

BaltAnestIC 2023

Tartu, Estonia

September 2023

# Beyond the state-of-art in anaesthesia and intensive care: pitfalls in the path of innovations

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Senior researcher

Vilnius university

Faculty of medicine

LITHUANIA

MD, Consultant

Anaesthesiology and Intensive Care

South-western group of hospitals

Republic of IRELAND

# Conflict of interest

I received consultant's fees from Masimo Corp., Irvine, CA, USA.

I am an inventor in US Patent No. 7,788,045 B2, non-provisional US patent application PCT/US2011/057,362, and US and EU non-provisional patent application No. 61/692,904.

# A century of innovations

> [Anesth Analg](#). 2022 Aug 1;135(2S Suppl 1):S48-S61. doi: 10.1213/ANE.0000000000006027.  
Epub 2022 Jul 15.

## A Century of Technology in Anesthesia & Analgesia

Jane S Moon <sup>1</sup>, Maxime Cannesson

Affiliations + expand

PMID: 35839833 PMCID: [PMC9298489](#) DOI: [10.1213/ANE.0000000000006027](#)

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ANESTHESIA  
&  
ANALGESIA



1922–1939	<ol style="list-style-type: none"><li>1. Invention of fundamental tools to facilitate anesthetic delivery and patient safety</li><li>2. Growing use of monitoring devices (ie, the sphygmomanometer and electrocardiogram) for physiological assessment</li><li>3. A preliminary recognition of the need for standardization of anesthesia equipment</li><li>4. Methods to mitigate explosion risk during the era of flammable anesthetics (ie, ether, ethylene, and cyclopropane)</li></ol>
1940–1959	<ol style="list-style-type: none"><li>1. Continued refinement of tools for inhalational, regional, and IV anesthetic delivery</li><li>2. Birth of continuous ECG and EEG</li><li>3. Eventual use of electricity for external cardiac defibrillation</li><li>4. Early twitch monitoring to assess degree of neuromuscular blockade</li><li>5. Origins of technological improvement and standardization on a systemic scale</li></ol>
1960–1979	<ol style="list-style-type: none"><li>1. Continued introduction of new tools and machines for safer and more efficient anesthetic delivery</li><li>2. Rapid development of new monitoring and measuring devices with increasing portability and automation</li><li>3. Proliferation of research on the physiological effects of various anesthetic agents</li><li>4. Technology's role in facilitating effective resuscitation and treatment measures</li><li>5. Early use of computers for scheduling, knowledge sharing, and data processing</li></ol>
1980–1999	<ol style="list-style-type: none"><li>1. Continued refinement of tools and machines for anesthetic delivery and airway management</li><li>2. Consolidation of the foundational monitoring devices in anesthesia (ie, pulse oximeter and capnograph)</li><li>3. Use of computer processing to develop simulation for crisis management, to improve health system efficiency, and to conduct large-scale outcomes trials</li></ol>
2000–2022	<ol style="list-style-type: none"><li>1. Development of advanced physiological monitoring systems</li><li>2. The electronic health record</li><li>3. Use of clinical research methodologies to evaluate technological impact on patient outcomes</li><li>4. Applications of <u>computer science, robotics, and control engineering to the perioperative environment</u></li><li>5. Promotion of patient safety and cybersecurity through coordination between devices (device interoperability) and health informatics systems</li></ol>

# Presentation aims

Discuss pitfalls in a pathway from innovative idea to practical implication:

innovativeness

feasibility

IP protection

validation

commercialization

our team's experience "the hard way": lessons on the way to

perfect failures and

perfect wins

# Innovativeness. Pitfall 1

**Pitfall 1:** It is not innovative. An example:

- ❑ SoA: transcapillary fluid filtration-absorption (F-A) ratio determines how much of intravascular fluid is shifting from intra- to extra-vascular space in a capillary bed.
- ❑ Thus, an idea to measure transcapillary F-A ratio with an aim to assess transcapillary distribution of fluids is obvious from existing SoA.
- ❑ However, the know-how of technique for measuring the transcapillary F-A ratio, as well as methodology for the clinically feasible interpretation of these measurements would be innovative.

