Journal of Visualized Experiments

A protocol to set up needle-free connector with positive displacement on central venous catheter in intensive care unit

--Manuscript Draft--

Article Type:	Invited Methods Article - Author Produced Video
Manuscript Number:	JoVE59801R2
Full Title:	A protocol to set up needle-free connector with positive displacement on central venous catheter in intensive care unit
Keywords:	Infusions, intravenous; Intensive Care Unit; Central Venous Catheters; Vascular Access Devices; Needle-free Connectors; human
Corresponding Author:	Thomas Clavier Centre Hospitalier Universitaire de Rouen Rouen, FRANCE
Corresponding Author's Institution:	Centre Hospitalier Universitaire de Rouen
Corresponding Author E-Mail:	thomasclavier76@gmail.com
Order of Authors:	Thomas Clavier
	Sébastien Franchina
	Antoine Lefevre-Scelles
	Philippe Gouin
	Emmanuel Besnier
	Benoit Veber
Additional Information:	
Question	**Response**
Please indicate whether this article will be Standard Access or Open Access.	Standard Access (US$1200)

TITLE

A Protocol to Set Up Needle-Free Connector with Positive Displacement on Central Venous Catheter in Intensive Care Unit

AUTHORS AND AFFILIATIONS:

Thomas Clavier[1,2], Sébastien Franchina[1], Antoine Lefevre-Scelles[1], Philippe Gouin[1], Emmanuel Besnier[1,2], Benoit Veber[1]

[1]Department of Anesthesiology and Critical Care, Rouen University Hospital, Rouen, France
[2]Normandie Univ, UNIROUEN, INSERM U1096, Rouen, France

Corresponding author:

Dr Thomas Clavier (thomas.clavier@chu-rouen.fr)

Email Addresses of Co-authors:

Sébastien Franchina (sebastien.franchina@chu-rouen.fr)
Antoine Lefevre-Scelles (antoine.lefevre@chu-rouen.fr)
Philippe Gouin (philippe.gouin@chu-rouen.fr)
Emmanuel Besnier (emmanuel.besnier@chu-rouen.fr)
Benoit Veber (benoit.veber@chu-rouen.fr)

KEYWORDS:

Infusions, Intravenous, Intensive Care Unit, Central Venous Catheters, Vascular Access Devices, Needle-free Connectors.

SUMMARY:

We present a protocol to show the installation of a needle-free connector with positive displacement on a central venous catheter.

ABSTRACT:

Needle-free connectors were initially designed and promoted to avoid blood exposure for healthcare workers. Some recent data suggest that the latest generation of connectors (with positive displacement) may be of interest for reducing central venous line infections. We have been using needle-free connectors for several years in our intensive care unit and here we present a protocol for installing these connectors on central venous catheters. After insertion of the catheter and control of the permeability of the lines, the connectors must be purged with 0.9% NaCl before being connected. The connectors replace all disposable caps used on infusion stopcocks and manifolds. All the connectors are changed every 7 days as recommended by the manufacturer (except when there is macroscopic contamination, which requires an immediate change of the connector). Before each injection, the connector must be disinfected for at least 3 seconds with 70% isopropyl alcohol. The connectors must not be disconnected (unless changed), as the injection is done through the device. Setting up the connectors slightly increases the total time required to place the catheter and there is no formal evidence that these connectors reduce the incidence of infectious or thrombotic complications. However, these devices simplify the

management of central venous lines and prevent the catheter circuit from "opening" once it has been sterilely installed.

INTRODUCTION:

Central venous catheter-related infections (CRI) are a severe complication of central venous catheters in intensive care unit (ICU). The decline in CRI remains an ever-present objective, with a final goal of “zero catheter related infection”[1]. Needle-free connectors were initially designed and promoted to avoid blood exposure for healthcare workers. There are two main designs of connectors: split septum (no internal moving parts) and closed valve systems (internal moving components) but both designs can be combined in one connector[2]. Needle-free connectors are categorized according to the type of fluid displacement that occurs after disconnection of a male Luer valve: negative (blood reflux into the catheter), neutral, and positive (with a push of blood out of the catheter lumen)[2,3].

Some connectors have been described as a cause of catheter-related infections, in particular in the intensive care unit (ICU)[4–6]. A new generation of needle-free connectors with minimal internal complexity, a reduction or elimination of interstitial or dead space, a visible fluid path to help assess proper flushing technique, and a flat access surface, etc. has been designed to lower the risk of infection. In vitro, these connectors have shown low bacterial colonization[7]. There are global recommendations from the laboratory manufacturing these connectors; however, there is no practical description of how to install them on catheters[8]. Hence, it is possible that each team uses them differently. Therefore, we propose a formalized protocol for the installation of these connectors on central venous lines in the ICU.

We present the installation of a positive pressure needleless connector (PPNC) with an internal silicone piston in our ICU but this protocol is applicable with any positive displacement valve. This valve is a mechanical needle-free connector with positive displacement.

PROTOCOL:

1. Preparation of connectors and infusion lines

1.1. Sterilely retrieve the connectors.

1.2. On the 3-way extension stopcock, screw 1 connector into each socket of the stopcock and 1 connector into the end of the extension line. Take 0.9% NaCl with a 50 mL syringe to purge the extension and the lines. Purge each 3-way extension with 0.9% NaCl through the 2 connectors of the stopcock.

1.3. Take the infusion manifold. Unscrew each single-use cap. Screw 1 connector into each socket of the manifold to replace the caps. Purge the infusion line through each connector by turning each stopcock sequentially.

NOTE: At the end of this step, there are 3 extensions with 3-way stopcock with purged connectors

and an infusion manifold with purged connectors.

2. Placement of the catheter

2.1. Place the central venous catheter sterilely according to usual practice in the unit or a previously described protocol[9].

2.2. Check the permeability of each line by aspiration of blood and then reinjection of 0.9% NaCl serum. Clamp the lines.

3. Installation of the connectors

3.1. Screw the extension's connector of each 3-way extension stopcock into each catheter line. These connectors, directly connected to the lines of the catheter, are the "proximal connectors". Unclamp the lines.

3.2. Connect the infusion manifold line to one of the connectors of the 3-way stopcock of the distal line.

NOTE: There is no need to place a vein guard on the manifold or extensions.

4. Use of connectors and infusion lines

4.1. Before each infusion, disinfect the end of the connector for 3 s with a sterile compress soaked in 70% isopropyl alcohol. Connect the syringe or tubing directly to the connector by screwing and injecting. After injection or infusion, unscrew the device. Do not remove the connector.

4.2. If needed, rinse an unused line with 3 mL of saline. There is no need to clamp or infuse an unused line with a vein guard. Leave the proximal valve in place even if the line is not perfused.

5. Replacement and maintenance of connectors and infusion lines

5.1. Always change the connectors every 7 days except for the proximal connectors. Thus, every week, the nurse prepares the extensions with 3-way stopcock and the infusion manifold in sterile conditions (see step 1).

5.2. Unscrew the used extensions at the proximal valve and screw the new sterile and purged extensions to the catheter on the proximal connector (see step 3).

5.3. Only change a proximal connector if it is soiled (to maintain the catheter in a "closed" system).

5.4. In case of macroscopic contamination, rinse the connector with 10 mL of 0.9% NaCl. If there

is still contamination, replace the connector. In the event of transfusion, infusion of lipid solution (e.g. propofol) or parenteral nutrition, change the tubing and connectors of the line concerned every 24 hours.

5.5. Change other infusion lines and tubing according to the practices and protocols of each unit.

REPRESENTATIVE RESULTS:

Once all the elements are in place, the catheter has connectors on almost all the junctions between two infusion lines (**Figure 1**). Thus, it has proximal connectors on each line and two connectors on the sockets of the 3-way extensions (**Figure 2**). Each infusion line has connectors at all its female sockets (**Figure 3**). Once the assembly is in place, any injection or infusion (continuous or discontinuous) must be made, after disinfection, through one of the connectors of the infusion lines or extensions (**Figure 4**).

Maintaining the connectors in place keeps the infusion system closed as well as sterile mounted and minimizes the risk of bacterial contamination. One of our previous works, the first study that prospectively analyzed these devices over several years, showed a significant decrease in CRI incidence during the six-year period framing the introduction of the connectors (**Figure 5**)[10]. In this work, the incidence of CRI before using connectors was 6.2 CRI/1000 catheter-day vs. 2.7 CRI/1000 catheter-days after using connectors[10]. Moreover, we did not find any increase of CRI after the beginning of connector use (**Figure 5**) and there was no significant difference concerning the kind of bacteria species involved in CRI[10]. We have not identified any specific complications associated with the use of these connectors during these years of use.

FIGURE AND TABLE LEGENDS:

Figure 1: Global view of the catheter once the connectors have been placed.

Figure 2: Proximal part of the catheter with proximal connectors (A) and connectors on the 3-way extension stopcock (B).

Figure 3: 4-port manifold with connectors.

Figure 4: Steps of injection through a connector. (A) Disinfect the surface of the connector for 3 seconds with 70% isopropyl alcohol. Wait until the connector is dry. (**B**) Insert the tip of the syringe or infuser into the connector. (**C**) Inject or infuse the medication. (**D**) Remove the syringe or infuser.

