard deviation) for an input impulse of 0.025 Ns, $67.6 \pm 7.6\%$ for an input impulse 0.0375 Ns, and $56.0 \pm 9.7\%$ for an input impulse of 0.05 Ns.

In order to investigate the effect of traveling through multiple curves in the vasculature to reach the CTO on the efficiency of the catheter, the catheter was evaluated in two configurations: (1) straight 0° configuration and (2) curved 1080° ($3 \times 360^\circ$) configuration with a curve radius r of 25 mm. The mean peak force efficiency of the hydraulic pressure wave catheter was not affected by the catheter curvature in terms of mean peak force efficiency, as determined by a two-tailed t-test ($t(32) = 2.0, p = 0.3$), allowing for very efficient energy transfer through tortuous environments. The measured peak force efficiency was $56.0 \pm 9.7\%$ for the straight 0° configuration and $58.7 \pm 5.1\%$ for the curved 1080° ($3 \times 360^\circ$) configuration.

In order to test the effect of the elasticity of the catheter shaft, two catheter types were tested in the straight configuration: (1) the elastic single-braided *Mach1 6F CLS4* guide catheter (Boston Scientific, Marlborough, MA) and (2) the stiffer double-braided *Impulse 6F AL3* angiographic catheter (Boston Scientific, Marlborough, MA). From the experiments it was determined that the efficiency of the catheter was influenced by the elasticity

of the catheter shaft ($t(32) = 2.0, p = 1.7 \cdot 10^{-5}$). The peak force efficiency was approximately 13% lower ($\eta = 56.0 \pm 9.7\%$) for the more elastic single-braided catheter as compared to the stiffer double-braided catheter ($\eta = 69.4 \pm 4.9\%$).

Table 1. Overview of experimental results per independent variable. The values are indicated as mean $\pm$ standard deviation ($n = 17$).

Independent Variable	Independent Variable Value	Input Peak Force [N]	Output Peak Force [N]	Mean Peak Force Efficiency η [%]
Input Impulse	0.025 Ns	8.3 ± 0.8	5.8 ± 0.5	71.0 ± 11.2
	0.0375 Ns	13.0 ± 1.1	8.7 ± 0.6	67.6 ± 7.6
	0.05 Ns	19.7 ± 1.9	11.0 ± 1.5	56.0 ± 9.7
Catheter Curvature at $J_{input} = 0.05$ Ns	0°	19.7 ± 1.9	11.0 ± 1.5	56.0 ± 9.7
	1080° (3x360° = 3 loops) ($r = 25$ mm)	18.4 ± 1.8	10.7 ± 0.7	58.7 ± 5.1
Catheter Type at $J_{input} = 0.05$ Ns	Single-braided	19.7 ± 1.9	11.0 ± 1.5	56.0 ± 9.7
	Double-braided	18.4 ± 1.8	10.7 ± 0.7	69.4 ± 4.9
Plunger Travel Distance (d) at $J_{input} = 0.05$ Ns	0 mm	19.7 ± 1.9	11.0 ± 1.5	56.0 ± 9.7
	2 mm	18.8 ± 1.6	37.3 ± 14.2	199.7 ± 26.1
	4 mm	19.0 ± 1.7	40.5 ± 1.5	213.0 ± 16.6

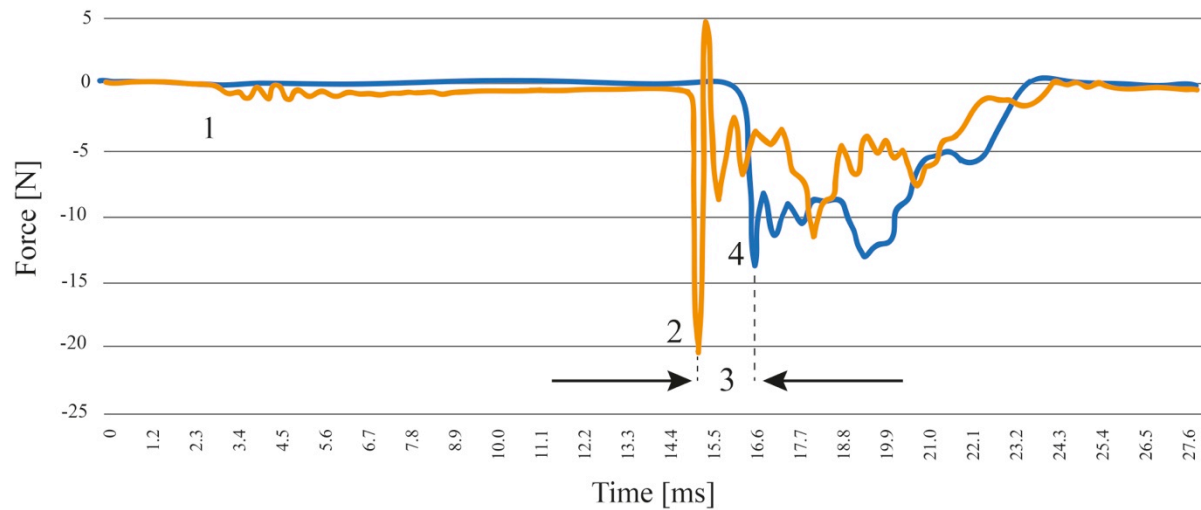


Fig 6. Measured input (orange) and output (blue) force characteristics of the impulse. Observations: (1) Release and acceleration of input mass, (2) Input peak force and oscillations of the input load cell, (3) Wave interval: time it takes for the hydraulic pressure wave to reach the output of the catheter, and (4) Output peak force and oscillations of the load cell.

The effect of the distance between the CTO and the output plunger, defined as the plunger travel distance d , on the peak force efficiency and output peak force was investigated, as in the clinical situation it might be challenging to establish direct contact with the CTO. Three plunger travel distances d were compared: (1) $d = 0$ mm, in which the output plunger was in direct contact with the load cell, (2) $d = 2$ mm, and (3) $d = 4$ mm. It was determined that the peak force efficiency was significantly influenced by the output plunger travel distance d as determined by a one-way ANOVA ($F(2, 48) = 285.6, p = 2.2 \cdot 10^{-27}$). The mean peak force efficiency was positively correlated with an increased travel distance and ranged from $56.0 \pm 9.7\%$ for $d = 0$ mm, $199.7 \pm 26.1\%$ for $d = 2$ mm, and $213.0 \pm 16.6\%$ for $d = 4$ mm, resulting in a maximum output peak force of 43 N for $d = 4$ mm. Looking at a typical measurement of the in-contact situation in which the plunger is in direct contact with the output load cell, and the no-contact situation in which the plunger travels either 2 or 4 mm until impact illustrated in Figure 7, it becomes clear that the output characteristic for both situations is significantly different. In the no-contact situation a more concentrated force-time characteristic was found, whereas a much broader force-time characteristic was found for the in-contact situation.