# Feasibility. Pitfall 2

*feasible*

\*capable of being carried out and used successfully (suitable & practical)

**Pitfall 2:** Innovation **is not** feasible\*. An example:

- A know-how for measuring and interpreting transcapillary fluid F-A ratio:
  - ❑ Is it needed? **Yes**
  - ❑ Can it improve outcomes and cost of treatment? **Yes**
  - ❑ Can it increase the safety of patients? **Yes**
  - ❑ Can it be practical – user friendly? (**probably**), and labour-effective? (**probably**)
  - ❑ Can it be developed using the current SoA tools? **Very unlikely**
  - ❑ Can it be protected, developed and validated, certified and commercialized using your own skills, workforce and budget? **No**

# IP protection: considering patent. Pitfall 3

Pitfall 3: It belongs to your employer.

A million dollar tip: It belongs to your employer **only if** your employer has given you a task to develop specifically the innovation you are considering to patent. Thus, even if you work as researcher in the university, you may still be free to patent your innovation without university's share or ownership.



# Co-founding private companies. Co-ownership

US Professor Richard J. Melker has more than 70 issued U.S. patents to his name.

Melker has cofounded the medical technology company Xhale® Inc. in Gainesville in 2005.



Richard Melker, MD, PhD, right, with Richard R. Allen, then the President and CEO of Xhale, in 2014. Photo by Erica Brough/Gainesville Sun.



# Professor businessman. Awards for innovations

In 2020, Richard J. Melker - a distinguished Emeritus Professor of Anesthesiology has been elected to the rank of the highest professional distinction awarded solely to academic inventors - National Academy of Inventors (NAI) Fellow.

# IP protection: patentability. Pitfall 3

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Pitfall 3: It **is not** patentable.

# Patentability. Pitfall 3

From US Patent (USPTO) website:

- ❖ an invention cannot be patented if the invention was known or used by others in this country, or patented or described in a publication, or in public use or on sale in this country **more than one year prior to the application for patent** in the United States.

**!** The inventor must file US patent application on the date of public use or disclosure to preserve patent rights in **many other countries**.

# Patents with a camouflage. Pitfall 4

Pitfall 4: You do not know that it is already patented.

- A similar idea is already patented with a camouflage.

# Patents with a camouflage. Pitfall 4

The patent game - peering into the soul of an organization's innovation

By Laura Gaze

6 MIN READ

- ❑ The “patent game”
  - ✓ A little known fact [...] nearly 80 percent of the information contained in patent documents is not publicly available anywhere else.
  - ✓ The patent application process is one of secrecy: IP attorneys protect the invention without giving away what is being developed.

\* <https://www.reuters.com/article/us-patent-game-new-idUSBRE99809D20131009>



World Business Markets Breakingviews

# Patents with a camouflage. Pitfall 4

An example:

- Filing a patent for a light bulb (assuming it is a novel, useful and non-obvious item):
  - ✓ Nowhere in the description would the words “light bulb” appear:
    - the filer might refer to it as a “fixture that illuminates the surrounding area with a glow to make things see-able”.
  - ✓ By doing so, the invention, once publicly disclosed, may not be detected by competitors, thereby giving the filing company additional time to be in front of competition.

\* <https://www.reuters.com/article/us-patent-game-new-idUSBRE99809D20131009>

# Cost of patenting. Pitfall 5

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Pitfall 5: Patenting **is not** affordable.



# Cost of patenting in USA (USPTO). Pitfall 5



US Patent Office requires payment of Maintenance fee: X



How much does it cost to hold a patent?

A patent can cost from \$900 for a do-it-yourself application to between \$5,000 and \$10,000+ with the help of patent lawyers. A patent protects an invention and the cost of the process to get the patent will depend on the type of patent (provisional, non-provisional, or utility) and the complexity of the invention.

