



**SAPIENZA**  
UNIVERSITÀ DI ROMA



**MicroFlu Lab**

**INVICTUS: IN VITRO CAVITATION  
THROUGH ULTRASOUND  
ERC-2017-PoC**

**C.M. CASCIOLA**

**DEPT. OF MECHANICAL AND  
AEROSPACE ENGINEERING  
SAPIENZA UNIVERSITY**







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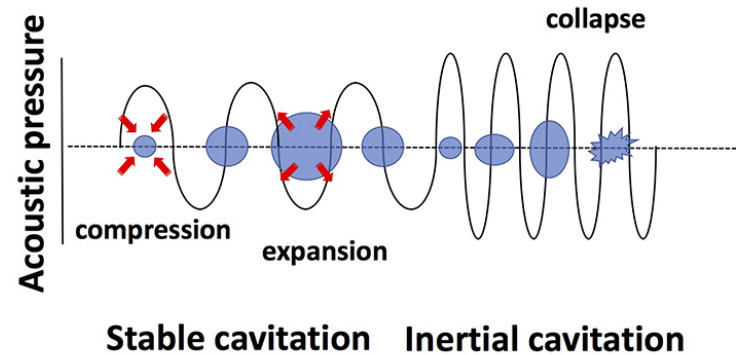
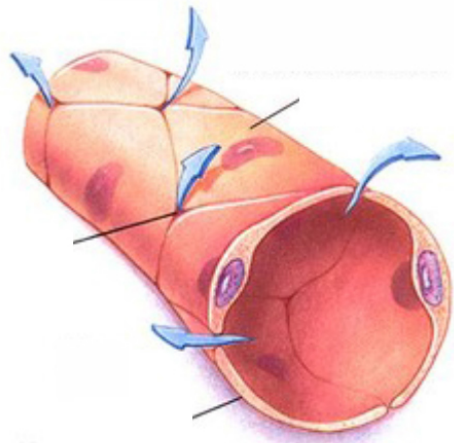
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# The Concept