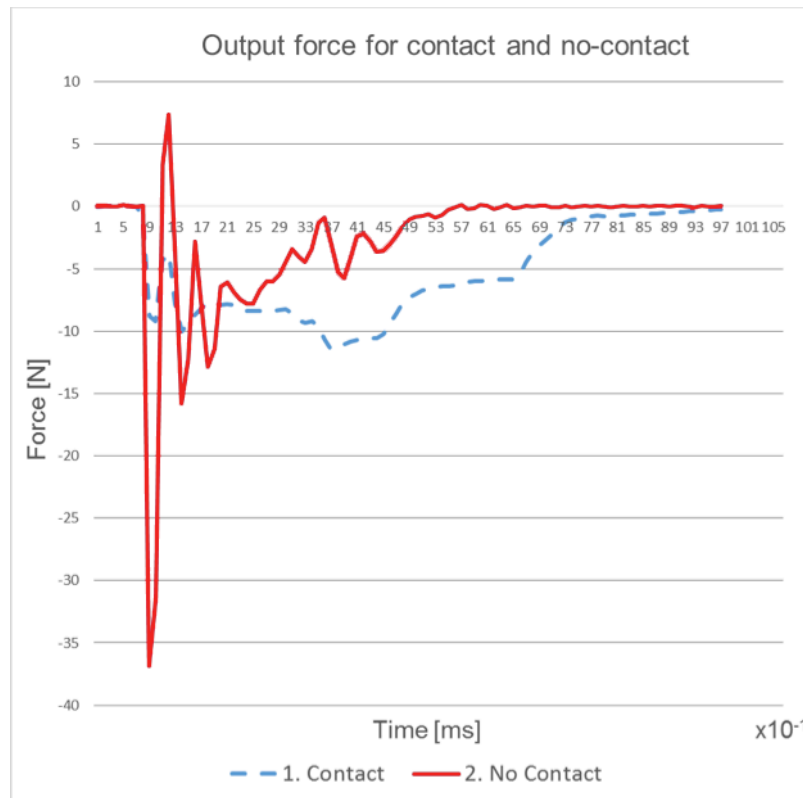


Fig 7. Typical output force-time characteristics of an in-contact ($d = 0$ mm; dotted blue line) and no-contact situation ($d = 2.0$ mm; red line). As can be seen from the figure, a higher output peak force is achieved in the no-contact situation when compared to the in-contact situation. Furthermore, the force-time characteristic of the in-contact situation is much broader than that of the no-contact situation.

Velocity

The velocity of the hydraulic pressure wave v was measured by dividing the length of the catheter ($L = 1$ m) through the elapsed time between the input and output peak force. Table 2 illustrates an overview of the experimental results with respect to the velocity of the hydraulic pressure wave. As can be seen from Table 2, the velocity of the hydraulic pressure wave was in between 330 and 820 m/s, with a mean of 569 m/s. The mean velocity of the hydraulic pressure wave was not significantly influenced by the input impulse, as determined by a one-way ANOVA ($F(2, 48) = 0.4, p = 0.7$). A mean wave velocity of 556.8 ± 134.0 m/s was found for an input impulse of 0.025Ns, 585.7 ± 87.3 m/s for an input impulse of 0.0375Ns, and 580 ± 70.0 m/s for an input impulse of 0.05Ns. The effect of the catheter type (single or double braided) on the mean velocity of the hydraulic pressure wave was not statistically significant either ($t(32) = 2.0, p = 0.9$).

Clinical Validation

The double-braided catheter was tested on artificial CTO models as described in the methods section. The CTO models consisted of a cap model representing the proximal cap, a core model representing the CTO body, and an environment model representing the clinical environment of the CTO. The entire model was submerged in Blood-Mimicking Fluid (BMF). In order to resemble the clinical situation more closely, the catheter was free to translate at the distal end and was not confined along the shaft. The hydraulic wave catheter was able to puncture all the artificial CTO models within 1 strike ($n = 5$).

Table 2. Measured wave velocities versus the input impulses and catheter types. The values are indicated as mean $\pm$ standard deviation ($n = 17$).

Independent Variable	Independent Variable Value	Velocity of the Hydraulic Pressure Wave [m/s]
Input Impulse	0.025 Ns	556.8 ± 134.0
	0.0375 Ns	585.7 ± 87.3
	0.05 Ns	580.0 ± 70.0
Catheter Type*	Single-braided	580.0 ± 70.0
	Double-braided	554.0 ± 73.6

* Using an input impulse of 0.05 Ns

Discussion

Summary of Main Findings

Efficiency Measurements

The feasibility experiment has illustrated the feasibility of using a hydraulic pressure wave to transfer an impulse through a flexible shaft with high efficiency. Our hydraulic pressure wave catheter was capable of transferring high output peak forces of up to 43 N through flexible catheter shafts (Ø2 mm) without buckling. The curvature of the catheter shaft did not significantly influence the efficiency of the system, which is beneficial since several tight curves need to be crossed in order to reach the CTO. The slight difference in the peak force efficiency between the straight and curve configuration can be explained by a slight difference in contact stiffness of the output and overall radial stiffness of the catheter in the curved configuration. The magnitude of the input peak force negatively affected the efficiency of the system. In other words, a higher magnitude pressure wave dissipated more over time than a lower magnitude pressure wave. This finding is in line with the results from a simulation on the effect of pipe wall friction on pressure loss (see Appendix A).

The flexibility of the catheter was found to significantly influence the efficiency, which is mainly due to the overall, radial and axial, expansion of the catheter shaft, absorbing a part of the impulse energy. However, even though the flexibility of the catheter negatively influenced the efficiency, the difference in efficiency was relatively low; approximately 13%. This is beneficial for the clinical application of the device as different catheters are often used for different procedures. A minimal dependency on the catheter elasticity allows the surgeon to pick the most suitable catheter for the procedure.

Changing the output plunger travel distance resulted in the ability to actively change the output characteristic. High output peak forces up to 43 N acting for a short ~0.3 ms time interval were generated when the plunger was not in direct contact with the sensor, whereas lower output peak forces up to 14 N over a longer time interval of ~0.4 ms were achieved with direct contact. The different force-time characteristic between these two situations is mainly caused by the rapid acceleration of the output plunger, and thus higher terminal velocity and momentum, which results in high, but short-lived, peak forces. Even though the overall efficiency decreased with increasing output plunger travel distance, mainly due to energy losses between the plunger and cylinder, the ability to achieve high peak forces is beneficial when puncturing heavily calcified CTOs. It must be noted, however, that in the clinical situation, the blood in front of the CTO will significantly damp the plunger. This

will potentially lead to lower peak forces in the clinical situation. Furthermore, due to the flexible environment of the CTO and the flexibility of the CTO itself, the peak force will be significantly less in the clinical situation.

Velocity Measurements

The mean pressure wave velocity was found to be approximately 570 m/s, which is slightly higher as expected from the calculated values in Appendix A. The experimental results illustrate no significant difference between the mean velocities of the hydraulic pressure waves for the different input impulses and catheter types. No significant difference in the wave velocity of the two different catheters was found either. One possible explanation is that the difference in elasticity of the chosen catheters was too small to cause a significant difference in the wave velocity. For more information on this topic, we would like to refer to Appendix A.

Clinical Feasibility

The hydraulic pressure wave was highly effective in puncturing the artificial CTO models. All the CTO models were punctured within 1 strike, while the catheter tip was free to translate, similar to what will be encountered in a clinical situation. This result clearly illustrates that the *Wave* catheter has great potential for puncturing CTO during PCIs in the near future.

Limitations of this Study

In the current measurement facility, the lack of a fluid seal between the plunger and the cylinder caused minor fluid leakage during operation; decreasing the efficiency, and required filling the catheter after each test. Furthermore, on some occasions this also caused air to become entrapped in the system, which decreased the efficiency due to the compressibility of the air bubbles.

Recommendations for Future Research

Modeling of the *Wave* Catheter

In order to get a better understanding of the working principles of the *Wave* catheter, it is recommended that a (mathematical) model is developed. This model can be used to run simulations and can aid in understanding the relevant properties of the shaft and output to optimize the efficiency of the system. Furthermore, this model can also be used to simulate different output characteristics and their effect on the catheter, as well as on a CTO model.