# Cost of patenting in USA (USPTO). Pitfall 5

Patent maintenance fees			
Fee code	37 CFR §	Description	Fee
1551/2551/3551	1.20(e)	For maintaining an original or any reissue patent, due at 3.5 years	2,000.00
1552/2552/3552	1.20(f)	For maintaining an original or any reissue patent, due at 7.5 years	3,760.00
1553/2553/3553	1.20(g)	For maintaining an original or any reissue patent, due at 11.5 years	7,700.00

❖ USPTO website:

# Hidden cost of patenting. Pitfall 5

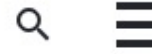
Cost of US patent: our experience (2003 – 2016). Our attorney's quotation

- “The U.S. Application will cost anywhere from \$5,500 to \$12,500 over the next 3-5 years. Obviously, this is just an estimate and things can happen for which we are not accounting.”

# Cost of patenting in EU (EPO). Pitfall 5

## EU (EPO) patenting costs

<https://www.epo.org/en/applying/fees>



### European fees (EPC)

Learn more about European fees (EPC) and consult decisions and notices related to fee changes.



### International fees (PCT)

Learn more about international fees (PCT), fee reductions and decisions and notices related to fee changes.

**1. 3 Filing fee**

<https://www.epo.org/en/applying/fees>

(Article 78, paragraph 2)

(i) where the European patent application or, if required, its translation (Article 14, paragraph 2) is filed online in character-coded format, or,

in the case of an international application, if within the 31-month period (Rule 159, paragraph 1) the form for entry into the European phase (EPO Form 1200) and the international application or, if required, its translation (Rule 159, paragraph 1(a)), and any amendments for processing in the European phase (Rule 159, paragraph 1(b)), are all filed online in character-coded format **105**

(ii) where all documents referred to in item 1(i) are filed online, **5** but any one of them is filed in a format other than character-coded format **135**

(iii) in all other cases **285**

**1a. 8 Additional fee**

# Hidden cost of patenting. Pitfall 5

Our experience:

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- ❖ Patent attorney's fees during first 3-5 yrs. after EPO application submission

# Hidden cost of patenting. Pitfall 5

✓ Extract from our attorney's quotation

- “If you intend to proceed with the referenced European patent application, the attorneys' services for European application will cost \$17,700 - \$20,700 over the next 3-5 years.”

# Hidden cost of patenting. Pitfall 5

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Time is money!



# It took 6 years after application for our US patent to be issued (2005-2011)


SYSTEMS AND METHOD FOR HOMEOSTATIC BLOOD STATES	US2011070210 (A1)	2011-03-24	ANDRIJAUSKAS AUDRIUS [LT]	MEDITASKS LLC	A A A B
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Total fees were USD 36000+

		<b>UNITED STATES PATENT AND TRADEMARK OFFICE</b>		UNITED STATES DEPARTMENT OF COMMERCE United States Patent and Trademark Office Address: COMMISSIONER FOR PATENTS P.O. Box 1450 Alexandria, Virginia 22313-1450 www.uspto.gov	
APPL NO.	FILING OR 371 (c) DATE	APT UNIT	FIL FEE REC'D	ATTY. DOCKET NO	DRAWINGS TOT CLMS IND CLMS
60/712,809	09/01/2005		225		1

CINDY MCLEAN  
3635 MONICA DRIVE  
MISSISSAUGA, ON L4T 2E8  
CANADA

**CONFIRMATION NO. 5166**  
**FILING RECEIPT**



\*OC000000017052833\*

Date Mailed: 09/21/2005

Receipt is acknowledged of this provisional Patent Application. It will not be examined for patentability and will become abandoned not later than twelve months after its filing date. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. **If an error is noted on this Filing Receipt, please mail to the Commissioner for Patents P.O. Box 1450 Alexandria Va 22313-1450. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts" for this application, please submit any corrections to this Filing Receipt with your reply to the Notice. When the USPTO processes the reply to the Notice, the USPTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).**

**Applicant(s)**  
Audrius Andrijauskas, Vilnius, LITHUANIA;



- ❖ E
- ❖ We could include of thousands
- ❖ We have US/EU
- ❖ We failed
- ❖ Who are
- ❖ Maybe we should have tried harder in fund raising?

our  
ent because of upcoming fees  
d sums counting in hundreds  
nd several patent pending  
2015 and 2019 calls

# Protection is not warranted by patent. Pitfall 6

- Innovation can be used in
- Similar patents may be f
- Will you afford suing a r



# Game of patents

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Pitfall 7: Unfair competition.

