Experimental studies on hemodialysis access innovations

Geelhoed, W.J.

A proof-of-principle study of the design and optimization of a novel fluid driven automated retracting needle system

W.J. Geelhoed[1,2], M. Boonekamp[3], H van de Stadt[3], S. Badulescu [1,2,3], R.A. Lalai[1,2], K.E Groeneweg[1], M. Koning[1], B. Florijn[1,2], T. Horeman[3], J.I. Rotmans[1]

Affiliations:

1. Dept. of Internal Medicine, Leiden University Medical Centre, The Netherlands.
2. Einthoven Laboratory of Vascular and Regenerative Medicine, Leiden University Medical Center, Leiden, The Netherlands.
3. Department of Instrumental Affairs, Leiden University Medical Centre, The Netherlands.
4. Dept. of Biomechanical Engineering, Delft University of Technology, Delft, The Netherlands

Abstract

The cannulation of blood vessels is one of the most basic and essential interventions in medical practice. A common adverse event of this procedure is miscannulation with infiltration of the second part of the vessel wall, often resulting in a perivascular hematoma. In hemodialysis patients, surgically created arteriovenous conduits are cannulated 3-4 times per week to provide sufficient blood supply to the hemodialysis machine. However, the high blood flow and pressure in these vascular access sites increase the risk of complications upon miscannulation. A novel needle system that allows for rapid automatic retraction of the needle in response to contact with blood after positioning the cannula in the blood vessel, was developed to reduce the risk of miscannulation. The device can easily be incorporated into existing needle designs. The mechanical functionality of the device was validated by testing prototypes in an ex vivo system. Optimization of the needle system was performed to enhance retraction speed and piston shape. A final prototype design was manufactured and validated. The optimal membrane composition and piston shape were determined, which resulted in a needle retraction speed of 40ms upon contact with fluid at a pressure of 100mmHg (arterial pressure). Here, we have successfully designed, mechanically validated, and tested a novel automated retraction system that allows incorporation into existing needle systems. This ... notably decrease the difficulty of vessel cannulation and the prevalence of ...ation.

Chapter 6

A proof-of-principle study of the design and optimization of a novel fluid driven automated retracting needle system

W.J. Geelhoed, M. Boonekamp, H van de Stadt, S. Badulescu, R.A. Lalai, K.E Groeneweg, M. Koning, B. Florijn, T. Horeman, J.I. Rotmans

Submitted

Abstract

The cannulation of blood vessels is one of the most basic and essential interventions in medical practice. A common adverse event of this procedure is miscannulation with infiltration of the second part of the vessel wall, often resulting in a perivascular hematoma. In hemodialysis patients, surgically created arteriovenous conduits are cannulated 3-4 times per week to provide sufficient blood supply to the hemodialysis machine. However, the high blood flow and pressure in these vascular access sites increase the risk of complications upon miscannulation. A novel needle system that allows for rapid automatic retraction of the needle in response to contact with blood after positioning the cannula in the blood vessel, was developed to reduce the risk of miscannulation. The device can easily be incorporated into existing needle designs. The mechanical functionality of the device was validated by testing prototypes in an ex vivo system. Optimization of the needle system was performed to enhance retraction speed and piston shape. A final prototype design was manufactured and validated. The optimal membrane composition and piston shape were determined, which resulted in a needle retraction speed of 40ms upon contact with fluid at a pressure of 100mmHg (arterial pressure). Here, we have successfully designed**,** mechanically validated, and tested a novel automated rapid needle retraction system that allows incorporation into existing needle systems. This device could notably decrease the difficulty of vessel cannulation and the prevalence of hematoma formation.