Increase of Efficiency & Safety

Even though our hydraulic pressure wave catheter has illustrated the ability to transfer impulses through tortuous shafts with high efficiency, we feel that a further increase in efficiency is possible by redesign. Energy loss can be mainly contributed to the expansion of the catheter wall (Appendix A). Therefore, the use of an even stiffer catheter shaft in which the overall, radial and axial, expansion is minimized could be researched. Furthermore, during the experiments it was found that small air bubbles in the system would significantly reduce the efficiency. In order to prevent entrapped air bubbles in the catheter, in future an alternative way of filling and sealing the catheter should be researched. Finally, in the current design, the cylinders contain a so-called series junction at the cylinder-catheter interface caused by the different inner diameters of both parts, which partly reflects the pressure wave; decreasing the efficiency of the system (Appendix A). In order to prevent this effect, as well as potentially reduce the friction between the output plunger and the cylinder, a different tip geometry can be looked into in which the output plunger is incorporated in the catheter shaft (see also Fig 8). Finally, it is imperative to test the catheter in an *ex-* or *in-vivo* situation to determine its effectiveness and safety in a clinical situation that closely resembles that of PCIs of CTOs.

Effectiveness on CTO Models

In order to get a conclusive answer on the feasibility of the hydraulic pressure wave catheter for increasing the success rate of PCI in CTOs, it is a necessity to test the catheter on animal CTO models. In theory, the system can deliver output forces high enough to puncture the caps of CTOs, as Thind *et al.* [6] measured a maximum force of 1.5 N to penetrate a rabbit CTO and forces up to 43 N were measured for our device. However, in a clinical situation the viscosity of the blood and flexibility of the environment will damp the output, resulting in significantly lower peak forces. Our catheter has illustrated the ability to puncture the artificial CTO models submerged in Blood-Mimicking-Fluid (BMF) within 1 strike. The catheter was allowed to translate, to more closely resemble the clinical situation and the CTO model. Even though the CTO model is artificial, it still illustrates the effectiveness of the catheter striking a flexible model.

The effect of the output characteristic on the effectiveness and efficiency to puncture CTOs should be researched. In the current experiment, single strikes, with different force-displacement characteristics, were used to test the performance. In the near future, research could be conducted to optimize this force-displacement characteristic for puncturing CTOs. Furthermore, it is also possible to exert multiple executive strikes by guiding multiple pressure waves through the catheter. Additionally, research could be conducted into different

tip shapes to determine the most effective and efficient shape to puncture CTOs (see also Sakes *et al.*[27] on this topic).

Miniaturization Outer Dimension

For a future clinical prototype the possibility of miniaturization should be looked into. Current dedicated coronary CTOs devices, such as guidewire and catheters, have a diameter in between Ø0.35–1.1 mm [24, 28]. Due to the simplicity of our design, miniaturization to a Ø1 mm size should be possible. For the catheter shaft, a regular double-braided Ø1 mm (3F) could be used, while the output plunger should be minimized towards a sub-millimeter scale. The main issue in miniaturization is achieving a proper fluid seal and filling of the catheter without air bubble entrapment. Therefore, redesign of the plungers, in which they are incorporated in the catheter shaft, may be a necessity.

Integration in Clinical Practice

Based on the findings in the proof-of-principle experiment and future clinical application, a conceptual design, named *Wave* catheter (Fig 8), containing a Ø1 mm double-braided radially stiff catheter shaft ($L = 1$ m) connected to a handle was developed. To allow for ergonomic handling and single-handed control the mechanisms are encompassed by a 3D-printed handle piece, which can be adjusted to the surgeon's preference. The handle contains an adjustable input impulse mechanism to set the preferred output peak force using a translating knob and a pistol-grip trigger mechanism to deliver the input impulse. An additional motor can be connected to the handle piece to allow for high-frequency pulsating inputs.

In the envisioned PCI “wave” procedure, the *Wave* catheter will be guided over a standard guidewire (Fig 9) towards the operation area. Once arrived at the CTO, the *Wave* catheter will be activated to puncture the proximal cap of the CTO. In order to prevent fragments from entering the blood stream we recommend to use an emboli filter proximal to the CTO at this stage. After angiographic confirmation that the proximal cap is fractured, a high stiffness guidewire is guided through the catheter and subsequently used to cross the CTO body. Finally, the *Wave* catheter is removed from the vasculature and a balloon catheter can be slid over the guidewire towards the CTO to reopen the coronary artery.

Additionally, the *Wave* catheter could potentially be used to open a passageway to the subintimal space by hitting the boundary layer between the CTO and blood vessel wall. This way, the CTO can be crossed subintimally. Future research, should be focused on investigating this possibility.

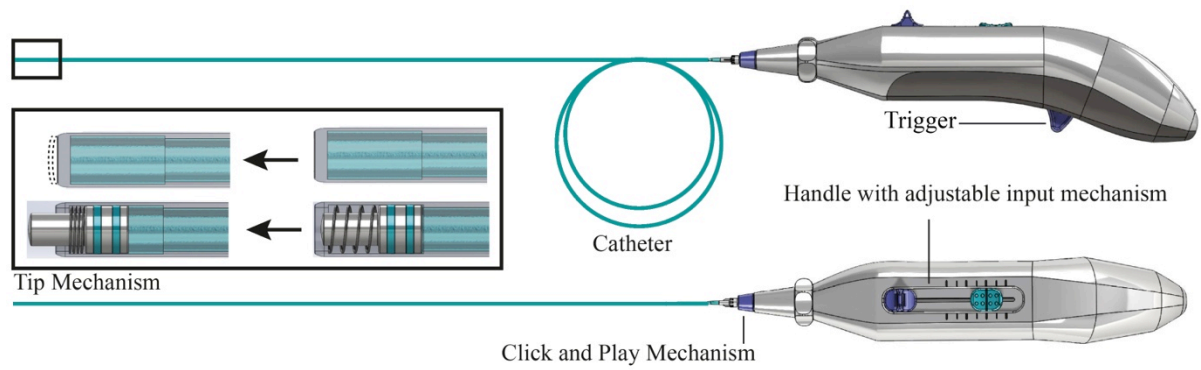


Fig 8. Conceptual Catheter Design. The *Wave* catheter consists of handle that allows for actively adjusting the input impulse and characteristic, as well as triggering the mechanism. A click-and-play mechanism is used to connect a pre-filled catheter shaft to the handle. The catheter tip shape can be altered based on the application; from blunt to sharp. Furthermore, the effect of an integrated or free-moving piston will be researched.

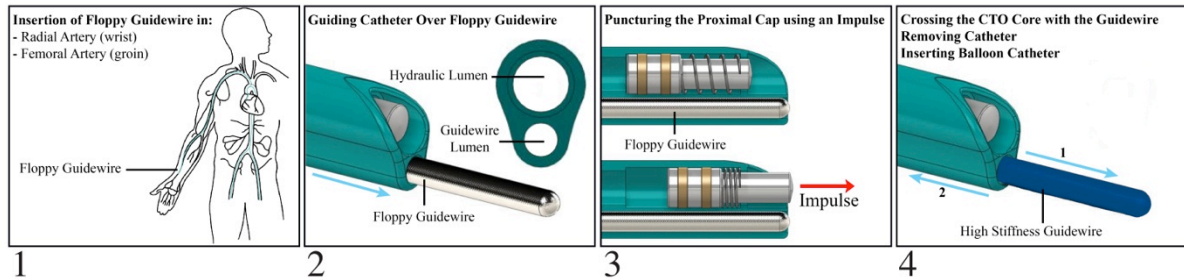


Fig 9. Envisioned PCI Procedure with the *Wave* catheter. (1) A floppy guidewire is inserted into the vasculature via the radial artery (wrist) or femoral artery (groin) and guided towards the CTO. (2) Once arrived at the CTO, the hydraulic pressure wave catheter is guided over the floppy guidewire. (3) The *Wave* catheter punctures the proximal cap of the CTO. (4) Once, the proximal cap is punctured, the floppy guidewire is retracted and a high stiffness guidewires is guided towards the CTO. Subsequently, the high stiffness guidewire is used to cross the CTO. Finally, the *Wave* catheter is removed and a balloon-stent catheter is guided over the guidewire to reopen the artery.