Figure 5: Evolution of catheter-related infection incidence before and after the use of connectors. Figure taken from Clavier et al.[10]

DISCUSSION:

Setting up the connectors slightly increases the total time required to place the catheter. However, their use has several advantages: no need to maintain a continuous saline perfusion for non-infused lines, rapid stopping of infusion of the lines if necessary (in case of urgent

transport of the patient for example), no need to use single-use caps several times a day to close the infusion lines. The use of connectors simplifies the daily use of catheter infusion lines without any particular complications. It should be noted that during our four year experience of these PPNC connectors there have been no complications with rapid fluid administration while this has been described with other types of connectors[11]. It is essential to maintain complete asepsis when installing the connectors in order to keep the infusion system closed. In addition, regular examination of the connectors for contamination is essential to be able to rinse or change the implicated connectors and avoid bacterial growth. A recent work reports the in vitro efficacy of a pulsative flushing technique to prevent bacterial colonization of vascular access devices but this technique has not been evaluated directly on needleless connectors[12]. Due to the technical aspect of this kind of connector, nurses must be trained before using these connectors in everyday practice. In this context, the use of Aseptic Non Touch Technique, which is a safe method for managing intravascular devices, is very relevant[13]. Thus, even after the connectors are set up, direct contact with the connectors should be minimized as much as possible to minimize the risk of contamination. In this context, the use of a disinfectant cap on needleless connectors can help to limit the contact with connectors and is effective in reducing central line-associated bloodstream infections[14].

The inclusion of extension tubing, stopcocks and manifolds increase the complexity of the system and expose it to a risk of contamination of stopcocks and manifolds[15]. Our choice of extensions and infusion lines is the result of a reflection on the balance between patient safety and infectious risk. In the ICU, continuous uninterrupted infusion of certain drugs is essential (e.g., catecholamine, sedation). In our protocol, the use of a 3-way extension stopcock allows medication relays to be easily made without ever interrupting the infusion, which is a guarantee of safety for the patient. The use of a unique 4-port manifold with a perfusion line allows the infusion of several drugs simultaneously (e.g., antibiotics, analgesics, insulin) but the number of these manifolds should be limited to prevent the risk of infection.

Some studies have shown interest in a closed system to prevent colonization and catheter infections[16,17]. Additionally, several studies have reported a decrease in catheter infection after using PPNCs[10,18,19]. It is also possible that these connectors may decrease thrombotic catheter occlusions, but there is insufficient evidence to conclude a direct causal link between needleless connectors and catheter occlusions[20,21]. Moreover, data in the literature support the safe and prolonged use of these devices[10,16,19]. However, different department may sometimes use different methods to mount connectors on infusion lines and most studies do not describe the method used to install connectors on catheters. It could appear interesting that studies on connectors report their installation protocol to better assess potential differences of practice between teams.

ACKNOWLEDGMENTS:
The authors are grateful to Nikki Sabourin-Gibbs, Rouen University Hospital, for her help in editing the manuscript. The authors would like to thank the communication department of Rouen University Hospital and the teams of the Medical Training Center for their participation in the video shoot.

DISCLOSURES:

TC, PG and BV previously conducted a study on PPNC valves. BD provided the connectors for this previous work but had no role in the trial initiation, study design, data collection, data analysis, data interpretation, writing of the report, or the decision to submit. The other authors have nothing to disclose. The drafting of this protocol was formalized in 2013 with validation by Carefusion consultants.

REFERENCES:

1. Worth, L.J., McLaws, M.-L. Is it possible to achieve a target of zero central line associated bloodstream infections? *Current Opinion in Infectious Diseases*. **25** (6), 650–657 (2012).
2. Kelly, L.J., Jones, T., Kirkham, S. Needle-free devices: keeping the system closed. *British Journal of Nursing (Mark Allen Publishing)*. **26** (2), S14–S19 (2017).
3. Casey, A.L., Karpanen, T.J., Nightingale, P., Elliott, T.S. The risk of microbial contamination associated with six different needle-free connectors. *British Journal of Nursing (Mark Allen Publishing)*. **27** (2), S18–S26 (2018).
4. Salgado, C.D., Chinnes, L., Paczesny, T.H., Cantey, J.R. Increased rate of catheter-related bloodstream infection associated with use of a needleless mechanical valve device at a long-term acute care hospital. *Infection Control and Hospital Epidemiology*. **28** (6), 684–688 (2007).
5. Jarvis, W.R. et al. Health care-associated bloodstream infections associated with negative- or positive-pressure or displacement mechanical valve needleless connectors. *Clinical Infectious Diseases: An Official Publication of the Infectious Diseases Society of America*. **49** (12), 1821–1827 (2009).
6. Btaiche, I.F., Kovacevich, D.S., Khalidi, N., Papke, L.F. The effects of needleless connectors on catheter-related bloodstream infections. *American Journal of Infection Control*. **39** (4), 277–283 (2011).
7. Chernecky, C., Waller, J. Comparative evaluation of five needleless intravenous connectors. *Journal of Advanced Nursing*. **67** (7), 1601–1613 (2011).
8. Infusion Resource Library - BD. at <https://www.bd.com/en-us/offerings/capabilities/infusion/infusion-resource-library?contenttype=22&productline=115>.
9. Kim, S.-C., Klebach, C., Heinze, I., Hoeft, A., Baumgarten, G., Weber, S. The supraclavicular fossa ultrasound view for central venous catheter placement and catheter change over guidewire. *Journal of Visualized Experiments.* (94), 52160 (2014).
10. Clavier, T. et al. Impact of MaxZero™ needle-free connector on the incidence of central venous catheter-related infections in surgical intensive care unit. *Australian Critical Care: Official Journal of the Confederation of Australian Critical Care Nurses*. (2018).
11. Lehn, R.A., Gross, J.B., McIsaac, J.H., Gipson, K.E. Needleless connectors substantially reduce flow of crystalloid and red blood cells during rapid infusion. *Anesthesia and Analgesia*. **120** (4), 801–804 (2015).
12. Ferroni, A. et al. Pulsative flushing as a strategy to prevent bacterial colonization of vascular access devices. *Medical Devices (Auckland, N.Z.)*. **7**, 379–383 (2014).
13. Flynn, J.M., Keogh, S.J., Gavin, N.C. Sterile v aseptic non-touch technique for needle-less connector care on central venous access devices in a bone marrow transplant population: A

comparative study. *European Journal of Oncology Nursing: The Official Journal of European Oncology Nursing Society*. **19** (6), 694–700 (2015).

14. Merrill, K.C., Sumner, S., Linford, L., Taylor, C., Macintosh, C. Impact of universal disinfectant cap implementation on central line-associated bloodstream infections. *American Journal of Infection Control*. **42** (12), 1274–1277 (2014).
15. Mermel, L.A., Bert, A., Chapin, K.C., LeBlanc, L. Intraoperative stopcock and manifold colonization of newly inserted peripheral intravenous catheters. *Infection Control and Hospital Epidemiology*. **35** (9), 1187–1189 (2014).
16. Rosenthal, V.D., Maki, D.G. Prospective study of the impact of open and closed infusion systems on rates of central venous catheter-associated bacteremia. *American Journal of Infection Control*. **32** (3), 135–141 (2004).
17. Bouza, E. et al. A needleless closed system device (CLAVE) protects from intravascular catheter tip and hub colonization: a prospective randomized study. *The Journal of Hospital Infection*. **54** (4), 279–287 (2003).
18. Tabak, Y.P., Jarvis, W.R., Sun, X., Crosby, C.T., Johannes, R.S. Meta-analysis on central line-associated bloodstream infections associated with a needleless intravenous connector with a new engineering design. *American Journal of Infection Control*. **42** (12), 1278–1284 (2014).
19. Wallace, M.C., Macy, D.L. Reduction of Central Line-Associated Bloodstream Infection Rates in Patients in the Adult Intensive Care Unit. *Journal of Infusion Nursing: The Official Publication of the Infusion Nurses Society*. **39** (1), 47–55 (2016).
20. Btaiche, I.F., Kovacevich, D.S., Khalidi, N., Papke, L.F. The effects of needleless connectors on catheter-related thrombotic occlusions. *Journal of Infusion Nursing: The Official Publication of the Infusion Nurses Society*. **34** (2), 89–96 (2011).
21. Williams, A. Catheter Occlusion in Home Infusion: The Influence of Needleless Connector Design on Central Catheter Occlusion. *Journal of Infusion Nursing: The Official Publication of the Infusion Nurses Society*. **41** (1), 52–57 (2018).