Introduction

The cannulation of blood vessels is one of the most basic and essential interventions in medical practice. A common adverse event of this procedure is miscannulation with infiltration of the second part of the vessel wall, often resulting in a hematoma [1]. Although hematoma formation always results in a burden for patients, its effects on end stage kidney disease (ESKD) patients requiring hemodialysis can be particularly detrimental [2]. Patients on hemodialysis require a long-term vascular access site in the form of an arteriovenous fistula (AVF), or arteriovenous graft (AVG), in order to dialyze efficiently with a high volume of blood being purified by the dialysis machine per minute. These conduits allow the cannulation of a patient's blood stream 3-4 times per week using two dialysis needles per session and are accordingly referred to as a patient's "lifeline" [3]. A vessel is usually cannulated at an angle of ~25-35° with the aim of placing the needle and cannula directly in the middle of the blood vessel. However, when the dorsal- or lateral part of the vessel wall is also penetrated by the needle, a hematoma can occur (Figure 1). Due to the high blood flow going through a vascular access site (often > 1000ml/min) [4] miscannulation and subsequent hematoma formation carries added risks for hemodialysis patients. Indeed, the occurrence of a hematoma can hinder the dialysis procedure as the vascular access may not be suitable for cannulation. In such a case an alternative vascular access must be found, or the dialysis procedure may be discontinued. In the worst case the hematoma can even lead to the vascular access site being lost [2].

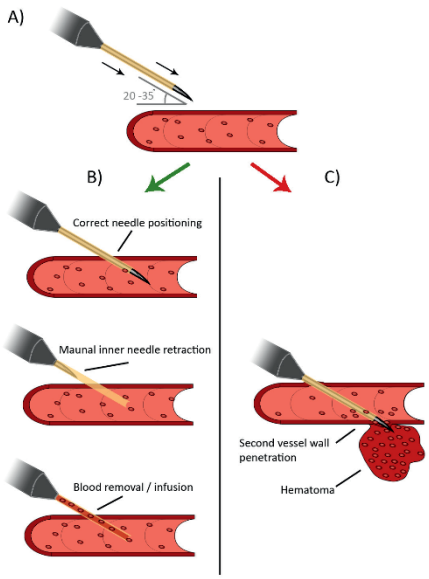

Figure 1: showing A) the cannulation of blood vessel the correct way, (B) and with back wall penetration leading to hematoma formation (C).

A 2006 study by Lee and coworkers found that the prevalence of major needle infiltration, where a fistula is unusable for at least a week, occurs with a prevalence of 5.2% in the United States [2]. As many as 31% of patients experience miscannulation within the first 6 months after a new vascular access has been placed, with a higher complication rate in AVF than AVG [1]. Moreover, patients in which major needle miscannulation occurs, require 2.4 additional procedures per patient for vascular access salvage (e.g. percutaneous transluminal angioplasty). This is associated with pain and discomfort for the patient, not to mention the fear for future cannulation procedures [5]. Moreover, 0.4% of all hemodialysis deaths are due to bleeding complications at the vascular access site [2], making miscannulation for hemodialysis a very serious problem. As such, the creation of a novel needle system that would make the cannulation procedure easier and decrease the risk of hematoma formation could improve the patients' quality of life (QOL) and hemodialysis efficacy.

Currently there are two types of cannulas for use in dialysis patients. Metal cannulas use a single large (commonly 16 gauge) cutting edge to cannulate the vessel. Plastic cannulas use an inner needle surrounded by a plastic sheath. The metal inner needle is used to place the sheath in the vessel, after which the inner metal needle can be retracted manually leaving only the sheath in the vessel. The plastic cannulas have been shown to have a favorable patient outcome compared to metal needles [6]. However, neither needle type allows automated retraction of a needle in response to blood vessel cannulation and both rely on manual user retraction. Currently, no known commercially available needle design allows for automated retraction upon cannulation of a fluid vessel. The aim of the current study was to conceive, design, and validate a novel needle that would decrease the probability of hematoma formation through the automated retraction of the needle into the sheet following vessel cannulation and blood contact.

Methods

Design requirements

The design requirements set for the system were that it should **i**) automatically retract in response to a user penetrating a first vessel wall, **ii**) automatically retract by a fluid (blood) driven mechanism, **iii**) retract fast enough to prevent the second vessel wall being penetrated, **iv**) only retract when the cannulation sheet is safely in the vessel, **v**) allow incorporation in any existing needle design, and **vi**) be simplistic enough to allow mass manufacturing at a competitive price, An unknown factor for the design of the system is the speed by which vascular access conduits are normally cannulated, as there are currently no data available regarding this parameter. Therefore, a range of needling speeds is tested in this study in which the system may be effectively used. In order to determine a minimal retraction speed threshold for vascular access cannulation several aspects must be known. The blood pressure, blood flow, vessel diameter, and cannulation speed must all be known. Moreover, there is no worldwide consensus on the speed at which dialysis needles are inserted. Based in the retraction speed determined in this study, a maximum cannulation speed may be determined. The aim here is therefore to attain the lowest possible retraction speed.