Expansion of Application Areas

The simplicity and versatility of the *Wave* catheter makes it highly suitable for other medical applications as well, for example, to fragment, penetrate, or drill through other types of brittle materials or tissues, such as gall-, kidney-, bladder-, and liver-stones, bone, and (calcified) tumors.

Conclusions

The proposed system has proven to transfer high-force impulses up to 43 N (1.5 N required) through a highly curved shaft with high efficiency, allowing for high force delivery onto the CTO, independent from the shaft

shape and under any tip angle. Different catheter types only minimally affected the efficiency, with a decrease of approximately 13% for a more flexible shaft, allowing the surgeon to choose the most suitable catheter type for the application. In future the catheter will be further developed into a smaller, Ø1 mm, handheld device that allows for single-handed control and easy adjusting of the output peak force. The hydraulic pressure wave catheter may pave the way towards a more widespread adoption of PCIs of CTOs for even the less experienced interventionists by allowing for easy puncture of the most heavily calcified CTOs in the most distal and difficult to reach areas.

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Author Contributions

AS wrote the main manuscript text. AS, TN, JK, and JWS designed and manufactured the measurement facility. AS, TN, JK, and JWS designed the experimental protocol. TN and JK performed the experiments. JWS and PB have given advice on the structure and content of paper. All authors reviewed the manuscript.

Additional Information

Competing financial interest statement.

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Appendix A: The Hydraulic Pressure Wave

A.1. What is a Hydraulic Pressure Wave?

In order to understand the mechanics of a periodic longitudinal pressure wave, we consider a long tube filled with a fluid and two plungers at each end, as in Fig. A1. If we push the input plunger in, we compress the fluid near plunger; increasing the pressure in this region. This region then pushes against the neighboring region of fluid, and so on, resulting in a wave pulse that moves along the tube until it reaches the output plunger. The output plunger is accelerated by the wave and can exert an impulse on the environment.

Now we suppose we move the input plunger back and forth along a line parallel to the main axis of the tube with simple harmonic motion. This motion forms regions in the fluid where the pressure and density are greater or less than the equilibrium values. We call a region of increased density a “compression” and a region of reduced density a “rarefaction”. The compressions and rarefactions move towards the output plunger with constant velocity v .

For a mathematical description of the wave, a so-called wave function is required that describes the position of a fluid particle in the medium at any time (see Eq. A1). The displacement of such a particle y is a function of the position x and the point in time t .

$$y(x, t) = A \cos \left[\omega \left(\frac{x}{v} - t \right) \right] = A \cos 2\pi f \left(\frac{x}{v} - t \right) \quad (\text{A1})$$

with A = the amplitude [m], ω = the angular frequency ($2\pi f$) [rad/s], x = is the position along this axis [m], v = the wave velocity, t = the point in time [s], and f = frequency [Hz].

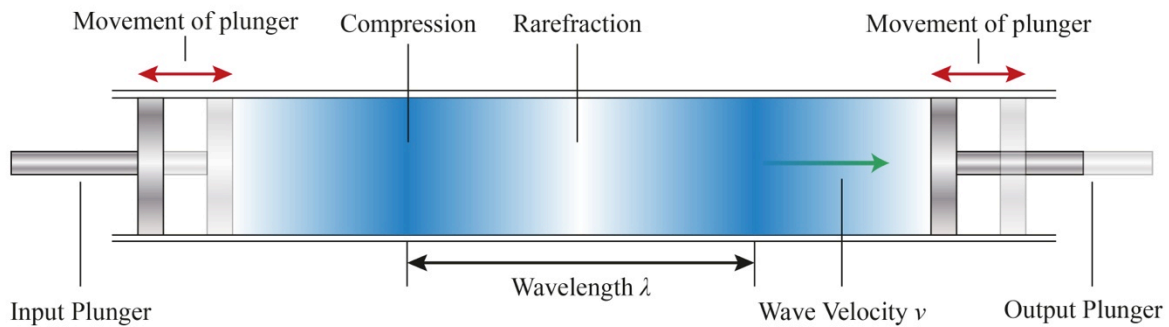


Figure A1. A longitudinal hydraulic pressure wave travelling to the right. First, we move the input plunger to the right, which compresses the fluid near the plunger. The compressed region subsequently pushes against the neighboring region, and so on, resulting in a pressure wave that travels from the input to the output plunger. Once arrived at the distal end, the pressure wave pushes against the output plunger, which subsequently starts to accelerate. Note also that if we pull the input plunger back also rarefactions (low pressure regions) can be generated.

A.2. Transfer of the hydraulic pressure wave

A.2.1. Velocity of the Hydraulic Pressure Wave

On what properties of the medium does the velocity depend? A pressure wave causes compressions and rarefaction in the fluid, so the velocity is related to how easy or difficult it is to compress the fluid. This value is represented by the bulk modulus K [N/m²] of the fluid. On the other hand, inertia, which is related to mass and thus its density ρ [kg/m³], resists the return to the equilibrium state. Thus the velocity of the unconfined pressure wave can be described as:

$$v = \sqrt{\frac{K}{\rho}} \quad (\text{A2})$$

The velocity of a hydraulic pressure wave confined in an elastic pipe is different, usually much lower, from that in unconfined water. This difference was first described by Frizell ¹ and can be deduced from Eq. A3, in which the velocity of the hydraulic pressure wave (v [m/s]) in a thin-walled cylindrical pipe is calculated ². From Eq. A3 it can be seen that the wave velocity v can be increased by increasing ρ and K of the fluid or E and e of the shaft ³. When the Young's modulus E of the shaft becomes large, which is the case in a perfectly rigid shaft, the wave velocity would approach that of an unconfined pressure wave. Furthermore, it can be seen that within this linearized model the amplitude (or magnitude) of the pressure wave does not affect the wave velocity (see also Marey *et al.* ⁴ on this topic).

$$v = \sqrt{\frac{1}{\rho \left(\frac{1}{K} + \frac{D}{Ee} \right)}} \quad (\text{A3})$$

with ρ = density of fluid [kg/m³], K = bulk modulus of fluid [Pa], D = diameter of pipe [m], E = Young's modulus of the shaft [Pa], e = wall thickness of the shaft [m].

The effect of pipe wall elasticity on the wave velocity can be explained by fluid-structure interaction, in which the propagating pressure wave interacts with the elastic and deformable catheter shaft. In general, three interaction mechanisms can be distinguished: shear stresses between the fluid and shaft, the axial compression of the shaft by radial deformation during pressure surges (called Poisson coupling ⁵), and movement of shaft generated by an imbalance of forces in curves. Shear stresses between the fluid and shaft are dependent on the dynamic viscosity and velocity of the fluid at the boundary. At the boundary, the velocity of the fluid particles is almost zero, also known as the no-slip condition (see A.2.2), so the most determining factors are the dynamic viscosity of the fluid, which is approximately 1.0 mPas at 20 °C. Axial compression of the shaft is caused by radial extension of the catheter shaft that results from the passing pressure wave. Increased elasticity increases the radial extension and thus decreases wave velocity as it partly absorbs the volume displaced by the pressure wave. Movement of the catheter shaft also decreases the amplitude of the wave as it partly takes the momentum of the pressure wave.

With Eq. A1 and A3 we can make a prediction on the wave velocity of the hydraulically actuated catheter

using a density ρ of 999 kg/m³ (water), a bulk modulus K of $2.19 \cdot 10^9$ Pa, diameter D of 2 mm, and wall thickness e of 0.2 mm. The effect of the Young's modulus E on the wave velocity v is plotted in Figure A2. The plotted line approaches a horizontal asymptote, which represents the wave velocity through a perfectly rigid shaft. As the Young's moduli of the single- and double-braided catheter are unknown, an estimation is made based on the volume ratio and Young's moduli of the PolyTetraFluoroEthylene (PTFE or Teflon; $E = 0.4$ GPa and $V = 98\%$) liner and stainless steel braiding ($E = 180$ GPa and $V = 2\%$)⁶. Using Eq. 1, a wave velocity of 580 m/s is estimated.