# Unfair competition. Pitfall 6

Masimo sues Apple in 2020 accusing Apple Watches of copying its technology

<https://www.reuters.com/legal/litigation/apple-lawsuits-say-health-monitoring-company-masimo-copied-apple-watch-2022-10-20/>

Masimo also seeks co-ownership of five Apple patents.

<https://orangeoast.com/2023/mistrial-declared-in-masimo-lawsuit-against-apple>



Who is the winner?



And the winner is...

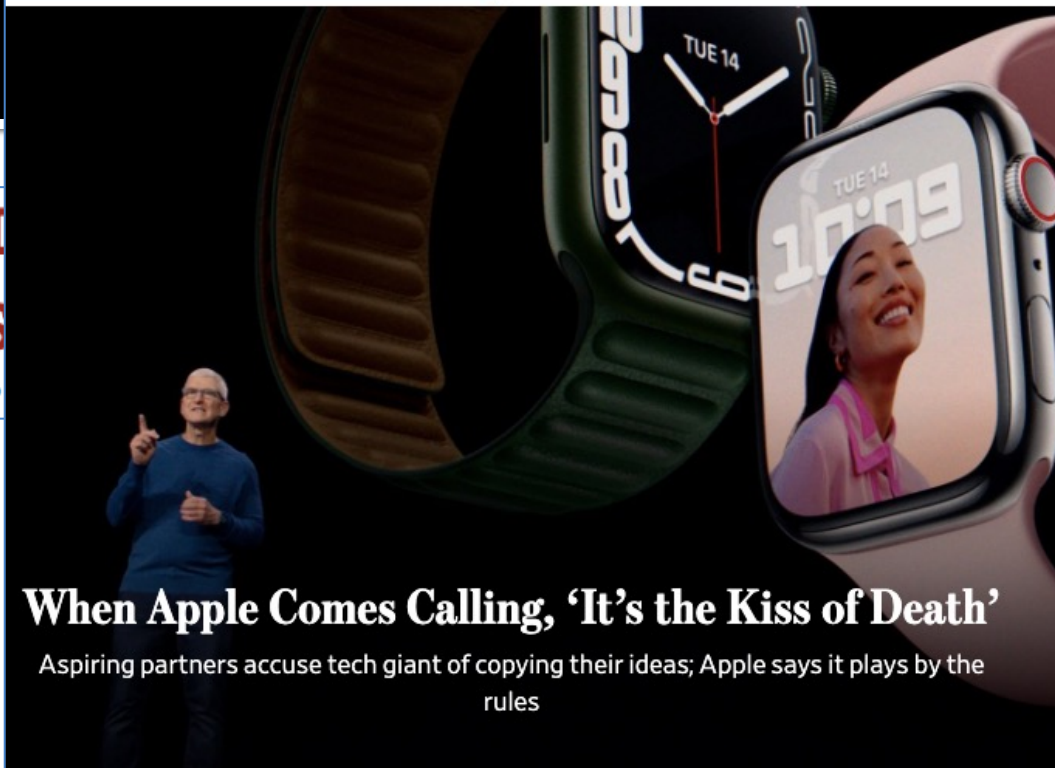


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## When Apple Comes Calling, 'It's the Kiss of Death'

Aspiring partners accuse tech giant of copying their ideas; Apple says it plays by the rules

Apple CEO Tim Cook introduces Apple Watch Series 7 at a 2021 event. Many of Apple's patent battles with smaller companies hinge on technology used in the Apple Watch. PHOTO: APPLE INC/REUTERS



# Validation. Our experience

Validation of our patented and patent-pending innovations:

- A proof of concept: preliminary proof obtained; research published.
- A prototype device was developed.
- Technology and methodology successfully tested *in silico* and *clinical* RCT.
- Clinical feasibility assessed: practical and improving outcomes.