Figure 1

Click here to access/download;Figure;Figure 1.pdf

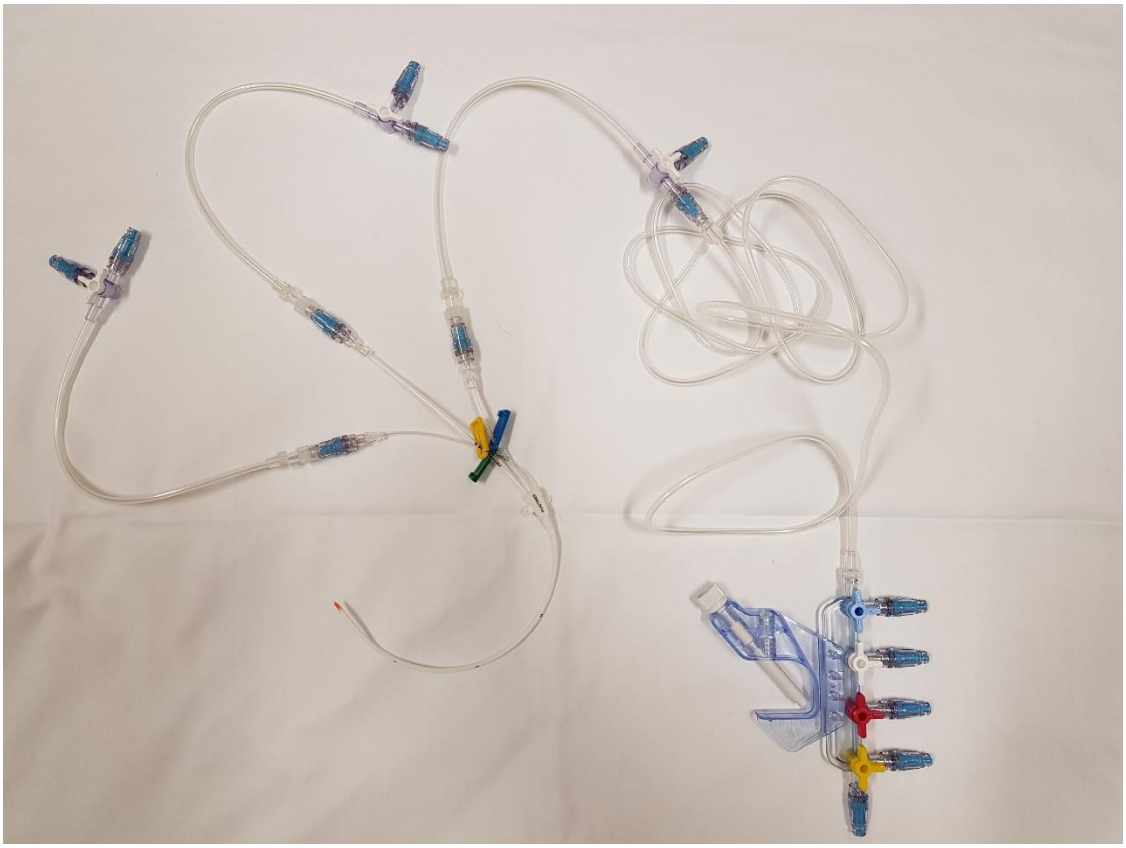


Figure 2

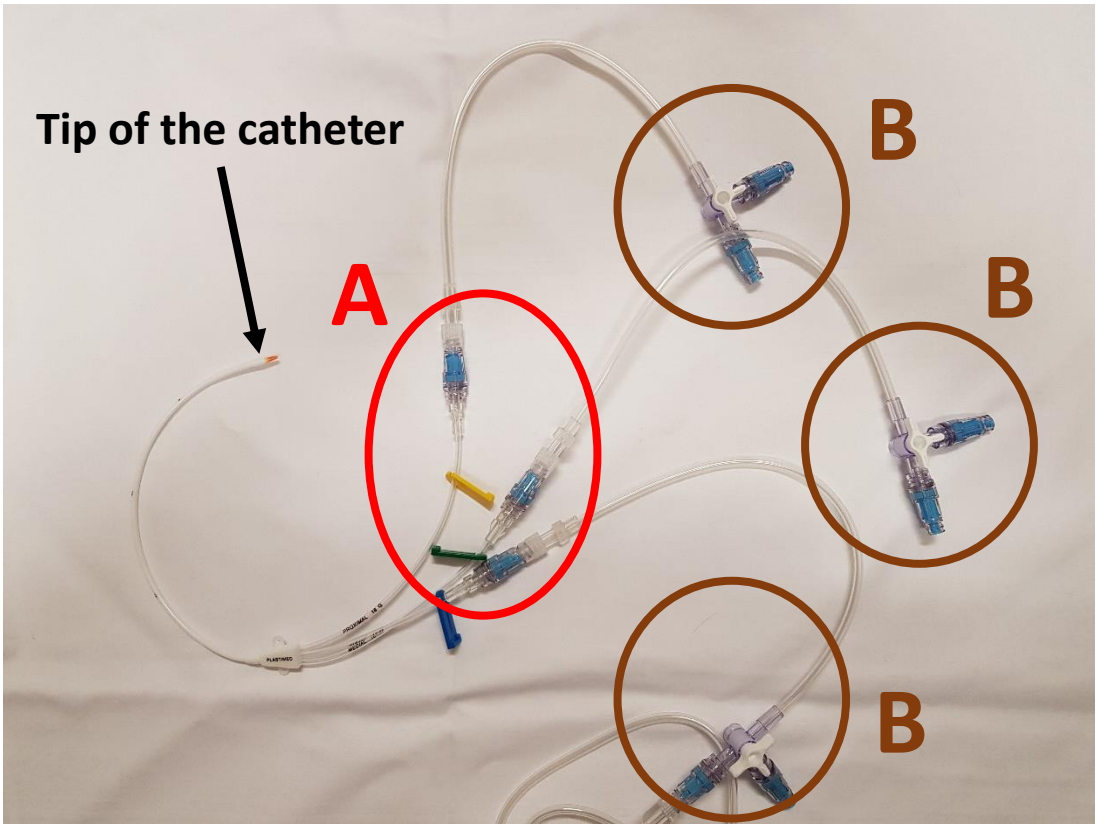
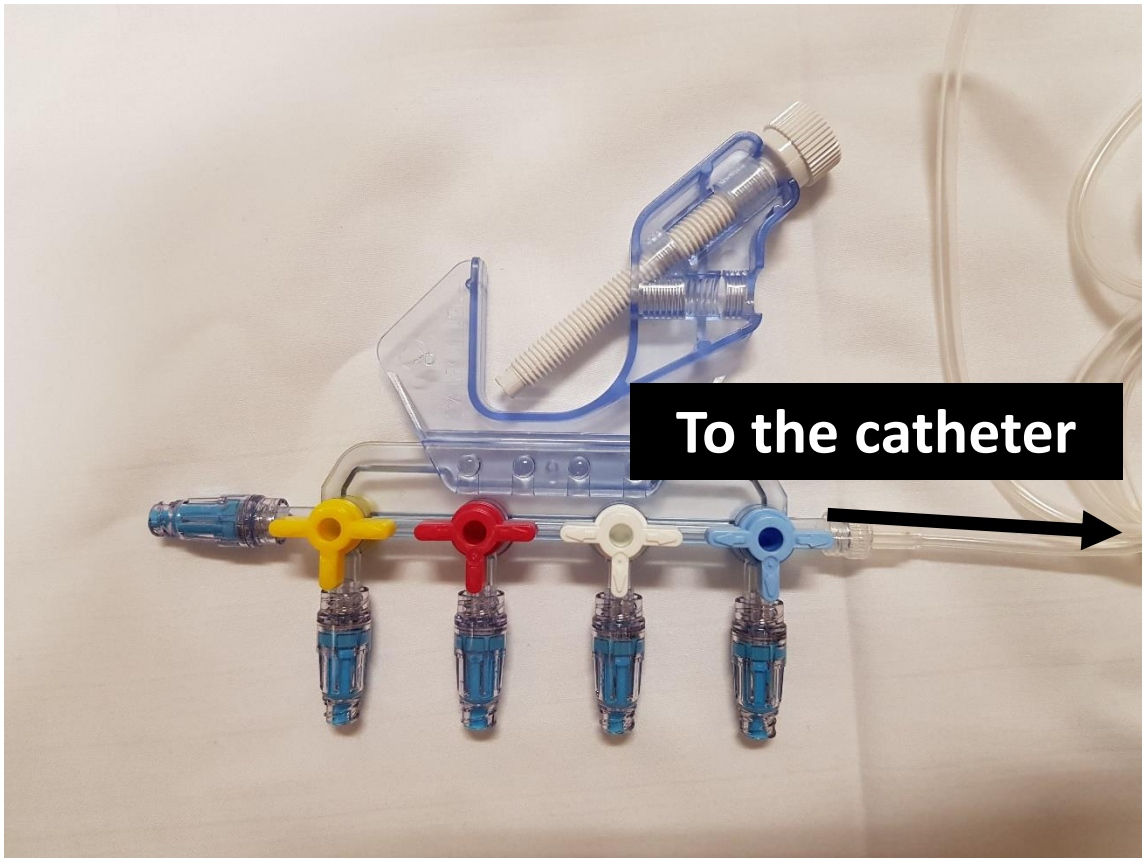