Core concept

The proposed retracting needle system is composed of a standard inner needle and outer cannula, which have been adapted to include: i) a piston, ii) a membrane, and iii) a spring. The core concept is based on the instant loss of tensile strength of a cellulose membrane material following fluid contact (Figure 2). When the needle system penetrates a vessel, blood enters the needle and travels through the lumen of the needle to reach the membrane component. Once fluid contacts the membrane, the membrane loses its tensile strength instantly, allowing the spring to overcome the restraining force of the membrane, and retract the inner needle into the cannula. The position of the hole at the side of the needle (instead of the conventional location at the tip) results in a preferred delay of needle retraction in order to prevent retraction of the needle before the cannula is safely positioned inside the vessel.

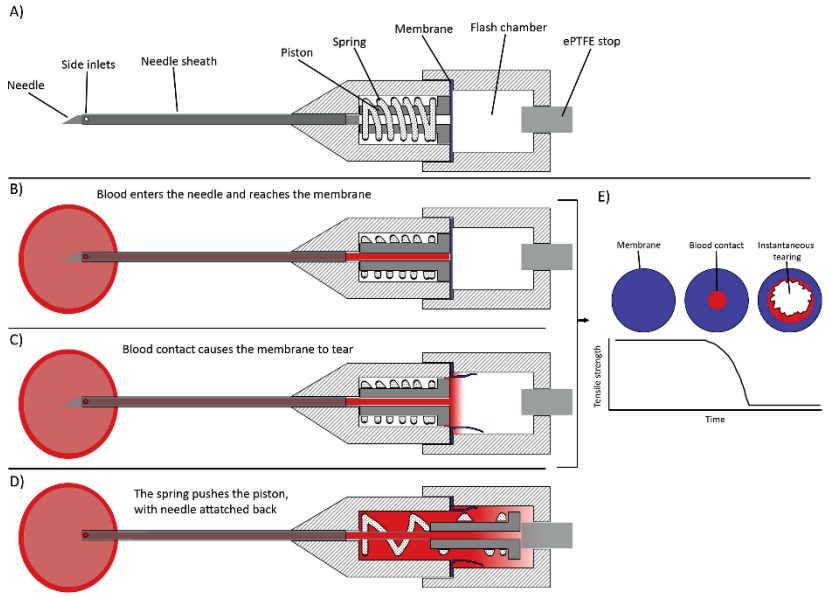

Figure 2. The concept of the system. A, B) Blood enters the needle through the hole in the tip of the sheath and moves through the needle towards the membrane. C) The membrane breaks due to fluid contact. D) the rupturing of the membrane allows the spring to expand and the needle to retract. E) Rupturing of the membrane is caused by an instant loss of tensile strength of the membrane materials upon fluid contact.

When a vessel is pressurized (as in an arteriovenous vascular access) the retraction will prevent the user from puncturing the second vessel wall and causing a hematoma. Also, it allows the user to perform a single-handed cannulation of a vessel, as no additional act is required to retract the needle. The system can be modified in order to alter **i**) the speed of

retraction, **ii**) the distance the needle retracts, iii) the force the membrane can restrain prior to retraction, and **iv**) the location of the system within existing needle systems.

Piston shape assessment

To assess the impact of the curvature of the piston, the effect of three different piston shapes on the tensile strength of the membrane was studied. The piston shape may have a considerable impact on the retraction speed as the piston conveys the force from the spring to the membrane. A custom-made probe burst pressure set-up was designed and fabricated (Figure 3). This set-up consisted of stainless-steel plates with a cavity of 6mm in diameter in the center, between which a membrane could be placed. Pistons with curvatures with a radius of 0, 1, and 2mm were placed into the pressure sensor of a Mark-10 tensile tester (Mark-10, United States) and driven through the membrane with a constant speed of 50mm. min. The force exerted on the membrane was recorded using MESUR gauge plus software (MESUR Version 2.0.5, Mark-10, United States) at 50hz.