A.2.2. Energy Losses of the Hydraulic Pressure Wave

In the proposed system a pressure wave travels from the handle to the tip. Between the input and the output the pressure wave can decrease in pressure, and thus energy, as the result of:

1. Friction between the fluid and the surface of the wall, also known as friction coupling;
2. Pressure loss due to elasticity of the shaft walls;
3. Partial reflection losses in bends, valves and tees, also known as junction coupling, and
4. Mechanical friction losses in junction couplings.

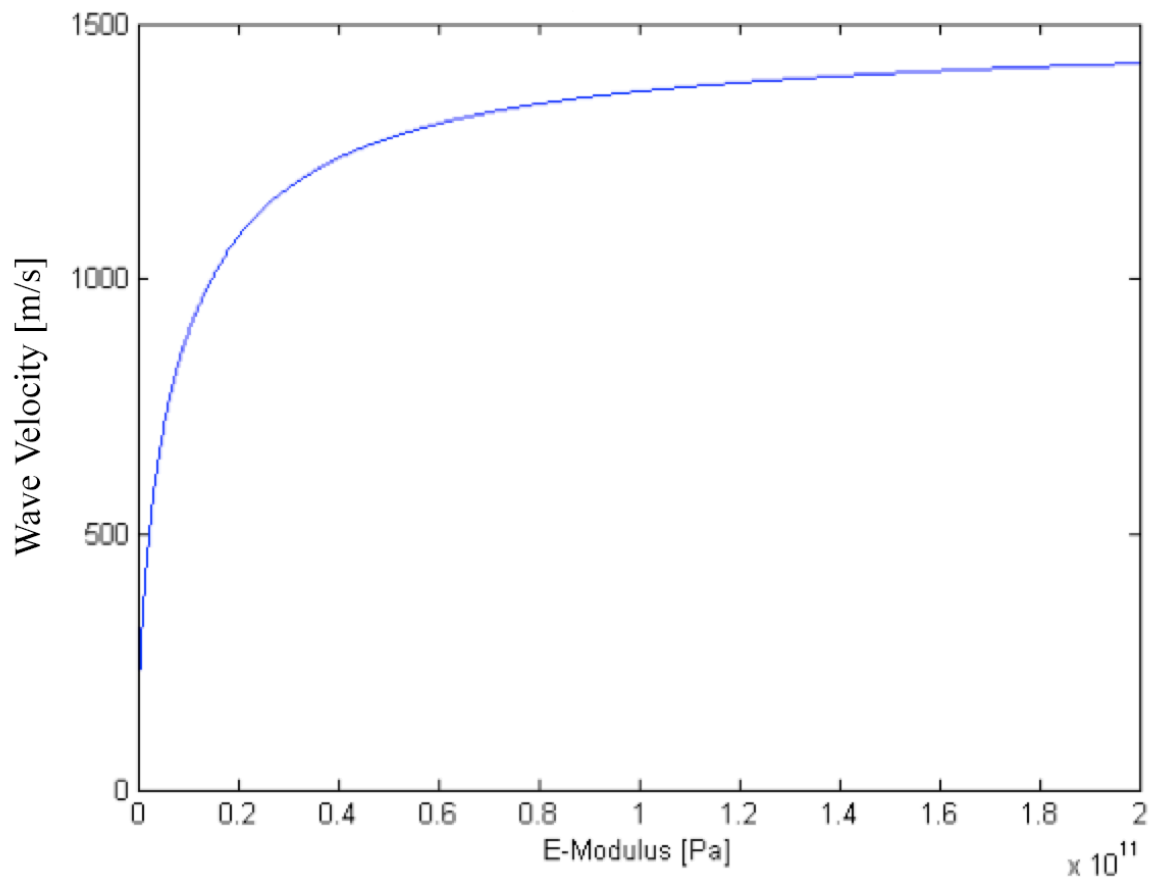


Figure A2. Wave velocity versus the Young's Modulus of the shaft. The graph illustrates that a slight change in the Young's modulus of the shaft has a large effect on the velocity as the slope of the graph is high in the 0 – 20 GPa range.

In conventional pipe flow, friction between the fluid and catheter shaft surface can be mainly attributed to the surface roughness of the inner surface (see Fig. A3). This can be explained by the no-slip boundary condition that states that the velocity at the fluid–solid boundary is equal to that of the solid boundary. At the fluid-solid boundary, the adhesive forces between the fluidic and solid particles are larger than the cohesive forces within the fluid, which brings the fluid velocity to zero at the boundary. This effect is amplified by an increase of surface roughness on a molecular level. Especially in the case of a small diameter tube, the boundary layer is relatively large.

Unfortunately, the effects of friction on propagating pressure waves are not that well described. Therefore, the effect of pressure loss due to friction between the fluid and the surface of the wall was simulated using COMSOL. When this friction effect was turned off the pressure wave did not dissipate over time and traveled back and forth along the pipe. This demonstrates no other pressure loss effects are included in the model and the wave is perfectly reflected. The loss in pressure over time showed a logarithmic decay when friction was included using the Churchill friction model ⁷ (see Fig. A4). The exponential decay illustrates that the friction effect depends on the magnitude of the pressure wave. A higher magnitude pressure wave dissipates faster due to surface roughness than a lower magnitude pressure wave.

Energy losses can also be caused by partial deflection and friction in abrupt bends, valves, and tees, as well as by catheter wall elasticity. As there is little information available on energy losses due to these effects, it was decided to perform the feasibility experiment. The feasibility experiment is described in detail in the main manuscript.

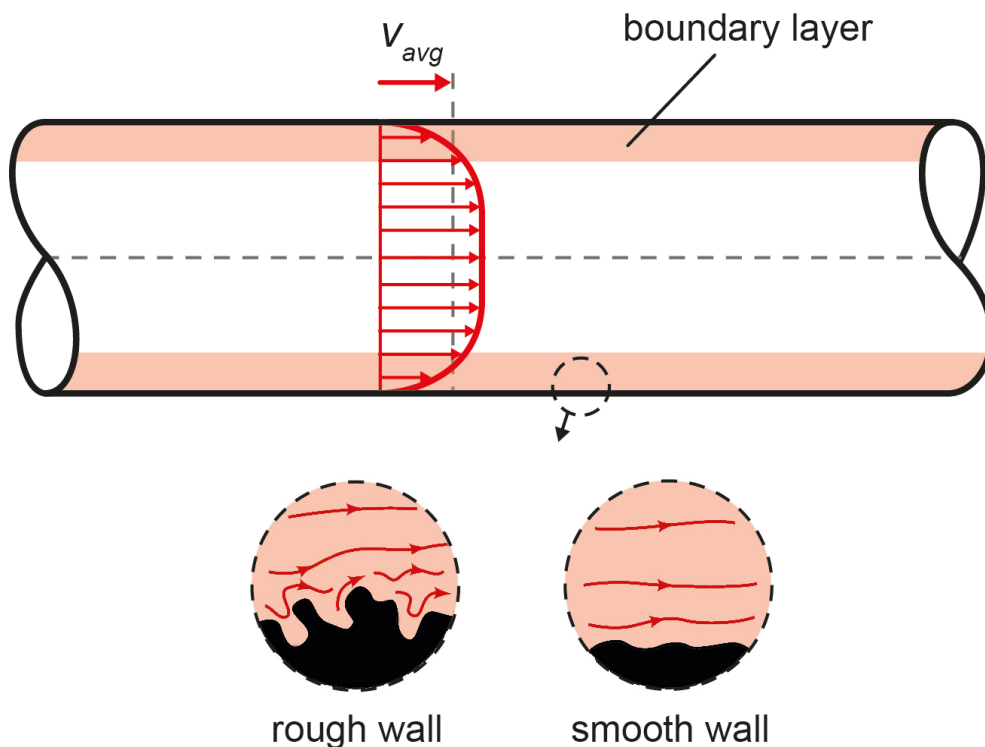


Figure A3. Pressure loss effect due to surface roughness. No-slip behavior at the boundary layer results in a decreased average velocity (v_{avg}) and pressure losses.