Figure 3



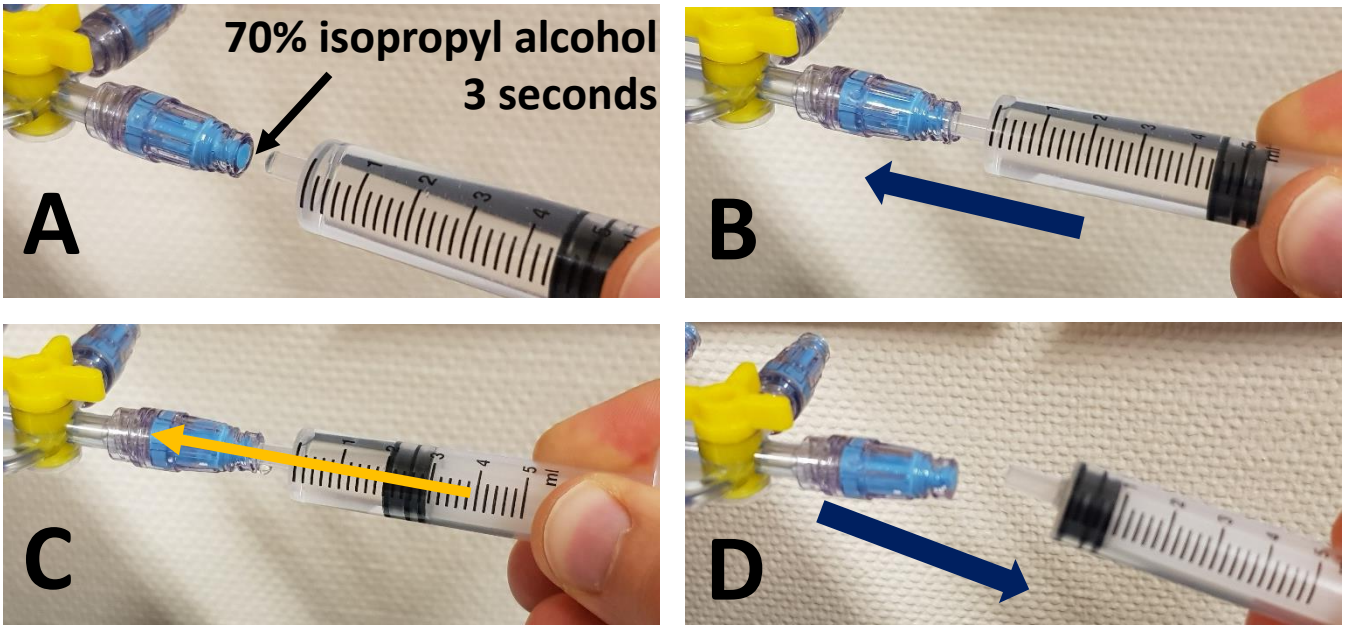


Figure 4: Steps of injection through a connector.

A. Disinfect the surface of the connector for 3 seconds with 70% isopropyl alcohol. Insert the tip of the syringe or infuser through the connector.

C. Inject or infuse the medication

D. Remove the syringe or infuser

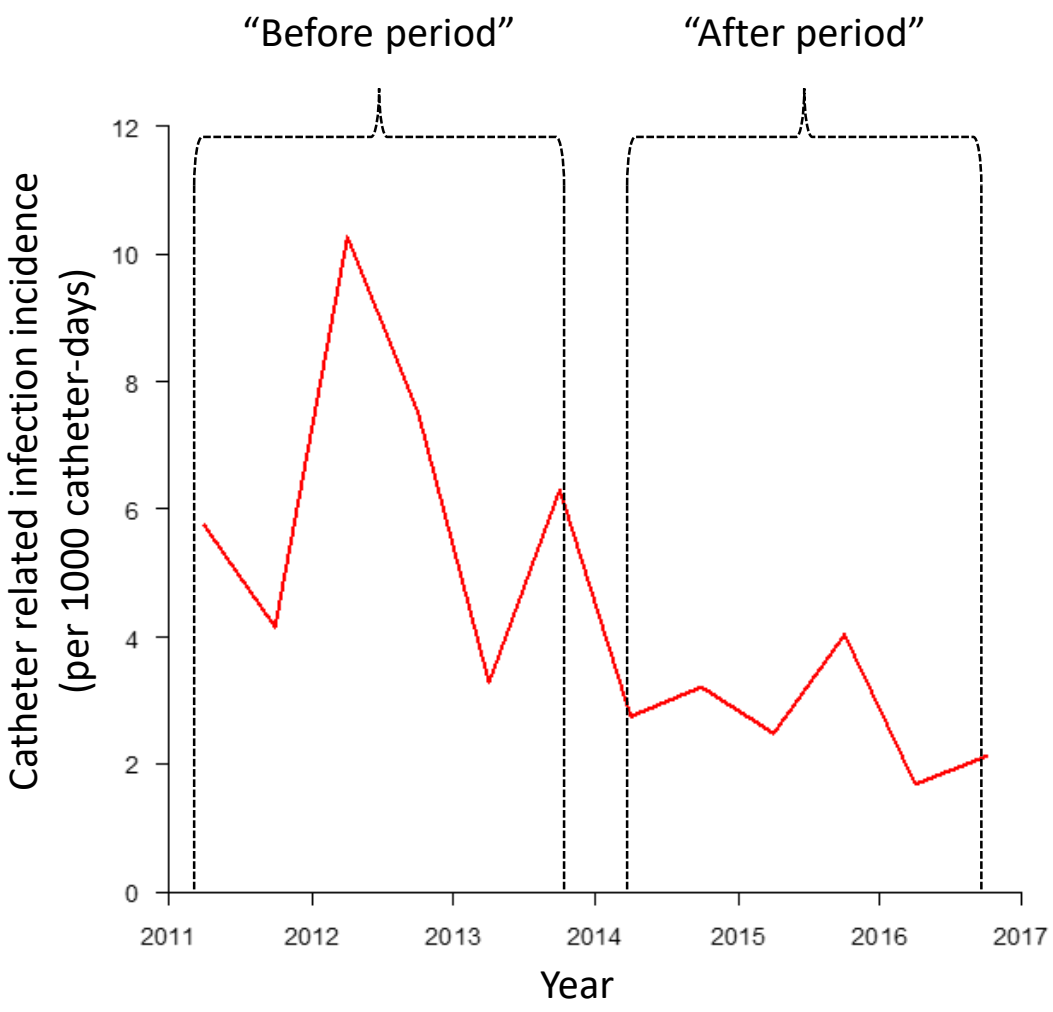


Figure 5: Evolution of the catheter related infection incidence before and after the use of connectors (figure taken from Clavier *et al*. [10]**).**

Name of Material/ Equipment	Company	Catalog Number	Comments/Description
BD MaxZero™ needle-free connector	Becton Dickinson	MZ1000-07	we present the installation of the connector with MaxZero but thi
4-port mannifold with PE/PVC extension	Cair-LGL	RPB4310A	
PE/PVC extension line with 3-way stopcock	Cair-LGL	PE3302M	
NaCl 0.9% 250 ml	Baxter	2B1322	
BD Plastipak™ 50mL Luer-Lock Syringe	BECTON DICKINSON MEDICAL	613-3925	

is protocol is applicable with any positive displacement valve.

jove JOURNAL OF VISUALIZED EXPERIMENTS
1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

Title of Article: A PROTOCOL TO SET UP NEEDLE FREE CONNECTOR WITH POSITIVE DISPLACEMENT ON CENTRAL VENOUS CATHETER IN INTENSIVE CARE UNIT

Author(s): THomas CLAVIER, Sebastien FRANCHINA, Ancaine LEFEVRE-SCELLES, Philippe GOUIN, Emmanuel BESNIER, Benoit VEBER.

Item 1: The Author elects to have the Materials be made available (as described at http://www.jove.com/publish) via:

☒ Standard Access ☐ Open Access

Item 2: Please select one of the following items:

☒ The Author is **NOT** a United States government employee.

☐ The Author is a United States government employee and the Materials were prepared in the course of his or her duties as a United States government employee.

☐ The Author is a United States government employee but the Materials were NOT prepared in the course of his or her duties as a United States government employee.

ARTICLE AND VIDEO LICENSE AGREEMENT

1. **Defined Terms.** As used in this Article and Video License Agreement, the following terms shall have the following meanings: "**Agreement**" means this Article and Video License Agreement; "**Article**" means the article specified on the last page of this Agreement, including any associated materials such as texts, figures, tables, artwork, abstracts, or summaries contained therein; "**Author**" means the author who is a signatory to this Agreement; "**Collective Work**" means a work, such as a periodical issue, anthology or encyclopedia, in which the Materials in their entirety in unmodified form, along with a number of other contributions, constituting separate and independent works in themselves, are assembled into a collective whole; "**CRC License**" means the Creative Commons Attribution-Non Commercial-No Derivs 3.0 Unported Agreement, the terms and conditions of which can be found at: http://creativecommons.org/licenses/by-nc-nd/3.0/legalcode; "**Derivative Work**" means a work based upon the Materials or upon the Materials and other pre-existing works, such as a translation, musical arrangement, dramatization, fictionalization, motion picture version, sound recording, art reproduction, abridgment, condensation, or any other form in which the Materials may be recast, transformed, or adapted; "**Institution**" means the institution, listed on the last page of this Agreement, by which the Author was employed at the time of the creation of the Materials; "**JoVE**" means MyJove Corporation, a Massachusetts corporation and the publisher of The Journal of Visualized Experiments; "**Materials**" means the Article and / or the Video; "**Parties**" means the Author and JoVE; "**Video**" means any video(s) made by the Author, alone or in conjunction with any other parties, or by JoVE or its affiliates or agents, individually or in collaboration with the Author or any other parties, incorporating all or any portion of the Article, and in which the Author may or may not appear.

2. **Background.** The Author, who is the author of the Article, in order to ensure the dissemination and protection of the Article, desires to have the JoVE publish the Article and create and transmit videos based on the Article. In furtherance of such goals, the Parties desire to memorialize in this Agreement the respective rights of each Party in and to the Article and the Video.

3. **Grant of Rights in Article.** In consideration of JoVE agreeing to publish the Article, the Author hereby grants to JoVE, subject to **Sections 4** and **7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Article in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Article into other languages, create adaptations, summaries or extracts of the Article or other Derivative Works (including, without limitation, the Video) or Collective Works based on all or any portion of the Article and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and(c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. If the "Open Access" box has been checked in **Item 1** above, JoVE and the Author hereby grant to the public all such rights in the Article as provided in, but subject to all limitations and requirements set forth in, the CRC License.

jove JOURNAL OF VISUALIZED EXPERIMENTS
1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

4. **Retention of Rights in Article.** Notwithstanding the exclusive license granted to JoVE in **Section 3** above, the Author shall, with respect to the Article, retain the non-exclusive right to use all or part of the Article for the non-commercial purpose of giving lectures, presentations or teaching classes, and to post a copy of the Article on the Institution's website or the Author's personal website, in each case provided that a link to the Article on the JoVE website is provided and notice of JoVE's copyright in the Article is included. All non-copyright intellectual property rights in and to the Article, such as patent rights, shall remain with the Author.