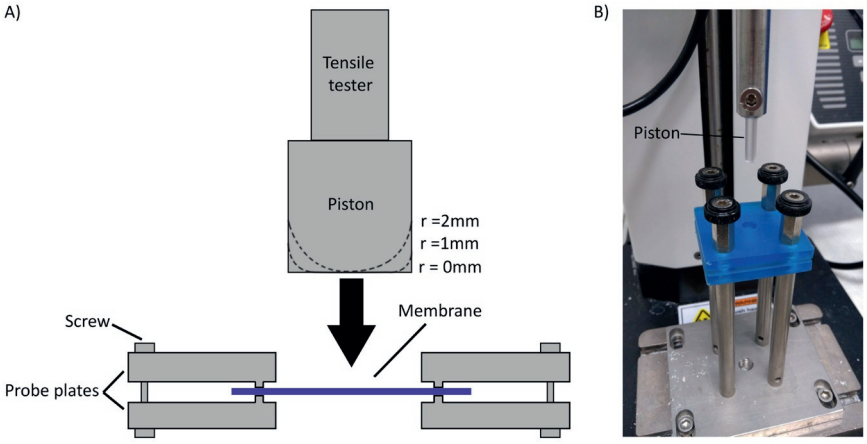

Figure 3. The experimental set-up to assess the impact of the curvature of the piston. A) showing a schematic of the system. B) showing an image of the experimental set-up with the tensile tester.

Optimization of the cellulose membranes

Ten variations of cellulose-based membranes were assessed for their applicability in the system. Ultrathin cellulose membranes were purchased from SWM medical (SWM international, United States) and tested for their effect on retraction speed (Table 1). Ultrathin cellulose membranes were chosen due to their high dry tensile strength yet express a rapid loss of tensile strength when exposed to fluid. The tensile strength of the membranes was assessed in their dry state by driving a piston with an edge radius of zero through a sample at 50mm.min using a custom-made probe burst pressure set-up. The tensile test was then repeated with the same membrane type after addition of 10ul of PBS

with glycerol to attain a 3×10−3Pa.s solution with a similar viscosity to blood. All tests were carried out in triplicates.

Table 1. An overview of the composition of the tested membrane materials.

Designation	Company paper code	Density	Porosity	Calcium carbonate concentration
M1	*EP140*	++	++++	++
M2	*EP80*	++	+++	++
M3	*1.1C*	++	++	++
M4	*16-17.5*	+	+	+
M5	*10.18*	+	+	-
M6	*10.23.1*	++	-	+
M7	*10.23.2*	++	-	+
M8	*10.23.3*	++	-	+
M9	*0.8C*	+++	++	++++
M10	*0.35C*	+++	+	+++

Retraction speed of membrane compositions

The retraction speed of the needle was assessed with various compositions of cellulose membranes (Figure 4) in order to determine the optimal membrane composition. A custom-made needle retraction device (Figure 5) was placed in the pressure sensor of the tensile tester. The needle was primed using a membrane and driven through a shore A60 silicone tube (J. Lindemann GmbH, Germany, wt: 3mm, ID: 6mm) at a constant speed of 50mm.min. ShoreA60 silicone was selected as this is provides a robust model of tissue cannulation. A thickness of 3mm was chosen as this allowed for optimal cannulation in the retraction speed set-up. As this experiment only evaluated the retraction speed upon puncture of the fluid vessel lumen itself, the wall thickness of the silicone. By comparison, the shore value of skin of the human forearm is approximately 30 [7]. A wall thickness of 3mm was used as this assured all fluid entered the needle and did not leak past the cannulation site. The start coordinates of the system were recorded. The silicone lumen was filled with PBS with glycerol up to a pressure of 100 mmHg. The needle was allowed to puncture the silicone tubing, causing fluid to enter the needle and induce retraction of the needle. The tensile tester software recorded the increase in pressure as the needle entered the silicone, as well as the drop-in resistance following retraction, allowing the retraction speed to be determined. After the optimal membrane composition was ascertained, the retraction speed of the optimal membrane was assessed at varying pressures (10-100mmHg) in the same experimental set-up in order to determine the impact of pressure on the needle.