# Validation. Our experience

Validation of our patented and patent-pending innovations:

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RESULTS BY YEAR

2006 2023

TEXT AVAILABILITY

Abstract

1 [A mini volume loading test for indication of preoperative dehydration in surgical patients.](#)  
Cite **Andrijauskas A**, Ivaškevičius J, Porvaneckas N, Stankevičius E, Svensen CH, Uvarovas V, Švedienė S, Kvederas G.  
Share *Medicina (Kaunas)*. 2015;51(2):81-91. doi: 10.1016/j.medic.2015.02.001. Epub 2015 Mar 18. PMID: 25975876 **Free article.** Clinical Trial.

2 [The maintenance and monitoring of perioperative blood volume.](#)  
Cite Iijima T, Brandstrup B, Rodhe P, **Andrijauskas A**, Svensen CH.  
Share *Perioper Med (Lond)*. 2013 May 7;2(1):9. doi: 10.1186/2047-0525-2-9. PMID: 24472160 **Free PMC article.**

# Peer review. False sense of independence



Published Online  
January 8, 2014  
[http://dx.doi.org/10.1016/  
S0140-6736\(13\)62329-6](http://dx.doi.org/10.1016/S0140-6736(13)62329-6)

Peer review and peer decision making in funding, publication, and promotion decisions give a false sense of independence. At every stage, every atomised individual in these processes is affected by the different drivers. Ambitious for success, advancement, and

# Publications. Biased?

GLOBAL HEALTH POLICY

By Matthew Harris, Joachim Marti, Hillary Watt, Yasser Bhatti, James Macinko, and Ara W. Darzi

## Explicit Bias Toward High-Income-Country Research: A Randomized, Blinded, Crossover Experiment Of English Clinicians

DOI: 10.1377/hlthaff.2017.0773  
HEALTH AFFAIRS 36,  
NO. 11 (2017): 1997-2104  
©2017 Project HOPE—  
The People-to-People Health  
Foundation, Inc.

## Physicians May Be Biased

By Ronnie Cohen

November 17, 2017

(Reuters Health) - Physicians in England appear to favor research from high-income countries over research from low-income countries, a bias that could lead to reluctance to adopt cost-saving healthcare innovations, a new study suggests.

"High-income research is disproportionately overvalued, and low-income research is undervalued," said lead author Dr. Matthew Harris, clinical senior lecturer in public health at the Institute of Global Health Innovation, Imperial College London.

# Efficacy of publishing

- 254 PubMed publications co-authored by Cannesson M. from 2011 to 2023.

**PubMed**®

Cannesson M[Author]

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254 results

Page 26

RESULTS BY YEAR

2002 2023

TEXT AVAILABILITY

Abstract

251 **Monitoring in the intensive care unit: its past, present, and future.**  
Cannesson M, Broccard A, Vallet B, Bendjelid K.  
Cite Crit Care Res Pract. 2012;2012:452769. doi: 10.1155/2012/452769. Epub 2012 Se  
PMID: 23019523 **Free PMC article.** No abstract available.

252 **Perioperative hemodynamic therapy: quality improvement progra  
to resolve our uncertainty.**  
Michard F, **Cannesson M**, Vallet B.  
Cite Crit Care. 2011;15(5):445. doi: 10.1186/cc10336. Epub 2011 Oct 10.  
Share PMID: 21989107 **Free PMC article.** No abstract available.

# Big name, big game

**Prof. Maxime Cannesson**, Department of Anesthesiology and Perioperative Medicine, University of California, Los Angeles.