5. **Grant of Rights in Video – Standard Access.** This **Section 5** applies if the "Standard Access" box has been checked in **Item 1** above or if no box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby acknowledges and agrees that, Subject to **Section 7** below, JoVE is and shall be the sole and exclusive owner of all rights of any nature, including, without limitation, all copyrights, in and to the Video. To the extent that, by law, the Author is deemed, now or at any time in the future, to have any rights of any nature in or to the Video, the Author hereby disclaims all such rights and transfers all such rights to JoVE.

6. **Grant of Rights in Video – Open Access.** This **Section 6** applies only if the "Open Access" box has been checked in **Item 1** above. In consideration of JoVE agreeing to produce, display or otherwise assist with the Video, the Author hereby grants to JoVE, subject to **Section 7** below, the exclusive, royalty-free, perpetual (for the full term of copyright in the Article, including any extensions thereto) license (a) to publish, reproduce, distribute, display and store the Video in all forms, formats and media whether now known or hereafter developed (including without limitation in print, digital and electronic form) throughout the world, (b) to translate the Video into other languages, create adaptations, summaries or extracts of the Video or other Derivative Works or Collective Works based on all or any portion of the Video and exercise all of the rights set forth in (a) above in such translations, adaptations, summaries, extracts, Derivative Works or Collective Works and (c) to license others to do any or all of the above. The foregoing rights may be exercised in all media and formats, whether now known or hereafter devised, and include the right to make such modifications as are technically necessary to exercise the rights in other media and formats. For any Video to which this **Section 6** is applicable, JoVE and the Author hereby grant to the public all such rights in the Video as provided in, but subject to all limitations and requirements set forth in, the CRC License.

7. **Government Employees.** If the Author is a United States government employee and the Article was prepared in the course of his or her duties as a United States government employee, as indicated in **Item 2** above, and any of the licenses or grants granted by the Author hereunder exceed the scope of the 17 U.S.C. 403, then the rights granted hereunder shall be limited to the maximum rights permitted under such statute. In such case, all provisions contained herein that are not in conflict with such statute shall remain in full force and effect, and all provisions contained herein that do so conflict shall be deemed to be amended so as to provide to JoVE the maximum rights permissible within such statute.

8. **Protection of the Work.** The Author(s) authorize JoVE to take steps in the Author(s) name and on their behalf if JoVE believes some third party could be infringing or might infringe the copyright of either the Author's Article and/or Video.

9. **Likeness, Privacy, Personality.** The Author hereby grants JoVE the right to use the Author's name, voice, likeness, picture, photograph, image, biography and performance in any way, commercial or otherwise, in connection with the Materials and the sale, promotion and distribution thereof. The Author hereby waives any and all rights he or she may have, relating to his or her appearance in the Video or otherwise relating to the Materials, under all applicable privacy, likeness, personality or similar laws.

10. **Author Warranties.** The Author represents and warrants that the Article is original, that it has not been published, that the copyright interest is owned by the Author (or, if more than one author is listed at the beginning of this Agreement, by such authors collectively) and has not been assigned, licensed, or otherwise transferred to any other party. The Author represents and warrants that the author(s) listed at the top of this Agreement are the only authors of the Materials. If more than one author is listed at the top of this Agreement and if any such author has not entered into a separate Article and Video License Agreement with JoVE relating to the Materials, the Author represents and warrants that the Author has been authorized by each of the other such authors to execute this Agreement on his or her behalf and to bind him or her with respect to the terms of this Agreement as if each of them had been a party hereto as an Author. The Author warrants that the use, reproduction, distribution, public or private performance or display, and/or modification of all or any portion of the Materials does not and will not violate, infringe and/or misappropriate the patent, trademark, intellectual property or other rights of any third party. The Author represents and warrants that it has and will continue to comply with all government, institutional and other regulations, including, without limitation all institutional, laboratory, hospital, ethical, human and animal treatment, privacy, and all other rules, regulations, laws, procedures or guidelines, applicable to the Materials, and that all research involving human and animal subjects has been approved by the Author's relevant institutional review board.

11. **JoVE Discretion.** If the Author requests the assistance of JoVE in producing the Video in the Author's facility, the Author shall ensure that the presence of JoVE employees, agents or independent contractors is in accordance with the relevant regulations of the Author's institution. If more than one author is listed at the beginning of this Agreement, JoVE may, in its sole

jove JOURNAL OF VISUALIZED EXPERIMENTS
1 Alewife Center #200
Cambridge, MA 02140
tel. 617.945.9051
www.jove.com

ARTICLE AND VIDEO LICENSE AGREEMENT

discretion, elect not take any action with respect to the Article until such time as it has received complete, executed Article and Video License Agreements from each such author. JoVE reserves the right, in its absolute and sole discretion and without giving any reason therefore, to accept or decline any work submitted to JoVE. JoVE and its employees, agents and independent contractors shall have full, unfettered access to the facilities of the Author or of the Author's institution as necessary to make the Video, whether actually published or not. JoVE has sole discretion as to the method of making and publishing the Materials, including, without limitation, to all decisions regarding editing, lighting, filming, timing of publication, if any, length, quality, content and the like.

12. **Indemnification.** The Author agrees to indemnify JoVE and/or its successors and assigns from and against any and all claims, costs, and expenses, including attorney's fees, arising out of any breach of any warranty or other representations contained herein. The Author further agrees to indemnify and hold harmless JoVE from and against any and all claims, costs, and expenses, including attorney's fees, resulting from the breach by the Author of any representation or warranty contained herein or from allegations or instances of violation of intellectual property rights, damage to the Author's or the Author's institution's facilities, fraud, libel, defamation, research, equipment, experiments, property damage, personal injury, violations of institutional, laboratory, hospital, ethical, human and animal treatment, privacy or other rules, regulations, laws, procedures or guidelines, liabilities and other losses or damages related in any way to the submission of work to JoVE, making of videos by JoVE, or publication in JoVE or elsewhere by JoVE. The Author shall be responsible for, and shall hold JoVE harmless from, damages caused by lack of sterilization, lack of cleanliness or by contamination due to the making of a video by JoVE its employees, agents or independent contractors. All sterilization, cleanliness or decontamination procedures shall be solely the responsibility of the Author and shall be undertaken at the Author's expense. All indemnifications provided herein shall include JoVE's attorney's fees and costs related to said losses or damages. Such indemnification and holding harmless shall include such losses or damages incurred by, or in connection with, acts or omissions of JoVE, its employees, agents or independent contractors.

13. **Fees.** To cover the cost incurred for publication, JoVE must receive payment before production and publication of the Materials. Payment is due in 21 days of invoice. Should the Materials not be published due to an editorial or production decision, these funds will be returned to the Author. Withdrawal by the Author of any submitted Materials after final peer review approval will result in a US$1,200 fee to cover pre-production expenses incurred by JoVE. If payment is not received by the completion of filming, production and publication of the Materials will be suspended until payment is received.

14. **Transfer, Governing Law.** This Agreement may be assigned by JoVE and shall inure to the benefits of any of JoVE's successors and assignees. This Agreement shall be governed and construed by the internal laws of the Commonwealth of Massachusetts without giving effect to any conflict of law provision thereunder. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together shall be deemed to me one and the same agreement. A signed copy of this Agreement delivered by facsimile, e-mail or other means of electronic transmission shall be deemed to have the same legal effect as delivery of an original signed copy of this Agreement.

A signed copy of this document must be sent with all new submissions. Only one Agreement is required per submission.

CORRESPONDING AUTHOR

Name:	Thomas CLAVIER
Department:	Department of Anesthesiology and Critical Care
Institution:	ROUEN UNIVERSITY HOSPITAL
Title:	M.D.
Signature:	
Date:	01-28-2019

Please submit a **signed** and **dated** copy of this license by one of the following three methods:

1. Upload an electronic version on the JoVE submission site
2. Fax the document to +1.866.381.2236
3. Mail the document to JoVE / Attn: JoVE Editorial / 1 Alewife Center #200 / Cambridge, MA 02140

Dear Dr Steindel,

We are glad to submit the revised version of our manuscript entitled "**A protocol to set up needle-free connector with positive displacement on central venous catheter in intensive care unit**". The manuscript is revised by following the suggestion and comments of the reviewers (with a tracking of the modifications). We also submit a version of the video following your suggestions and comments and those of the reviewers.

Thank you for the attention you have given to our protocol and thank you to the reviewers for their accurate and relevant comments that have contributed to improve the quality of our work. We remain of course at your disposal (and/or at the disposal of reviewers) if any further clarification is required.

We would like to thank you again for taking this manuscript into consideration for publication in *JoVE*,

Sincerely yours,

Dr Thomas Clavier
Department of Anesthesiology and Critical Care
Rouen University Hospital, Rouen, France

Response to Editor and Reviewers

Editorial and production comments:

General:

1. Please take this opportunity to thoroughly proofread the manuscript to ensure that

2. JoVE cannot publish manuscripts containing commercial language. This includes trademark symbols (™), registered symbols (®), and company names before an instrument or reagent. Please limit the use of commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials and Reagents.