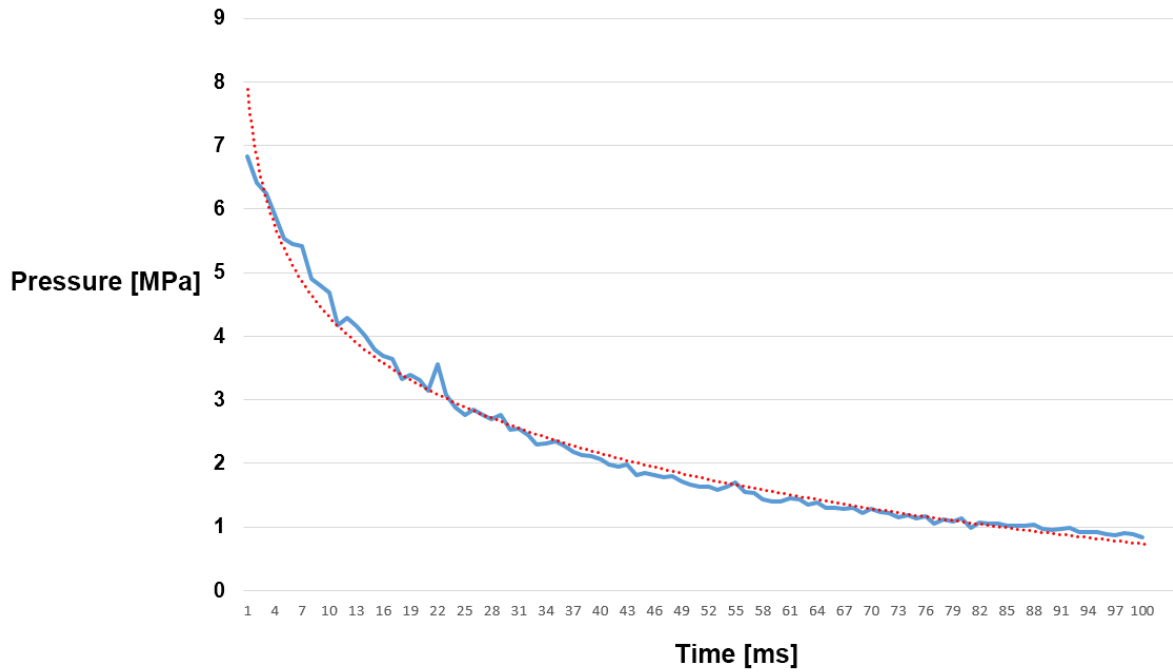


Figure A4. COMSOL simulation showing the pressure drop over time in an elastic pipe as a result of surface roughness (blue line). A logarithmic trend line provides an approximation of the simulation (red line). Formula of the trendline: $y = -1.552 \cdot \ln(x) + 7.8797$.

A.3. Wave Reflection and Transmission

A.3.1. Reflection coefficient

When a pressure wave approaches a boundary, such as a dead end in the system, the wave is reflected. The reflection coefficient describes the ratio between the incident wave (the pressure wave before reflection) and the reflected wave (see Eq. A4). In case of a dead end, the reflected pressure wave has the same sign and same magnitude as that of the incident wave ($r = 1$)³. In the hydraulic system of the proposed concept, a moving piston is present, which represents an active dead end. Therefore, the reflected pressure wave has the same sign as the incident wave but a significantly decreased magnitude. In the ideal situation, the reflected pressure wave would be zero. The movement and properties of the piston, the friction of the seal and the contact of the piston with a material determine the magnitude of the reflected wave in case of the proposed concept.

$$r = \frac{wave_{reflected}}{wave_{incident}} \quad (A4)$$

A.3.2. Series junction

In a junction, a pressure wave can get reflected and/or transmitted. A series junction represents the transition of two pipes with different diameters, wall thicknesses, and/or friction factors. When a pressure wave approaches a series junction, the pressure wave is partly reflected back into the same pipe and partly transmitted further down

the pipe. For a series junction a specific reflection coefficient (r ; see Eq. A5) and transmission coefficient (s ; see Eq. A6) exists³.

$$r = \frac{\text{wave}_{\text{reflected}}}{\text{wave}_{\text{incident}}} = \frac{\frac{A_1 - A_2}{v_1} \frac{v_2}{v_1}}{\frac{A_1 + A_2}{v_1} \frac{v_2}{v_1}} \quad (\text{A5})$$

$$s = \frac{\text{wave}_{\text{transmitted}}}{\text{wave}_{\text{incident}}} = \frac{\frac{2A_1}{v_1}}{\frac{A_1 + A_2}{v_1} \frac{v_2}{v_1}} \quad (\text{A6})$$

Where A = cross-sectional area of pipe 1 or 2 [mm²] and v = wave velocity of pipe 1 and 2 [m/s].

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Appendix B: Artery Modeling

This appendix provides a detailed description of the travel path through the human vascular system to reach the occlusion site. This information, together with geometrical details of the vascular system and calculations, was used to define the geometrical design requirements of the prototype.

B.1. Endovascular Routes

The most prevalent location of a coronary CTO is the Right Coronary Artery (RCA)⁸. For the peripheral arteries, the Superficial Femoral Artery (SFA) is the most common location⁹. To approach the RCA and SFA, several endovascular routes can be taken. Two common approaches for each of the occlusion locations were selected for this analysis:

1. RCA–Transfemoral approach
2. RCA–Radial approach
3. SFA–Ipsilateral antegrade approach
4. SFA–Contralateral retrograde approach

Per approach, the vascular route is specified in detail in Table B1 and illustrated in Figure B1. In the case of a transfemoral approach, the vascular system is entered at the groin into the Common Femoral Artery (CFA). From here, the path travels upwards, towards the heart. For the radial approach, the vascular system is entered at the wrist into the Radial Artery (RA). In this approach, the path travels upwards through the arm and shoulder towards the heart. For both the ipsilateral antegrade and contralateral retrograde approaches, the vascular system is entered at the groin, either on the ipsilateral or the contralateral side of the body.

B.2. Artery Diameters, Curve Radii, and Bifurcation Angles

The geometry of the four described endovascular routes was analyzed in more detail. This analysis included the determination of the average artery diameters, curve radii of the arteries, and the artery bifurcation angles. The artery diameters of all arteries that are passed in one of the four approaches have been obtained from literature (see Table B2). It can be seen that the diameters differ slightly between sources. Therefore, an average diameter (defined as the mean of the smallest and largest number given in Table B2) was calculated. The curve radii and bifurcation angles have been estimated based on illustrations and data in⁸⁻¹⁹, and are given in Tables B3 and B4, respectively.

The presented artery diameters, curve radii, and bifurcation angles that are encountered in the analyzed endovascular approaches have been used to model the routes in simplified nodes. These nodes represent the curves and bifurcations that need to be passed by the guidewire or crossing tool to reach the RCA or SFA. The annotations of the nodes, as well as the simplified illustrations of the nodes, are given in Fig. B2.

Table B1. The detailed arterial paths of the four selected endovascular approaches.