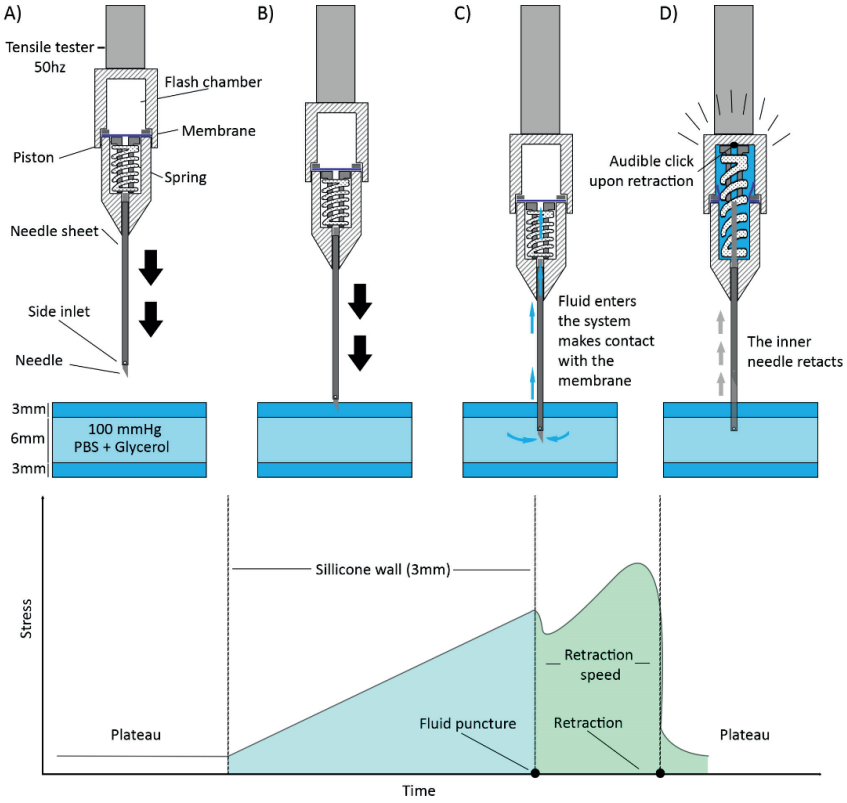

Figure 4. The experimental retraction speed set-up where a) the loaded system is driven through the silicon, a) the needle begins to penetrate the silicone wall, increasing the recorded stress, c) the first silicone vessel wall is penetrated, which provides a momentary decrease in stress, and d) fluid enters the needle, and makes contact with the membrane causing the needle to retract

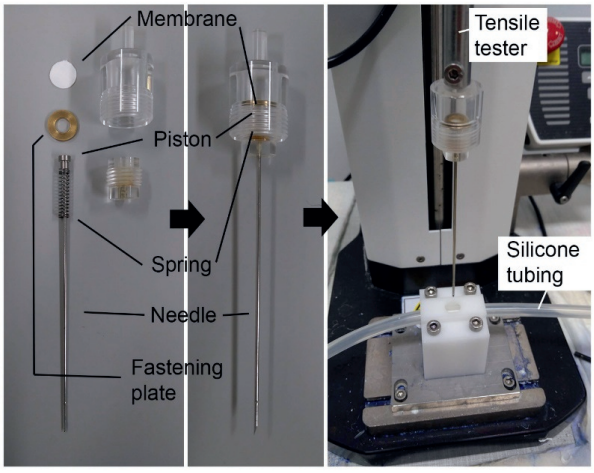

Figure 5. Showing the experimental setup of the retraction speed device. For the retraction speed device, a fastening plate was used to keep the membrane in place to allow high-throughput measurements.

Results

Optimal shape of the needle piston

To determine the optimal shape of the piston, the impact of curvature of the piston was assessed. Various curvatures of the piston were assessed with a fixed membrane diameter (Figure 6). The piston with a radius close to 0 displayed the largest difference in strength required to break the membrane in dry versus wet state. This highest piston surface area relative to the membrane was therefore desirable.

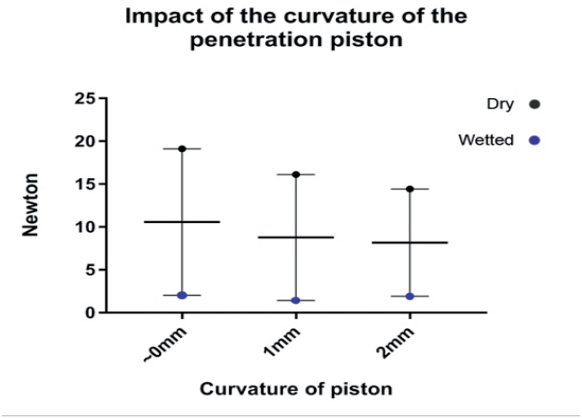

Figure 6. The impact of the curvature of the piston on dry and wet tensile strength, performed in triplicates.