For example: BD MaxZero

RESPONSE: As asked we suppressed all the references to commercial language in the manuscript.

Protocol:

1. For each step, please ensure you answer the "how" question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. If revisions cause a step to have more than 2-3 actions and 4 sentences per step, please split into separate steps or substeps.

RESPONSE: Thanks you for this comment. The steps we describe involve basic technical knowledge of nurses and physicians (screwing a line on a catheter, purging an infusion line, etc.). For the most complex step (catheter placement) we referred to a JoVE publication. If particular points of the protocol need to be more explicit, do not hesitate to let us know.

Specific Protocol steps:

1. 4.1: Which alcohol-ethanol? Do you mean 90%? See also Figure 4 and the video

RESPONSE: Thank you for this remark, our presentation was indeed confusing. We switched "alcohol" to "isopropyl alcohol" and after a reviewer suggestion we switched to 70% alcohol.

Results:

1. Please include at least one figure or table (including in the video) demonstrating typical outcomes and/or effectiveness of this procedure. These can be from other works; if so, please cite them appropriately in the legend and obtain permission from the journal they were originally published in.

RESPONSE: This remark is indeed relevant, thank you very much. As requested, we have reproduced a figure from a previous study on the subject that we published to illustrate the effect of our protocol.

Table of Materials:

1. Please ensure the Table of Materials has information on all materials and equipment used, especially those mentioned in the Protocol.

RESPONSE: We added the information about NaCl 0.9% and syringe that we used.

Video Content:

1. 0:09: 'mannequin', not 'manikin'.

2. 0:12 - It should be "venous", instead of "venus".

RESPONSE: Yes, absolutely, thank you for these remarks, we made the corrections.

Video Production:

1. The logos should be removed from the front title card. They can remain on the ending title card.

RESPONSE: As asked we removed them.

2. 0:00-0:15, 9:40-9:50 - There is a black border on the right side of the frame. The white background should fill the entire frame.

RESPONSE: We corrected this technical problem

3. 0:10 - The logos should be removed from this title card. The wording of the text may need to be changed because of this.

4. 0:16-9:38 - The logo bug in the top right of the video should be removed.

RESPONSE: As asked we removed the logos.

5. 1:33, 1:54, 2:40, 3:21, 5:10, 5:42, 5:49, 5:56, 6:29, 6:43, 6:49, 6:57, 7:12, 7:42, 7:52, 8:31- The edits here are jump cuts, which tend to have a jarring effect on the viewer. They should be smoothed out with crossfades instead.

RESPONSE: We edited the video to replace jump cuts with crossfades.

6. 1:37-1:54 - There is a lot of time where the demonstrator is just waiting on screen. Some of this wait time could be edited out and crossfades inserted to help this step move more quickly.

RESPONSE: We edited the video to shorten this sequence.

7. 4:17-5:09 - This step plays out in real time over mostly silence. If it is necessary to show this entire step in real time, narration should be added that further explains some of the details of this procedure as it is happening. If it is not necessary, this step should be edited for length. Perhaps it is only necessary to show the purging of one of the four connectors.

RESPONSE/ We edited the video to shorten this sequence (with only one purge).

8. Chapter title cards need to be inserted, include one that reads "Conclusion" at 8:51. This is for the chaptering of the video that will be done on our website upon publication, and will help viewers navigate through the content.

RESPONSE: As asked, we inserted title cards in the video.

9. There is no representative results section. There is some discussion of results in the concluding statement, but no visuals for them.

RESPONSE: This protocol was submitted to the journal at the request of a JoVE editor after we had already published an article on the effect of these connectors on catheter-related infections. The objective of the submission to JoVE was to show the protocol we had used but it did not seem to us scientifically deontological to copy the results we have already published and which now belong to another journal. That is why we refer to our previous publication in the text. However, we added a figure at the end of the video to add a visual information.

10. 9:52 - Social media logos should be omitted, as we cannot include corporate branding in published articles.

RESPONSE: As asked we removed them.

Reviewers' comments:

Reviewer #1:

Manuscript Summary:

A very simple protocol regarding an important clinical ICU support that can help to standardize the procedure

RESPONSE: Thank you very much for your feedback on our work and for the time you spent reviewing it.

Reviewer #2:

Manuscript Summary:

The authors describe a protocol to install needleless connectors on an infusion system attached to a central venous line, a routine procedure in intensive care units.

Thank you very much for your feedback on our work and for the time you spent reviewing it.

Major Concerns:

1) Although novelty is not a prerequisite for publication, this protocol describes a routine procedure that is currently performed in many ICUs in industrialized countries. I agree with the authors that this procedure is not performed according to a national or international standardized protocol. However, the authors fail to show superiority of their protocol compared to other alternative protocols. They don't present any data concerning the incidence of bacteraemia, central line infections and venous thrombosis in their patient population and thus fail to prove the efficacy of the protocol even in comparison to a historical control group.

RESPONSE: Thank you for these comment that encourage us to better present our objectives. This protocol was submitted to the journal at the request of a JoVE editor after we had already published an article on the effect of these connectors on catheter-related infections. The objective of the submission to JoVE was to show the protocol we had used but it did not seem to us scientifically deontological to copy the results we have already published and which now belong to another journal. That is why we refer to our previous publication in the text. However, we added a paragraph in the result part to summarize our previous results and we added a figure for visual information (Figure 5).

2) The authors recommend to attach a needleless connector proximal at the central venous line as well as at each socket of the 3-way-stopcock and additionally at each socket of the infusion manifold. By doing so, they end up with up to 3 serially installed needleless connectors. In the setting, what is the exact function of the proximal and middle connector?

RESPONSE: Maintaining the connectors in place keeps the infusion system closed, sterile mounted and minimizes the risk of bacterial contamination. Placing several connectors in a row allows the system to be kept closed after unscrewing regardless of where the infusion line is unscrewed. This also allows, due to the positive pressure that is kept, to leave a line uninfused wherever the line has been unscrewed. This makes manipulations easier and a more convenient use of the catheter for nurses.

3) In the results section, the authors claim that: "Maintaining the connectors in place keeps the infusion system closed, sterile mounted and minimizes the risk of bacterial contamination" but do not show any data to support this assumption.

RESPONSE: Thank you for these comments, which lead us to better express our point of view. We added a reference to our previous work and a figure to illustrate our point. We also cited other references on the beneficial impact of a closed system on catheter infections.

4) In the representative results section, no representative results are shown.

RESPONSE: Thank you for this comment. As previously said in response to your first comment, this protocol was submitted to the journal at the request of a JoVE editor after we had already published an article on the effect of these connectors on catheter-related infections. The objective of the submission to JoVE was to show the protocol but it was clearly stated with this editor that we could not duplicate our results (which belong to another journal). However, we added a paragraph in the result part to summarize our previous results and we added a figure to add a visual information (Figure 5).

5) In the discussion section, the authors claim that "It is also possible that these connectors reduce the risk of deep vein thrombosis11". However, reference 11 reports on the influence of needleless connectors on thrombotic catheter occlusion and not on deep venous thrombosis and thus does not support the statement of the authors of the present manuscript.

RESPONSE: Yes, absolutely, thank you for that remark. This mistake, related to a translation problem, has been rectified. The sense of the original sentence was that these connectors decrease catheter occlusions (but they of course have no impact on venous occlusion).

Minor Concerns:

1) The authors recommend disinfecting the connector for 10 seconds with 90° alcohol. The manufacturer of the protocol recommends 3 seconds of disinfection with an alcohol-based disinfectant. How do the authors explain the superiority of their protocol compared to the recommendation of the manufacturer?

RESPONSE: This protocol was set up with the help of the manufacturer 7 years ago and their referent nurse suggested a duration of 10 seconds with 90% alcohol at that time (duration that remained in our protocol) but we have no arguments to affirm that 10 seconds of disinfection is better than 3 seconds. As things have evolved and according to your smart suggestion, we modified the protocol to set the disinfection time to 3 seconds. We also switched “90% alcohol” to “70% isopropyl alcohol” as it has also been included in the latest manufacturer's recommendations.

Reviewer #3:

I commend the authors on your manuscript and study of needleless connectors. However, I recommend attention to specific areas to add credibility to your work.

Thank you very much for your feedback on our work and for the time you spent reviewing it.

Manuscript Summary:

1. Your focus on a positive pressure needleless connector (NC) without providing a description of this product mechanism or comparison with other needleless connectors is deficient. Please add more information on needleless connector types (see Jarvis or Casey).

RESPONSE: This remark is indeed relevant, thank you very much. We added some sentences and references to describe NC mechanisms and to compare positive pressure NC with other needleless connectors.

2. Your frequent mention of MaxZero™ and the advantages of positive pressure NC come across as a sales pitch and a how to on placing this specific NC on tubing. Please change and add generic terms and include comparisons with other NC such as negative, neutral and anti-reflux.

RESPONSE: Thank you very much for this suggestion that we perfectly understand. As asked we suppressed all the references to commercial language in the manuscript. As specified in the manuscript, BD had no role in this work.

3. The protocol emphasizes importance of a standardized process without validation of steps or components. With the inclusion of extension tubing, stopcocks and manifolds there are risk concerns related to each of these add on devices that are not addressed. Please expand your discussion and include explanation of why you chose the add on components. Also include issues of contamination risk associated with stopcocks and manifolds.