## The Endothelial Barrier

*How to enhance endothelial layer permeability*

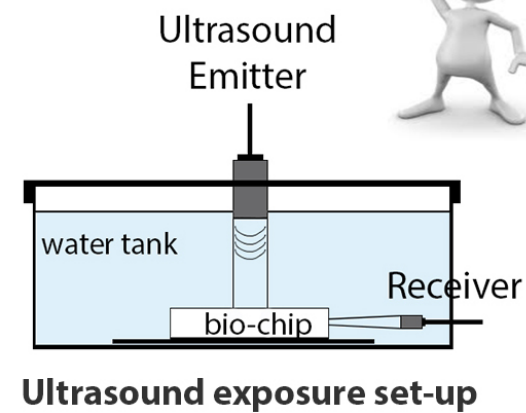


Microbubbles  
+  
Drugs

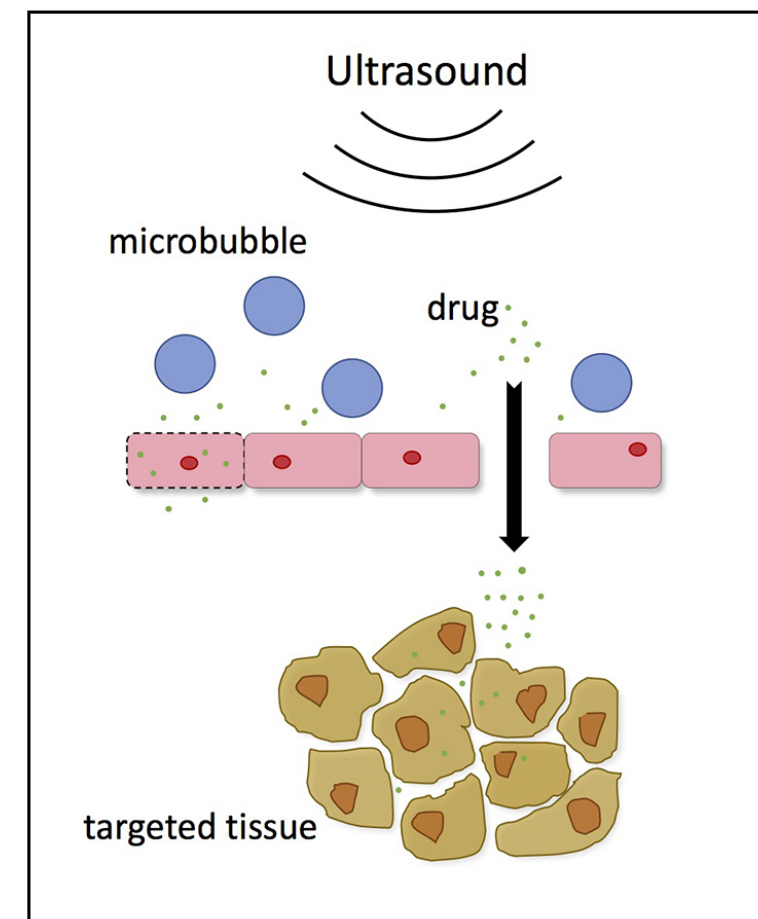