**Conflicts of Interest:** M. Cannesson is a Past Executive Section Editor of Technology, Computing, and Simulation for *Anesthesia & Analgesia*. He also has ownership interest in Sironis (Newport Beach, CA) and Perceptive Medical (Newport Beach, CA), consults for Edwards Lifesciences (Irvine, CA) and Masimo Corp (Irvine, CA), and receives research support from Edwards Lifesciences and Masimo through his department.

[Anesth Analg. 2022 Aug 1; 135\(2\): S48-S61.](#)

# Generation of scientists standing on the shoulders of giants

What could be better than this generation of scientists, standing on the shoulders of giants, and providing our own shoulders for future generations? And, if they are not really very good, careful, or precise, how would anyone know?



Published Online  
January 8, 2014  
[http://dx.doi.org/10.1016/S0140-6736\(13\)62329-6](http://dx.doi.org/10.1016/S0140-6736(13)62329-6)

Biomedical research: increasing value, reducing waste



# How might things be different

How might things be different? One protection from these distorting drivers would be the creation of a set of balancing counter-influences. So, instead of being judged on the basis of the impact factors of the journals in which their work is published, academics might be judged on the methodological rigour and full dissemination of their research, the quality of their reports, and the reproducibility of their findings. If these



**Biomedical research: increasing value, reducing waste**

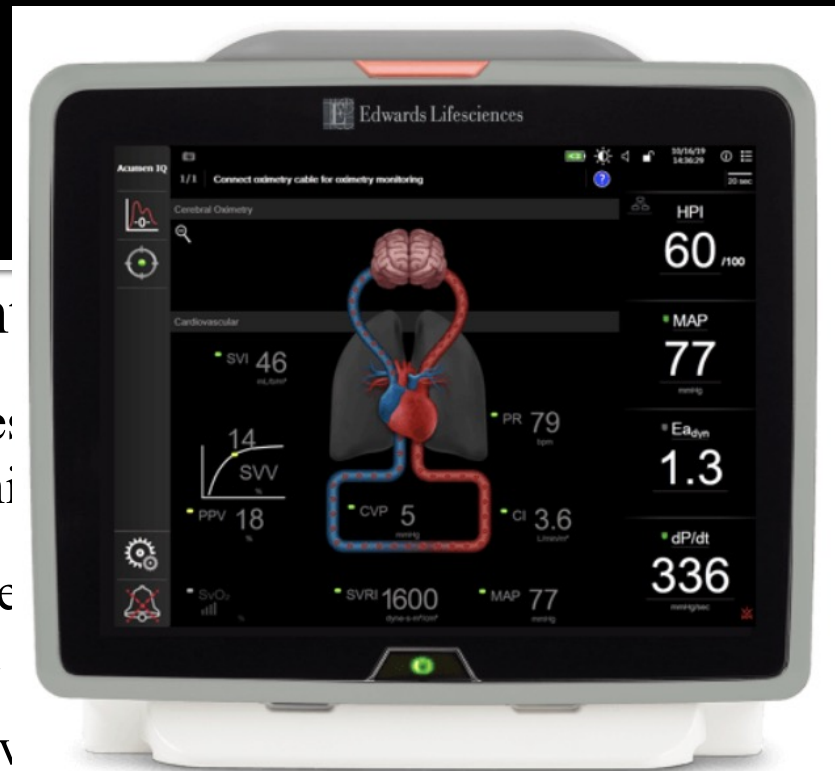




# Commercialization

## ❑ Industrial interests are key important

- Closed-loop system developed by Canne Lifesciences in 2014 - at the very beginning
- Because this company is one of the biggest monitoring devices and decision support
- Thus, they adopted the licensed innovative support in goal directed fluid therapy that used flow related parameters that their monitors are analyzing.



\* *J. Pers. Med.* 2022, 12(7):1168.






# Commercialization

## □ Our experience:

- Our Semi-Closed-Loop infusion system's development was supported by Masimo who provided free equipment and disposables for research but did not show intention to license the innovation or fund the validation studies.
- Our invention's background concept was against Masimo's interest because they marketed the noninvasive Hb device as alternative for invasive Hb measurement.
- Our vision is to raise funds for the development of our own device for measuring hemoglobin selectively in true capillaries where transcapillary fluid shifts occur.