RESPONSE: Thank you for this suggestion which allows us to better describe our protocol. We added an entire paragraph in the discussion to clarify these aspects of our protocol.

Major Concerns:

Bias, incomplete support for conclusions and lack of comparison with other products. Failure to report complications other than rapid flow concerns. Research on risk related to stopcocks and manifolds are not mentioned. Discussion is missing some vital points, see below. Failure to address other issues related to NC such as reflux and catheter occlusion.

RESPONSE: Thank you for these comment that encourage us to better present our objectives. This protocol was submitted to the journal at the request of a JoVE editor after we had already published an article on the effect of these connectors on catheter-related infections. The objective of the submission to JoVE was to show the protocol we had used but it did not seem to us scientifically deontological to copy the results we have already published and which now belong to another journal. That is why we refer to our previous publication in the text. The purpose of the present article was not to make a comparison with other connector devices (there is already several work on the subject) but to describe our experience with a positive pressure connector. However, we added a paragraph in the result part to summarize our previous results and we added a figure to add a visual information (Figure 5).

DISCUSSION:

1. Advantages of closed system not adequately reported or included with supporting evidence.

RESPONSE: Yes, absolutely, thank you for that remark. We added a sentence concerning the beneficial impact of closed systems.

2. Vein guard not defined.

RESPONSE: We have modified this sentence to make it easier to understand and deleted the term "Vein guard".

3. The term MaxZero™ was overused and should be omitted and replaced with positive pressure needleless connector (PPNC) or something generic.

RESPONSE: Thank you for this suggestion, we modified the text as asked.

4. The complications or lack thereof reported is of minimal importance in light of the failure to report all or any other complications related to the function of the device.

RESPONSE: We are sorry to observe that we do not fully understand this comment. We clearly discuss the infectious risk associated with these connectors in the introduction and discuss the impact of these connectors on infusion rate as reported in some studies. We also talk about the importance of training nurses that use this device to avoid misuse. If you want us to detail other complications, do not hesitate to specify them and we will of course add them on the manuscript.

4. Asepsis with installation was briefly mentioned, but, while included in the video as a sterile process, the sterile or completely aseptic application every 7 days at the bedside was ignored. Aseptic non touch ANTT could be mentioned in association with the nursing education.

RESPONSE: Thank you for this suggestion which improves the discussion section. We add two sentences on the ANTT.

5. The impact of connectors on complications related to central venous catheterization is poorly understood. - not true, issues of infection and occlusion are directly related to NC function and disinfection. Modify this conclusion and use evidence to support statements.

RESPONSE: Thank you for these comments, which lead us to better express our mind. We suppressed this sentence and we cite the references concerning catheter infection or occlusion in this paragraph.

6. In addition, regular examination of the connectors for contamination is essential to be able to rinse or change the implicated connectors and avoid bacterial growth. Due to the technical aspect of this kind of connector, nurses must be trained before using these connectors in everyday practice. -- Please read Ferroni and Guiffant on the impact of pulsatile flushing for catheters. Include this issue in your discussion on rinsing/flushing.

RESPONSE: As asked we cited this article in our manuscript.

7. It is also possible that these connectors reduce the risk of deep vein thrombosis11 167. - I question this conclusion. Please add more statements to support this or omit.

RESPONSE: Yes, thank you for that remark that point one error in the text. This mistake related to a translation problem has been rectified. The sense of the original sentence was that these connectors decrease catheter occlusions (but they of course have no impact on venous occlusion).

8. Although the potential beneficial effects have not been clearly demonstrated, data in the literature support the safe and prolonged use of these devices. - I question the first part of this sentence since there is quite a bit of literature on beneficial effects of NC. Please modify this sentence and add evidence and more content to support your statements.

RESPONSE: We have probably been too cautious in our interpretation of recent literature on these devices, thank you to raise this point. We modified this part of the discussion and cited more references to support our statement on the beneficial impact of NC.

9. However, different units may use different methods to mount connectors on infusion lines and most studies do not accurately describe the method used to install connectors on catheters. It seems appropriate that studies on connectors should rigorously report their installation protocol. --These are strange conclusions since NC are used on almost all intravenous devices in the United States by simply luer screwing the NC on the catheter hub without any additional extensions or supplies. Your use of the term "accurately" does not seem to apply since you have no validation of your procedure or steps. Please change these sentence and support your conclusions.

RESPONSE: As asked we modified this sentence to moderate our point of view. As you said, practices may vary from one country to another and in Europe the use of several infusion lines in addition to the NC is quite frequent. In our opinion, it costs nothing to write in an article studying NC the type of set-up that is used (even if it is very simple) and this contributes to the rigour of the scientific report. We therefore believe that our remark remains relevant.

Minor Concerns:

I recognize this was meant to be a short report of a protocol this facility is using, but without criteria to measure impact and outcomes the protocol has little credibility.

RESPONSE: As previously said in response one of your previous comment, this protocol was submitted to the journal at the request of a JoVE editor after we had already published an article on the effect of these connectors on catheter-related infections. The objective of the submission to JoVE was to show the protocol but it was clearly stated with this editor that we could not duplicate our results (which belong to another journal). However, we added a paragraph in the result part to summarize our previous results and we added a figure to add a visual information (Figure 5).

Dear Dr Steindel,

We are glad to submit the revised version of our manuscript entitled "**A protocol to set up needle-free connector with positive displacement on central venous catheter in intensive care unit**". The manuscript is revised by following your last suggestions. We also submit a version of the video following your suggestions and comments.

We remain of course at your disposal (and/or at the disposal of reviewers) if any further clarification is required.

We would like to thank you again for taking this manuscript into consideration for publication in *JoVE*,

Sincerely yours,

Dr Thomas Clavier
Department of Anesthesiology and Critical Care
Rouen University Hospital, Rouen, France

Response to Editor

1. 6:42-6:59 - The audio quality of this sentence of narration is noticeably different from the narration that surrounds it. This should be rerecorded so that it sounds similar to the rest of the narration. Also, it should say "...for three seconds..." instead of "...during three seconds..."

Answer: We have made a new audio recording of this sequence in our studio

2. There should be a separate representative results section (with title card) in the video, between the protocol and discussion.

Answer: We added a result part to the video with a figure and audio comments on the impact that the implementation of these connectors has had in our ICU.

3. Although the main focus of this should indeed be the procedure, as two reviewers have concerns about effectiveness, other readers/viewers may have the same concerns. It may be best to include more evidence in that regard, e.g., incidence of complications.

Answer: We understand the reviewers' comments on this point. That is why we insisted in our discussion on the fact that we had not encountered any complications related to the use of this protocol: no difficulty in infusing medication, no difficulties in vascular filling, no peaks of infection, etc. Figure 5 shows the effectiveness that this protocol has had in our department. In the results section, we have added data from our previous work to clarify the impact of this protocol on our patients.

4. Please obtain explicit copyright permission to reuse any figures from a previous publication. Explicit permission can be expressed in the form of a letter from the editor or a link to the editorial policy that allows re-prints. Please upload this information as a .doc or .docx file to your Editorial Manager account.

Answer: We provide in a document attached with the revised version of the manuscript a copy of Elsevier's authorization to use the figure. This document also contains a link to their site where the authorization form is located

Link to the form: https://s100.copyright.com/CustomerAdmin/PLF.jsp?ref=690a697d-930a-41c0-8d32-33c810a3eb07

ELSEVIER LICENSE
TERMS AND CONDITIONS

Jun 03, 2019

This Agreement between Thomas Clavier ("You") and Elsevier ("Elsevier") consists of your license details and the terms and conditions provided by Elsevier and Copyright Clearance Center.

License Number	4581360090602
License date	May 03, 2019
Licensed Content Publisher	Elsevier
Licensed Content Publication	Australian Critical Care
Licensed Content Title	Impact of MaxZero™ needle-free connector on the incidence of central venous catheter-related infections in surgical intensive care unit
Licensed Content Author	Thomas Clavier,Mathias Ferguen,Philippe Gouin,André Gillibert,Mikaël Dusenne,Véronique Merle,Benoit Veber
Licensed Content Date	Mar 1, 2019
Licensed Content Volume	32
Licensed Content Issue	2
Licensed Content Pages	5
Start Page	107
End Page	111
Type of Use	reuse in a journal/magazine
Requestor type	academic/educational institute
Intended publisher of new work	Other
Portion	figures/tables/illustrations
Number of figures/tables/illustrations	1
Format	electronic
Are you the author of this Elsevier article?	Yes
Will you be translating?	No
Original figure numbers	Figure 3
Title of the article	A protocol to set up needle-free connector with positive displacement on central venous catheter in intensive care unit
Publication new article is in	Journal of visual experiment (JoVE)
Publisher of the new article	MyJove Corp

Author of new article	Thomas Clavier
Expected publication date	May 2019
Estimated size of new article (number of pages)	6
Requestor Location	Thomas Clavier Inserm U982, Place Emile Blondel Mont-Saint,-Aignan, 76000 France Attn: Thomas Clavier
Publisher Tax ID	GB 494 6272 12
Total	0.00 EUR
Terms and Conditions	

INTRODUCTION

1. The publisher for this copyrighted material is Elsevier. By clicking "accept" in connection with completing this licensing transaction, you agree that the following terms and conditions apply to this transaction (along with the Billing and Payment terms and conditions established by Copyright Clearance Center, Inc. ("CCC"), at the time that you opened your Rightslink account and that are available at any time at http://myaccount.copyright.com).