*In vivo approach*



*In vitro approach*

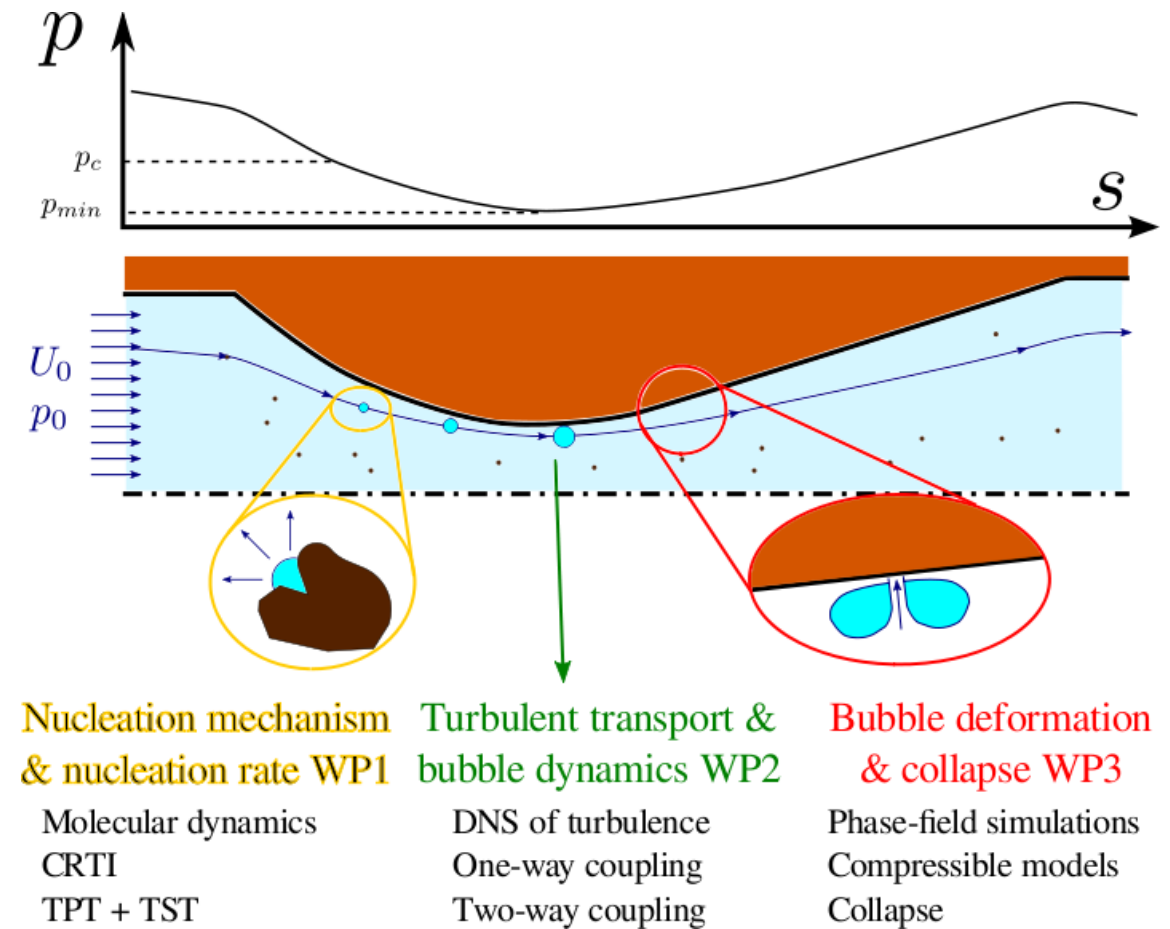


## Enhanced Drug Extravagation

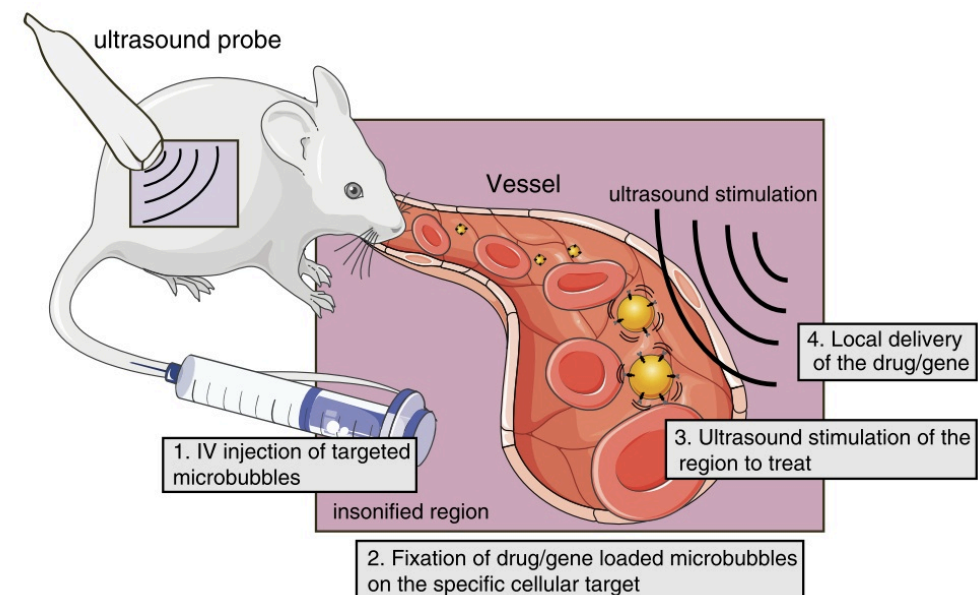