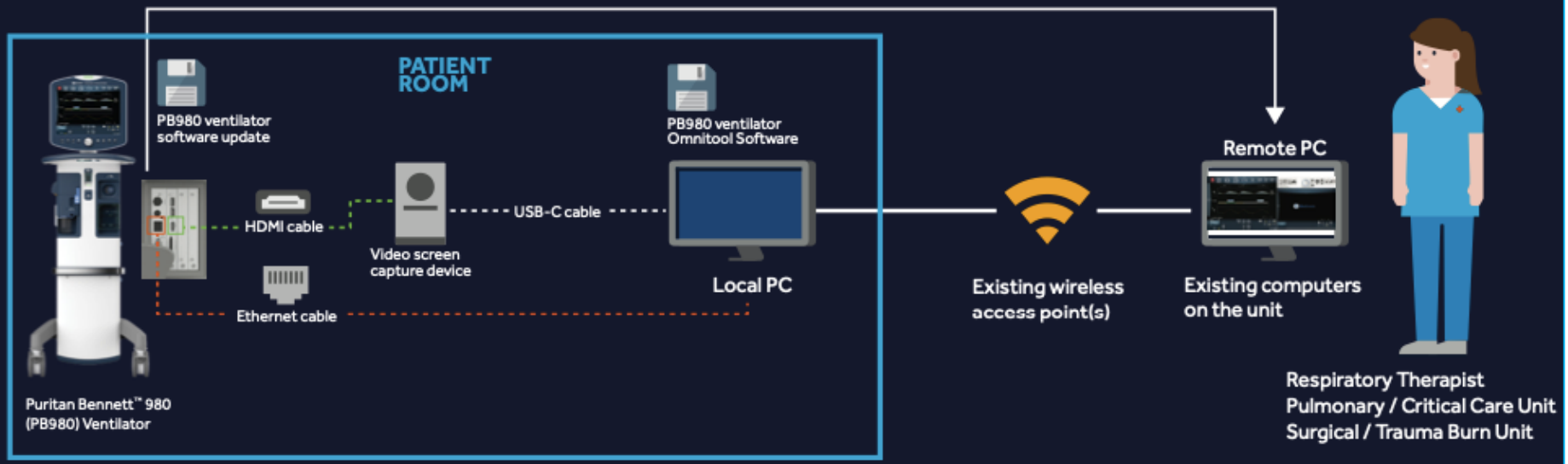
# We do not give up. Expanding the team

HYDRA-2021 project participants

No	Participant	Short name (EN)	Logo	Type	Country
1	Coordinator and lead institution: Vilniaus Universitetas (Vilnius University) <a href="https://www.vu.lt/en/">https://www.vu.lt/en/</a>	VU		University	Lithuania
2	Subcontractor: University of Limerick Optical Fibre Sensors Research Centre <a href="http://www.OFSRC.ul.ie">www.OFSRC.ul.ie</a> and Circuits and Systems Research Centre <a href="https://ulsites.ul.ie/csrc/">https://ulsites.ul.ie/csrc/</a>	UL		University	Ireland
3	Subcontractor: Sodersjukhuset <a href="https://www.sodersjukhuset.se">https://www.sodersjukhuset.se</a>	Sös		University hospital	Sweden
4	Subcontractor: Lietuvos sveikatos mokslų universitetas (Lithuanian University of Health Sciences) <a href="https://lsmuni.lt/en/">https://lsmuni.lt/en/</a>	LUHS		University	Lithuania
5	Subcontractor: Vilniaus Universiteto Igoninė Santaros Klinikos (Vilnius University Hospital Santaros Clinic) <a href="http://www.santa.lt/">http://www.santa.lt/</a>	VUHSC		University	Lithuania

# Innovating. Again?!

## REMOTE MONITORING AND CONTROL SETUP



# Innovating. Why not?!

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