GENERAL TERMS

2. Elsevier hereby grants you permission to reproduce the aforementioned material subject to the terms and conditions indicated.
3. Acknowledgement: If any part of the material to be used (for example, figures) has appeared in our publication with credit or acknowledgement to another source, permission must also be sought from that source. If such permission is not obtained then that material may not be included in your publication/copies. Suitable acknowledgement to the source must be made, either as a footnote or in a reference list at the end of your publication, as follows:
"Reprinted from Publication title, Vol /edition number, Author(s), Title of article / title of chapter, Pages No., Copyright (Year), with permission from Elsevier [OR APPLICABLE SOCIETY COPYRIGHT OWNER]." Also Lancet special credit - "Reprinted from The Lancet, Vol. number, Author(s), Title of article, Pages No., Copyright (Year), with permission from Elsevier."
4. Reproduction of this material is confined to the purpose and/or media for which permission is hereby given.
5. Altering/Modifying Material: Not Permitted. However figures and illustrations may be altered/adapted minimally to serve your work. Any other abbreviations, additions, deletions and/or any other alterations shall be made only with prior written authorization of Elsevier Ltd. (Please contact Elsevier at permissions@elsevier.com). No modifications can be made to any Lancet figures/tables and they must be reproduced in full.
6. If the permission fee for the requested use of our material is waived in this instance, please be advised that your future requests for Elsevier materials may attract a fee.
7. Reservation of Rights: Publisher reserves all rights not specifically granted in the combination of (i) the license details provided by you and accepted in the course of this licensing transaction, (ii) these terms and conditions and (iii) CCC's Billing and Payment terms and conditions.

8. License Contingent Upon Payment: While you may exercise the rights licensed immediately upon issuance of the license at the end of the licensing process for the transaction, provided that you have disclosed complete and accurate details of your proposed use, no license is finally effective unless and until full payment is received from you (either by publisher or by CCC) as provided in CCC's Billing and Payment terms and conditions. If full payment is not received on a timely basis, then any license preliminarily granted shall be deemed automatically revoked and shall be void as if never granted. Further, in the event that you breach any of these terms and conditions or any of CCC's Billing and Payment terms and conditions, the license is automatically revoked and shall be void as if never granted. Use of materials as described in a revoked license, as well as any use of the materials beyond the scope of an unrevoked license, may constitute copyright infringement and publisher reserves the right to take any and all action to protect its copyright in the materials.
9. Warranties: Publisher makes no representations or warranties with respect to the licensed material.
10. Indemnity: You hereby indemnify and agree to hold harmless publisher and CCC, and their respective officers, directors, employees and agents, from and against any and all claims arising out of your use of the licensed material other than as specifically authorized pursuant to this license.
11. No Transfer of License: This license is personal to you and may not be sublicensed, assigned, or transferred by you to any other person without publisher's written permission.
12. No Amendment Except in Writing: This license may not be amended except in a writing signed by both parties (or, in the case of publisher, by CCC on publisher's behalf).
13. Objection to Contrary Terms: Publisher hereby objects to any terms contained in any purchase order, acknowledgment, check endorsement or other writing prepared by you, which terms are inconsistent with these terms and conditions or CCC's Billing and Payment terms and conditions. These terms and conditions, together with CCC's Billing and Payment terms and conditions (which are incorporated herein), comprise the entire agreement between you and publisher (and CCC) concerning this licensing transaction. In the event of any conflict between your obligations established by these terms and conditions and those established by CCC's Billing and Payment terms and conditions, these terms and conditions shall control.
14. Revocation: Elsevier or Copyright Clearance Center may deny the permissions described in this License at their sole discretion, for any reason or no reason, with a full refund payable to you. Notice of such denial will be made using the contact information provided by you. Failure to receive such notice will not alter or invalidate the denial. In no event will Elsevier or Copyright Clearance Center be responsible or liable for any costs, expenses or damage incurred by you as a result of a denial of your permission request, other than a refund of the amount(s) paid by you to Elsevier and/or Copyright Clearance Center for denied permissions.

LIMITED LICENSE

The following terms and conditions apply only to specific license types:
15. **Translation**: This permission is granted for non-exclusive world **English** rights only unless your license was granted for translation rights. If you licensed translation rights you may only translate this content into the languages you requested. A professional translator must perform all translations and reproduce the content word for word preserving the integrity of the article.
16. **Posting licensed content on any Website**: The following terms and conditions apply as follows: Licensing material from an Elsevier journal: All content posted to the web site must maintain the copyright information line on the bottom of each image; A hyper-text

must be included to the Homepage of the journal from which you are licensing at http://www.sciencedirect.com/science/journal/xxxxx or the Elsevier homepage for books at http://www.elsevier.com; Central Storage: This license does not include permission for a scanned version of the material to be stored in a central repository such as that provided by Heron/XanEdu.
Licensing material from an Elsevier book: A hyper-text link must be included to the Elsevier homepage at http://www.elsevier.com . All content posted to the web site must maintain the copyright information line on the bottom of each image.

Posting licensed content on Electronic reserve: In addition to the above the following clauses are applicable: The web site must be password-protected and made available only to bona fide students registered on a relevant course. This permission is granted for 1 year only. You may obtain a new license for future website posting.
17. **For journal authors:** the following clauses are applicable in addition to the above:
Preprints:
A preprint is an author's own write-up of research results and analysis, it has not been peer-reviewed, nor has it had any other value added to it by a publisher (such as formatting, copyright, technical enhancement etc.).
Authors can share their preprints anywhere at any time. Preprints should not be added to or enhanced in any way in order to appear more like, or to substitute for, the final versions of articles however authors can update their preprints on arXiv or RePEc with their Accepted Author Manuscript (see below).
If accepted for publication, we encourage authors to link from the preprint to their formal publication via its DOI. Millions of researchers have access to the formal publications on ScienceDirect, and so links will help users to find, access, cite and use the best available version. Please note that Cell Press, The Lancet and some society-owned have different preprint policies. Information on these policies is available on the journal homepage.
Accepted Author Manuscripts: An accepted author manuscript is the manuscript of an article that has been accepted for publication and which typically includes author-incorporated changes suggested during submission, peer review and editor-author communications.
Authors can share their accepted author manuscript:

- immediately
    - via their non-commercial person homepage or blog
    - by updating a preprint in arXiv or RePEc with the accepted manuscript
    - via their research institute or institutional repository for internal institutional uses or as part of an invitation-only research collaboration work-group
    - directly by providing copies to their students or to research collaborators for their personal use
    - for private scholarly sharing as part of an invitation-only work group on commercial sites with which Elsevier has an agreement
- After the embargo period
    - via non-commercial hosting platforms such as their institutional repository
    - via commercial sites with which Elsevier has an agreement

In all cases accepted manuscripts should:

- link to the formal publication via its DOI
- bear a CC-BY-NC-ND license - this is easy to do

- if aggregated with other manuscripts, for example in a repository or other site, be shared in alignment with our hosting policy not be added to or enhanced in any way to appear more like, or to substitute for, the published journal article.

Published journal article (JPA): A published journal article (PJA) is the definitive final record of published research that appears or will appear in the journal and embodies all value-adding publishing activities including peer review co-ordination, copy-editing, formatting, (if relevant) pagination and online enrichment.
Policies for sharing publishing journal articles differ for subscription and gold open access articles:
Subscription Articles: If you are an author, please share a link to your article rather than the full-text. Millions of researchers have access to the formal publications on ScienceDirect, and so links will help your users to find, access, cite, and use the best available version.
Theses and dissertations which contain embedded PJAs as part of the formal submission can be posted publicly by the awarding institution with DOI links back to the formal publications on ScienceDirect.
If you are affiliated with a library that subscribes to ScienceDirect you have additional private sharing rights for others' research accessed under that agreement. This includes use for classroom teaching and internal training at the institution (including use in course packs and courseware programs), and inclusion of the article for grant funding purposes.
Gold Open Access Articles: May be shared according to the author-selected end-user license and should contain a CrossMark logo, the end user license, and a DOI link to the formal publication on ScienceDirect.
Please refer to Elsevier's posting policy for further information.
18. **For book authors** the following clauses are applicable in addition to the above: Authors are permitted to place a brief summary of their work online only. You are not allowed to download and post the published electronic version of your chapter, nor may you scan the printed edition to create an electronic version. **Posting to a repository:** Authors are permitted to post a summary of their chapter only in their institution's repository.
19. **Thesis/Dissertation**: If your license is for use in a thesis/dissertation your thesis may be submitted to your institution in either print or electronic form. Should your thesis be published commercially, please reapply for permission. These requirements include permission for the Library and Archives of Canada to supply single copies, on demand, of the complete thesis and include permission for Proquest/UMI to supply single copies, on demand, of the complete thesis. Should your thesis be published commercially, please reapply for permission. Theses and dissertations which contain embedded PJAs as part of the formal submission can be posted publicly by the awarding institution with DOI links back to the formal publications on ScienceDirect.

Elsevier Open Access Terms and Conditions
You can publish open access with Elsevier in hundreds of open access journals or in nearly 2000 established subscription journals that support open access publishing. Permitted third party re-use of these open access articles is defined by the author's choice of Creative Commons user license. See our open access license policy for more information.
Terms & Conditions applicable to all Open Access articles published with Elsevier:
Any reuse of the article must not represent the author as endorsing the adaptation of the article nor should the article be modified in such a way as to damage the author's honour or reputation. If any changes have been made, such changes must be clearly indicated.