# Background

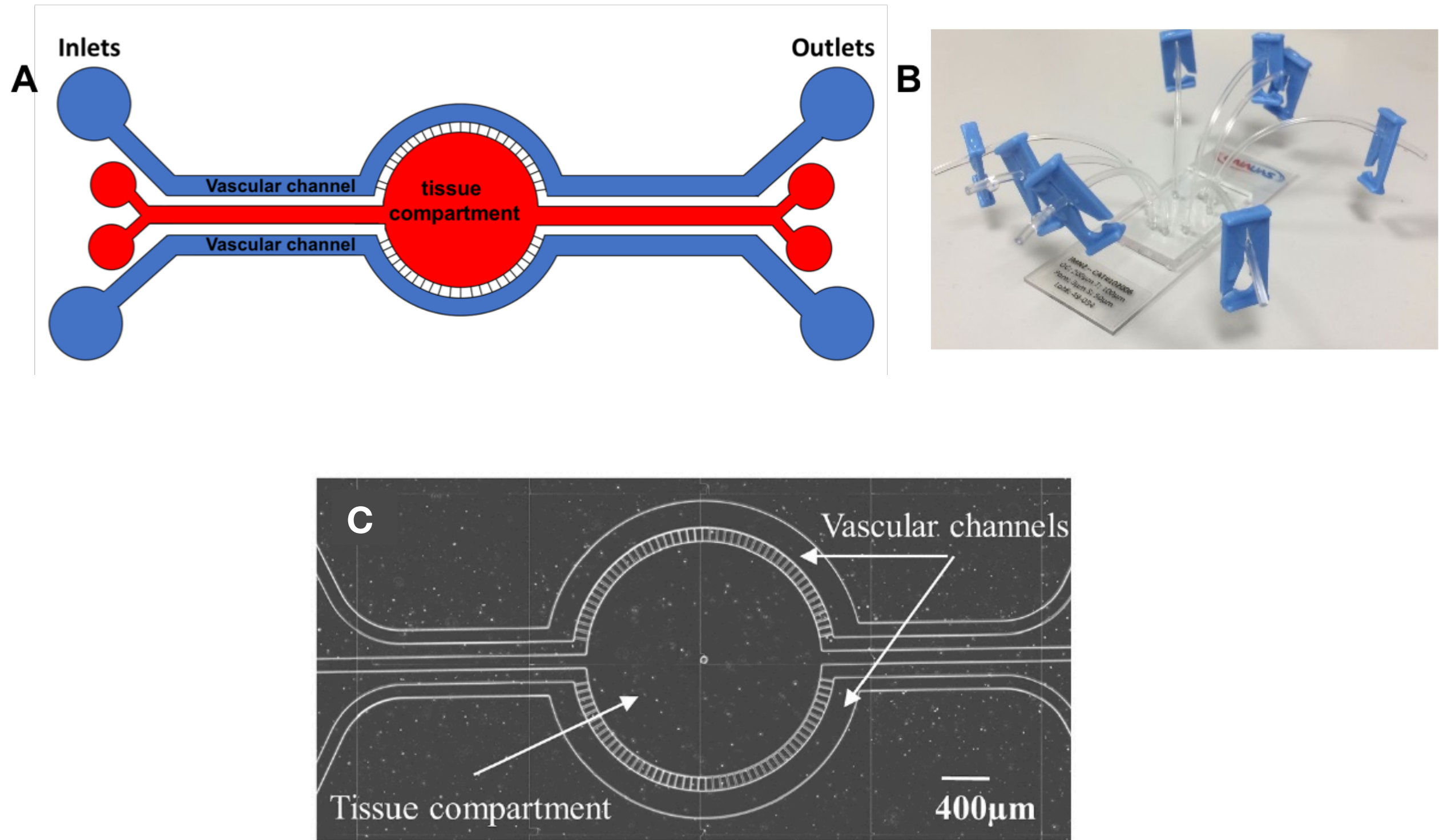
- ERC AdG 2013 (2014-2018)  
BIC, Cavitation across scales:  
following Bubbles  
from Inception to Collapse