Optimization of the cellulose membrane

The optimal membrane material was determined by comparing dry and wet tensile strength of the materials (Figure 7). The samples varied based on their density, porosity, and calcium carbonate levels (Table 1). Sample M10 was used as a control as this was composed of a cellulose material with a hydrophobic coating, as demonstrated by the identical tensile strength in dry and wetted state. It was concluded that features of sample M7-8 were optimal in this test as the delta between the dry and wetted state were the largest, and the wetted state had a low yield strength.

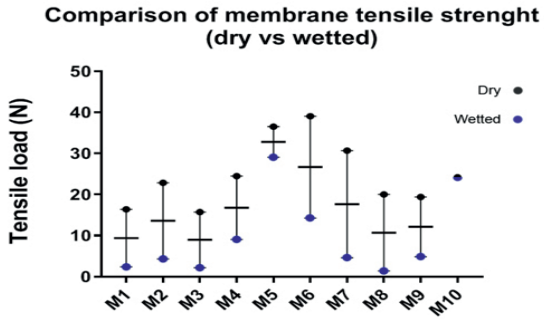

Figure 7. Comparison of the dry and wetted state of various membrane compositions. All measurements were performed in triplicates.

Retraction speed of membrane compositions

To assess the optimal material for the system, membrane types M1-10 were assessed for their retraction speeds (Figure 8). To assess the optimal membrane composition, samples were selected with the highest delta tensile strength when wetted, in combination with the lowest reaction time. Sample M8 was shown to have the highest delta tensile strength when wetted and fastest retraction speed at 100mmHg.

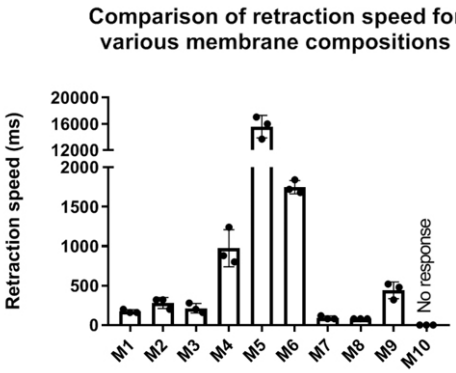

Figure 8. The retraction speed of the various membrane compositions. Sample M10 was hydrophobic and therefore had no response.

Next, retraction speed of the optimized membrane (M8) was assessed over a pressure range from a static pressure system. An increase in retraction time is observed with a decrease in pressure (Figure 9). Thus, assuming a static pressure system, the retraction speed of the needle is determined by the speed at which fluid moves towards the membrane component. The determining factor for retraction speed is the speed at which fluid enters the needle and contacts the membrane.

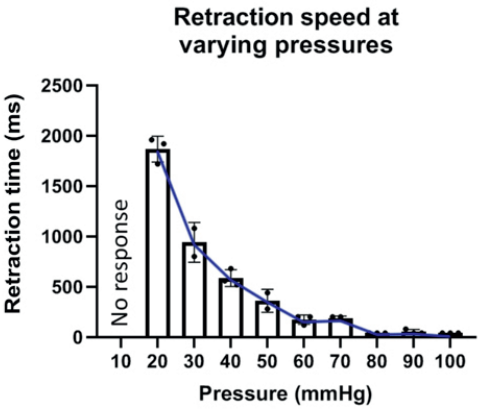

Figure 9. The retraction times of the optimized membrane system. An increase in retraction speed is observed when pressure in the static fluid compartment is decreased.