RCA–Transfemoral	RCA–Radial	SFA–Ipsilateral	SFA–Contralateral
Common femoral artery	Radial artery	Common femoral artery	Common femoral artery
External iliac artery	Brachial artery	Superficial femoral artery	External iliac artery
Common iliac artery	Axillary artery		Common iliac artery
Descending aorta	Subclavian artery		Common iliac artery
Aortic arch	Brachiocephalic artery		External iliac artery
Ascending aorta	Aortic arch		Common femoral artery
Right coronary artery	Ascending aorta		Superficial femoral artery
	Right coronary artery		

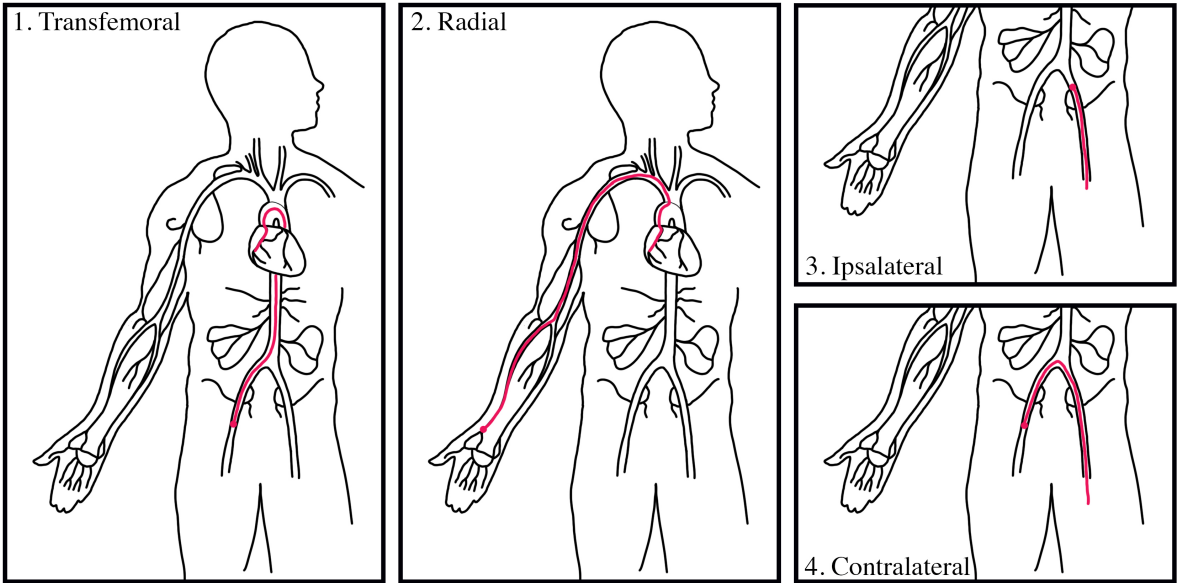


Figure B1. The arterial routes of the four selected endovascular paths in the body. (1) Right Coronary Artery (RCA)–Transfemoral approach, (2) RCA–Radial approach, (3) Superficial Femoral Artery (SFA)–Ipsilateral antegrade approach, and (4) SFA–Contralateral retrograde approach.

Table B2. Diameters [mm] of the encountered arteries in the in the 4 previously described coronary and peripheral interventional approaches.

	Diameters from Avolio ¹⁰	Diameters from Kahraman <i>et al.</i> ¹⁴	Diameters from 12,13,15-19	Mean Artery Diameter
Common iliac artery	10.4	9.1–10.4		10.0
External iliac artery	5.4–5.8	8.0		6.4
Common femoral artery			7.5 (<i>f</i>) ¹⁷ 10.4 (<i>m</i>) ¹⁷	8.9
Superficial femoral artery	4.8			4.8
Aortic arch	21.4–22.4			21.9
Ascending aorta	29.0	32.6		30.8
Brachiocephalic artery	12.4			12.4
Subclavian artery	8.0			8.0
Axillary artery	6.2–7.2			6.7
Brachial artery	4.8–5.6			5.2
Radial artery	3.2		2.3 ¹² 2.8 (<i>f</i>) ^{15,16} 3.1 (<i>m</i>) ^{15,16} 2.4 (<i>f</i>) ¹⁹ 2.7 (<i>m</i>) ¹⁹	2.8
Descending aorta	19.0–20.0 (<i>t</i>) 11.4–17.4 (<i>a</i>)	28.9		19.3
Right coronary artery		2.2 (<i>d</i>) 2.9 (<i>p</i>)	1.9 (<i>d</i>) ¹³ 4.0 (<i>p</i>) ¹³	2.8

Note. *f*= female, *m* = male, *d* = distal, *p* = proximal, *a* = abdominal, and *t* = thoracic

Table B3. Estimated curve radii [mm] of the encountered blood vessels in the 4 previously described coronary and peripheral interventional approaches.

Approach	Artery	Curve radius [mm]
RCA–Transfemoral SFA–Ipsilateral SFA–Contralateral	Common femoral artery → External iliac artery → Common iliac artery	100
RCA–Transfemoral	Brachial artery → Axillary artery → Subclavian artery	60
RCA–Transfemoral RCA–Radial	Aortic arch	20
RCA–Transfemoral RCA–Radial	Right coronary artery	29

Note. RCA: Right Coronary Artery. SFA: Superficial Femoral Artery

Table B4. Estimated curve angles [°] of the encountered nodes in the 4 previously described coronary and peripheral interventional approaches.

Approach	Node	Bifurcation Angle [°]
RCA–Radial	Radial artery to the Brachial artery	150
RCA–Radial	Brachiocephalic artery to the Aortic arch	90
RCA–Transfemoral RCA–Radial	Aortic arch to the Right coronary artery	90
SFA–Contralateral	Common iliac artery to contralateral Common iliac artery	90

Note. RCA: Right Coronary Artery. SFA: Superficial Femoral Artery

B.3. Endovascular Instrument Flexibility

Based on the previously described analysis, a guideline for the maximum stiff part length (L) of the prototype to pass through the curves and bifurcations was derived (Fig. B3). To do that, the bifurcation was translated into a curvature with the help of Eqs. B1–B3.

$$Y = D_{large} - \frac{1}{2}D_{small} , \quad (B1)$$

$$X = \frac{\cos\alpha \cdot Y}{1 - \cos\alpha} , \text{ and} \quad (B2)$$

$$R_{curve} = X + Y , \quad (B3)$$

with α = bifurcation angle [°], D_{large} = diameter of the largest artery [m], D_{small} = diameter of the smallest artery [m], and R_{curve} = curve radius [m]. Equations B4–B6 were subsequently used to derive the maximum stiff part length:

$$P = R_{curve} - R_{art} + \emptyset_{instr} , \quad (B4)$$

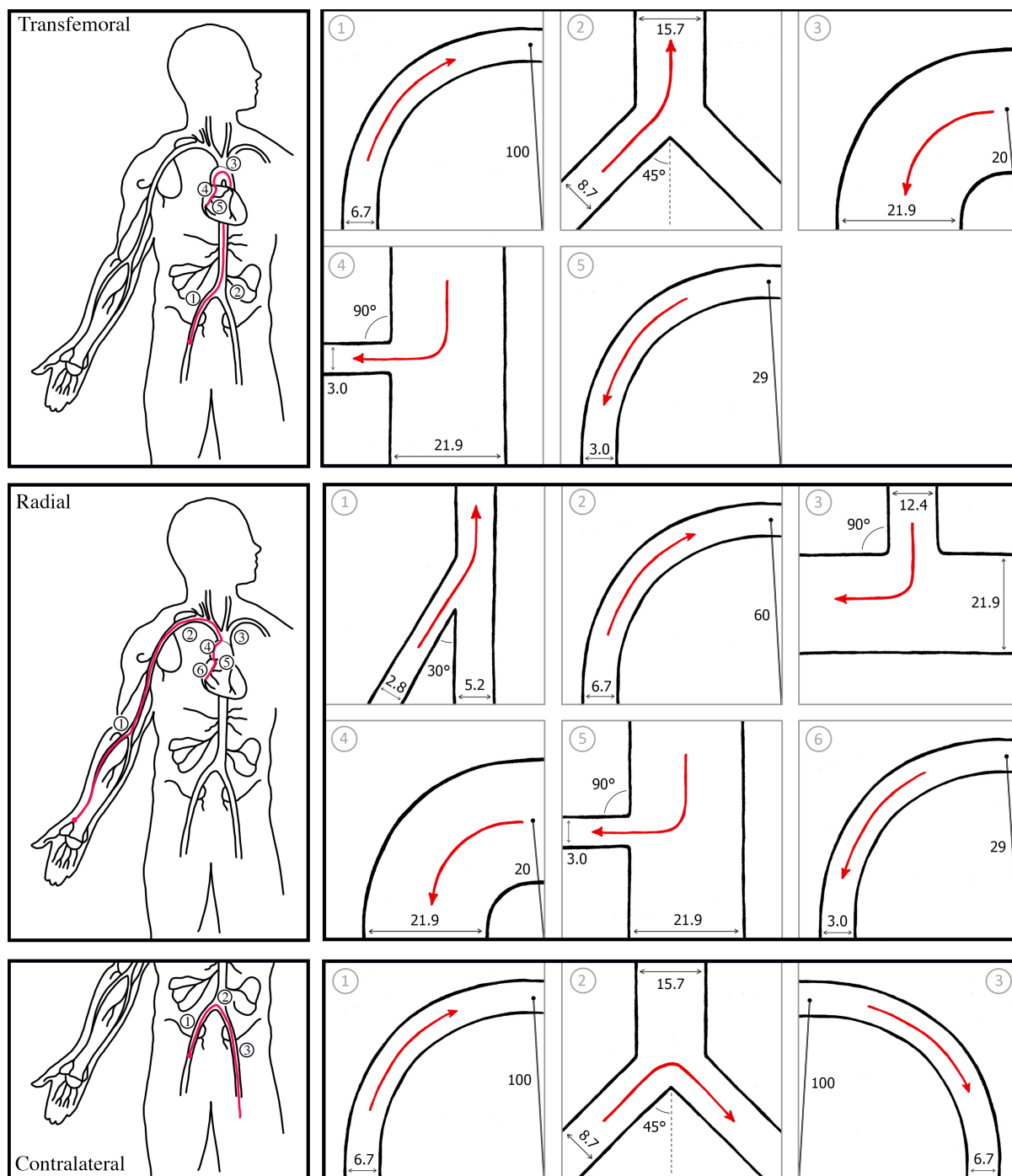


Figure B2. Analysis of the vascular routes and corresponding nodes. Top row: The nodes for Right Coronary Artery (RCA)–Transfemoral approach: (1) Common femoral artery, external Iliac artery, and common iliac artery, (2) Common iliac artery to the descending aorta, (3) Aortic arch and ascending aorta, (4) Ascending aorta to right coronary artery, and (5) Right coronary artery. Middle row: the nodes for the RCA–Radial approach: (1) Radial artery to brachial artery, (2) Axillary artery and subclavian artery, (3) Subclavian artery to the brachiocephalic artery, (4) Aortic arch and ascending aorta, (5) Ascending aorta to right coronary artery, (6) Right coronary artery. Bottom row: the nodes for the Superficial Femoral Artery (SFA)–Contralateral retrograde approach: (1) Common femoral artery, external Iliac artery, and common iliac artery, (2) Common iliac artery to contralateral common iliac artery, (3) Common iliac artery, external iliac artery, and common femoral artery. The SFA–Ipsilateral antegrade approach to the SFA may be described as part of the contralateral retrograde approach.

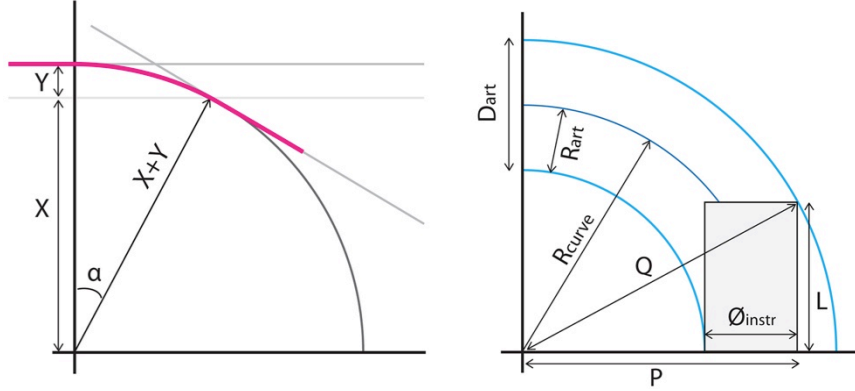
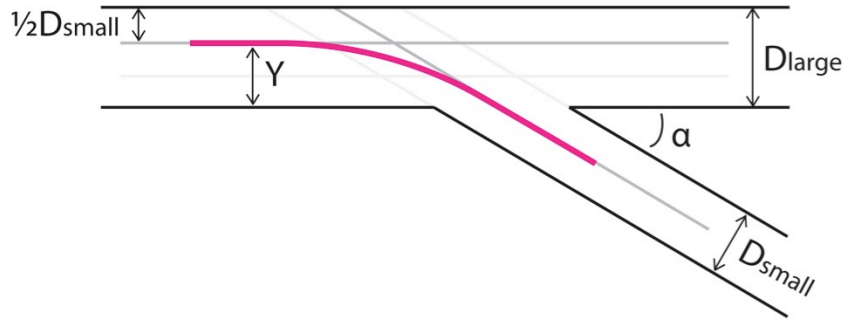


Figure B3. Simplified drawings showing the formula derivation for calculating the maximum stiff part length of an endovascular instrument to travel through set curvatures and bifurcations. Top: Input variables of Eqs. B1–B3. Bottom Left: Derivation of Eqs. B1–B3. Bottom Right: Inputs and derivation of Eqs. B4–B6.

$$Q = R_{curve} + R_{art} , \text{ and} \quad (B5)$$

$$L = \sqrt{Q^2 - P^2}, \quad (B6)$$

with L = rigid part length [m], R_{art} = radius of the smallest artery [m], and $\varnothing_{instr}$ = instrument diameter [m]. For the calculations, an instrument diameter of 2 mm was used.

In Table B5 the results of the calculations are presented. It can be seen that the bifurcation from the radial artery to the brachial artery and the curve in the RCA itself are the most restrictive nodes for reaching a lesion in the RCA, allowing for a maximum stiff part length (L) of only 6.9 mm. Reaching a CTO in the SFA is much less restrictive, with a minimum required stiff part length of 8.7 mm. Taking the estimated maximum stiff part lengths into account, and accounting for variability in artery diameter, curve radii, and bifurcation angles, the maximum stiff part length was set at 6.5 mm.

Table B5. Calculation results for the maximum rigid part length [mm] of the instrument tip for all of the modeled nodes illustrated in Figure B2.

RCA – Transfemoral		RCA – Radial		SFA – Ipsilateral		SFA – Contralateral	
Node	Length	Node	Length	Node	Length	Node	Length
1	29.8	1	6.9			1	29.8
2	36.7	2	23.9			2	8.7
3	28.9	3	18.6			3	29.8
4	7.0	4	28.9				
5	6.9	5	7.0				
		6	6.9				

Note. RCA: Right Coronary Artery. SFA: Superficial Femoral Artery. The most restrictive nodes are indicated in blue

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