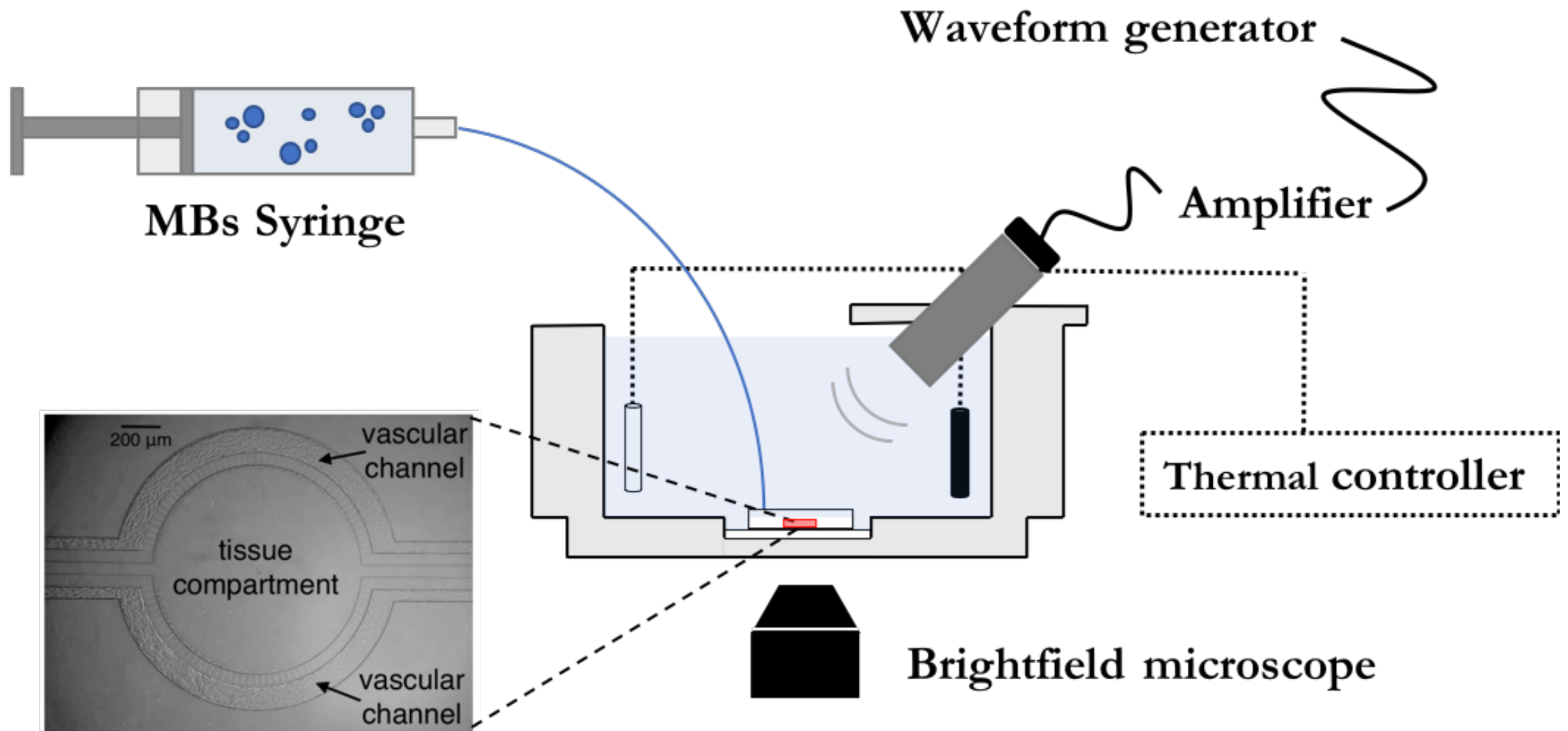
- Progetto Sapienza Award 2014,  
Nano & Microbubbles for Drug  
Delivery (60k€)