Discussion

Here, we have devised a method that allows a needle system to automatically retract upon contact with blood. The inner needle is connected to a spring system that is tensioned against a membrane. Once blood reaches this membrane, it instantaneously loses tensile strength and ruptures allowing the needle to retract safely into the flash chamber. In order to avoid the needle activating prior to the sheath having penetrated the blood vessel, a delaying mechanism is incorporated by positioning the blood inlets on the sides of the sheet, thus only allowing needle retraction if both the needle and the sheath are within the blood vessel. Benchtop optimization of the system showed that a low curvature of the piston, and a greater piston surface area is desired. Various membrane compositions were assessed for their applicability in the system. Automated retraction of the needle occurred within 40ms after puncturing a silicone tube containing PBS with glycerol at a pressure of 100 mmHg. This would indicate that the activation of the system (membrane rupture and spring activation) occurs within 40ms following fluid contact. An increase in retraction speed was observed with a decreasing pressure from a static fluid vessel. The primed needle with the M8 membrane was able to withstand a 20N load.

Owing to the high dry tensile strength of our membrane material, and the rapid loss of tensile strength upon fluid contact, ultrathin cellulose membranes were found to have the ideal characteristics for our application. Cellulose is a naturally occurring polysaccharide [8], and cellulose-based materials have previously been proposed as humidity sensors [9]. Through the process of water sorption an increase in the water content of the material results in the stiffness, tensile strength, and compression strength being affected adversely [10].

The pressure within an AVF decreases along a gradient from the high pressure arterial system (~120mmHg) to the low pressure venous system (~40mmHg) [11]. The high blood flow through the AVF will likely impact the speed at which blood enters and passes through the cannulation needle. This must be taken into account as the cannulation site may therefore also be determinant for the retraction speed. Assuming a retraction speed of 40ms at 100mmHg with a matured AVF vessel lumen diameter of 6mm a maximum cannulation speed of 15cm/s could be attained before the second vessel wall is punctured.

Few studies have been performed documenting the miscannulation rate in dialysis patients [1,2]. The conclusion is however clear that the rate of miscannulation is high, and that this can have serious implications for patient welfare. As stated earlier, plastic cannulation needles are preferred over metal needles [6]. Ultrasound guidance is often used to aid the cannulation of AVF. This however requires the user to multitask using one hand to operate the ultrasound device, and the other hand to cannulate the vessel. Regardless, the use of ultrasound has been shown to improve the success rate of venous cannulation procedures [12]. Currently, no other needle system exists that allows the fluid driven automated retraction of a needle upon blood vessel cannulation.

A limitation of this experiment was that the system was only assessed in response to pressure in a static system. In an AVF, blood flow is high (~1000ml.min), and the cannulation of a high flow system may lead to blood entering the needle faster than in a static system,

which would be favorable for our application. Although the cellulose membranes were commercially attained, only global characteristics of the membranes was received. And although current study outlines and validates the proof-o-principle of the automatic retraction concept, concurrent studies would require a more detailed examination of materials used. Moreover, in the current study cellulose membranes are focused on. Cellulose may induce complement activation which may be detrimental for the cannulation procedure [13]. Although the design of the needle system is such that following retraction the cellulose membrane is shielded form blood circulation this does need to be considered in future design iterations. Alternative membrane compositions such as methyl cellulose may be explored as potential alternatives. Moreover, silicone tubing was used in this study to allow for a highly controlled experimental set-up for concept validation. Ideally, a material more closely mimicking human skin and subcutaneous tissue would be assessed as well.

An alternative application for our needle design is the cannulation of arterial vessels, such as peripheral atrial cannulation that is a frequently performed procedure [14]. As mean arterial pressure is generally 90 mmHg, retraction time would approximately be 40ms. Therefore, our needle system may be of use for both the cannulation of AVF, and arterial cannulation procedures. Another alternative use of this needle system is venous cannulation. Currently, nursing staff requires both hands to cannulate a vein for an intravenous line. The needle system proposed here could be utilized to allow for single hand cannulation, freeing the other hand of the nursing staff (e.g. for ultrasound guidance). Although retraction times may be suboptimal for small veins due to the low pressure, the additive value of allowing single hand cannulation may be worth investigating.

Before this needle system can be introduced in the clinic, several steps need to be taken. Initially, the needle must be incorporated into either an existing needle system or designed to comply with medical device regulations. Further benchtop assessment of the system should be carried out to further optimize the needle design. The system should be assessed in a benchtop model mimicking the flow in an arteriovenous fistula, and a material may be used that more closely mimics human skin. Finally, animal studies must be performed in order to validate the needle system *in vivo* with real blood vessels prior to the start of clinical studies.

In conclusion, we have successfully designed, mechanically validated, and optimized a novel automated rapid needle retraction system that allows incorporation into existing cannulation designs. This device may notably decrease the difficulty of vessel cannulation and the prevalence of hematoma formation.

Acknowledgements

This research was funded by a Take-off grant (17769 to WJG) from the NWO (the Dutch Research Council). This had no influence on the outcome of the study.

References

1 van Loon, M. M., Kessels, A. G., van der Sande, F. M. & Tordoir, J. H. Cannulation practice patterns in haemodialysis vascular access: predictors for unsuccessful cannulation. *Journal of renal care* **35**, 82-89, doi:10.1111/j.1755-6686.2009.00092.x (2009).

2 Lee, T., Barker, J. & Allon, M. Needle infiltration of arteriovenous fistulae in hemodialysis: risk factors and consequences. *American journal of kidney diseases : the official journal of the National Kidney Foundation* **47**, 1020-1026, doi:10.1053/j.ajkd.2006.02.181 (2006).

3 Shiu, Y. T., Rotmans, J. I., Geelhoed, W. J., Pike, D. B. & Lee, T. Arteriovenous conduits for hemodialysis: how to better modulate the pathophysiological vascular response to optimize vascular access durability. *American journal of physiology. Renal physiology* **316**, F794-f806, doi:10.1152/ajprenal.00440.2018 (2019).

4 Robbin, M. L. *et al.* Arteriovenous Fistula Development in the First 6 Weeks after Creation. *Radiology* **279**, 620-629, doi:10.1148/radiol.2015150385 (2016).

5 Wilson, B. & Harwood, L. Outcomes for Successful Cannulation of the Arteriovenous Fistula: Perspectives from Patients on Hemodialysis. *Nephrol Nurs J* **44**, 381-388 (2017).

6 Marticorena, R. M., Dacouris, N. & Donnelly, S. M. Randomized pilot study to compare metal needles versus plastic cannulae in the development of complications in hemodialysis access. *The Journal of Vascular Access* **19**, 272-282, doi:10.1177/1129729817747535 (2018).

7 Falanga, V. & Bucalo, B. Use of a durometer to assess skin hardness. *Journal of the American Academy of Dermatology* **29**, 47-51, doi:10.1016/0190-9622(93)70150-r (1993).

8 Moon, R. J., Martini, A., Nairn, J., Simonsen, J. & Youngblood, J. Cellulose nanomaterials review: structure, properties and nanocomposites. *Chemical Society Reviews* **40**, 3941-3994, doi:10.1039/C0CS00108B (2011).

9 Mahadeva, S. K., Yun, S. & Kim, J. Flexible humidity and temperature sensor based on cellulose–polypyrrole nanocomposite. *Sensors and Actuators A: Physical* **165**, 194-199, doi:https://doi.org/10.1016/j.sna.2010.10.018 (2011).

10 Ramarao, B. V. in *Studies in Surface Science and Catalysis* Vol. 120 (ed A. Dąbrowski) 531-560 (Elsevier, 1999).

11 Hemodialysis Adequacy Work, G. Clinical practice guidelines for hemodialysis adequacy, update 2006. *American journal of kidney diseases : the official journal of the National Kidney Foundation* **48 Suppl 1**, S2-S90, doi:10.1053/j.ajkd.2006.03.051 (2006).

12 van Loon, F. H. J., Buise, M. P., Claassen, J. J. F., Dierick-van Daele, A. T. M. & Bouwman, A. R. A. Comparison of ultrasound guidance with palpation and direct visualisation for peripheral vein cannulation in adult patients: a systematic review and meta-analysis. *Br J Anaesth* **121**, 358-366, doi:10.1016/j.bja.2018.04.047 (2018).

13 Innes, A., Farrell, A. M., Burden, R. P., Morgan, A. G. & Powell, R. J. Complement activation by cellulosic dialysis membranes. *J Clin Pathol* **47**, 155-158, doi:10.1136/jcp.47.2.155 (1994).

14 Scheer, B., Perel, A. & Pfeiffer, U. J. Clinical review: complications and risk factors of peripheral arterial catheters used for haemodynamic monitoring in anaesthesia and intensive care medicine. *Critical care (London, England)* **6**, 199-204, doi:10.1186/cc1489 (2002).