# Blood-Vessel-on-a-chip (INVICTUS)

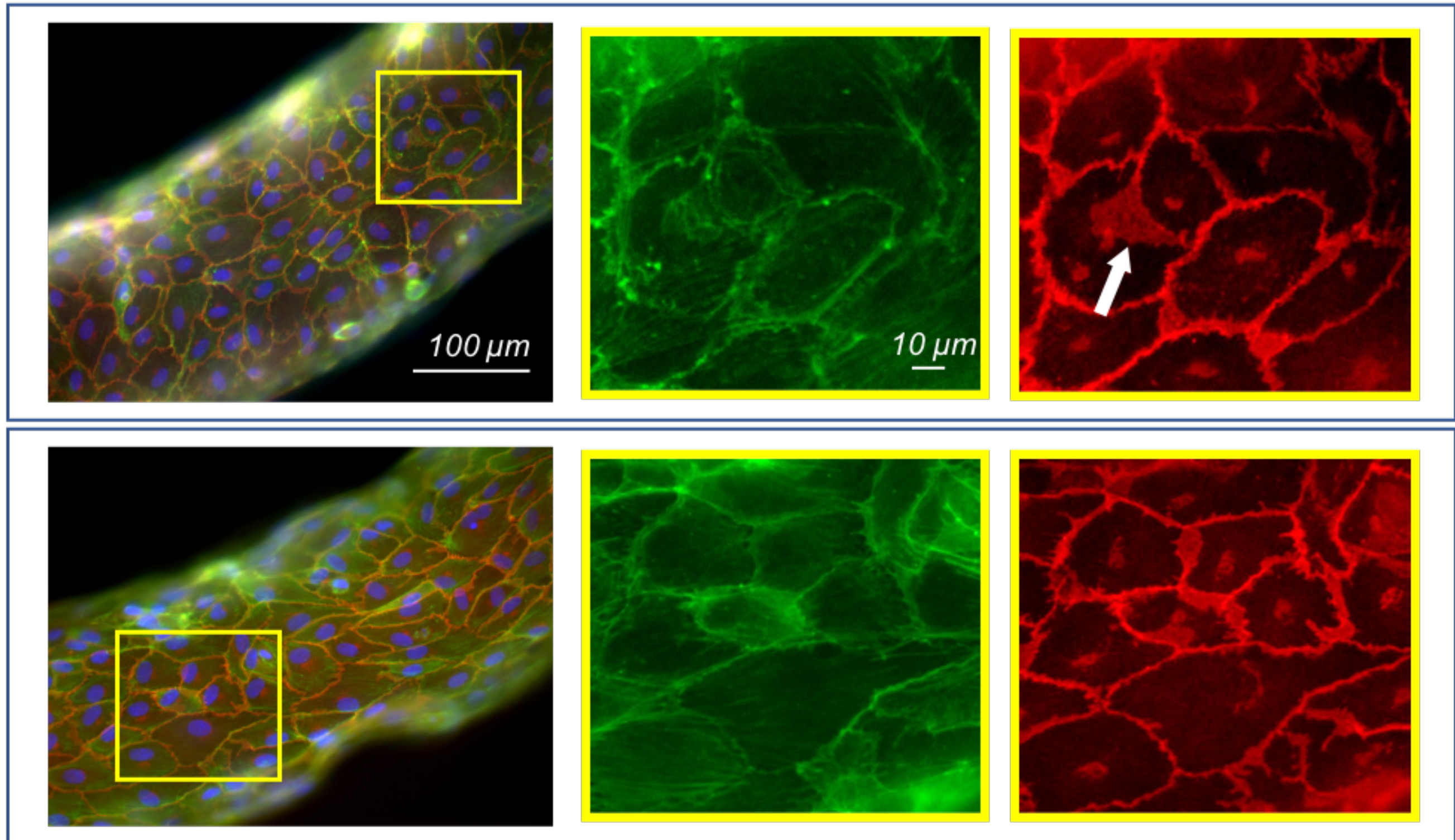


# Experimental Set-up





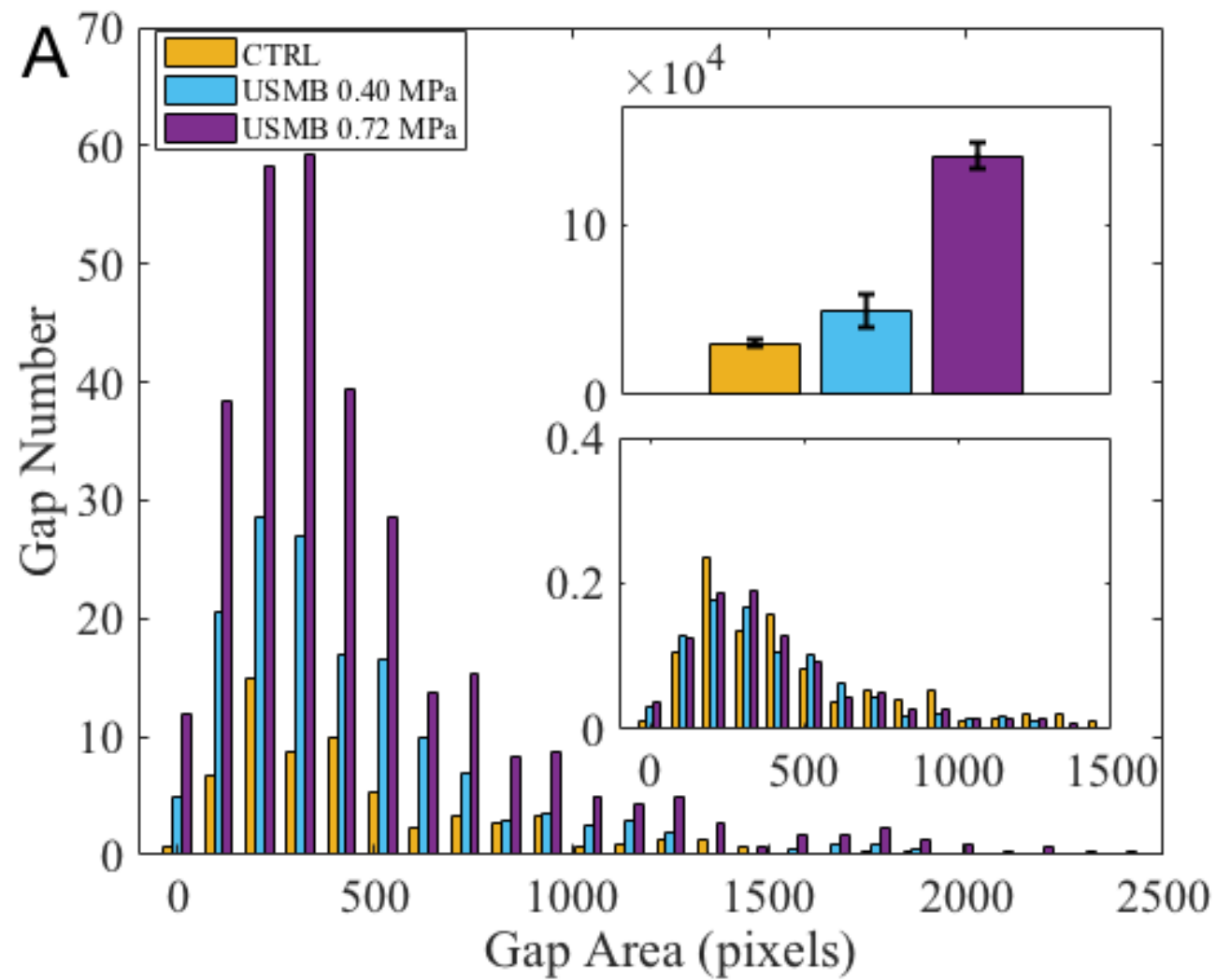
# Inter-endothelial Gaps



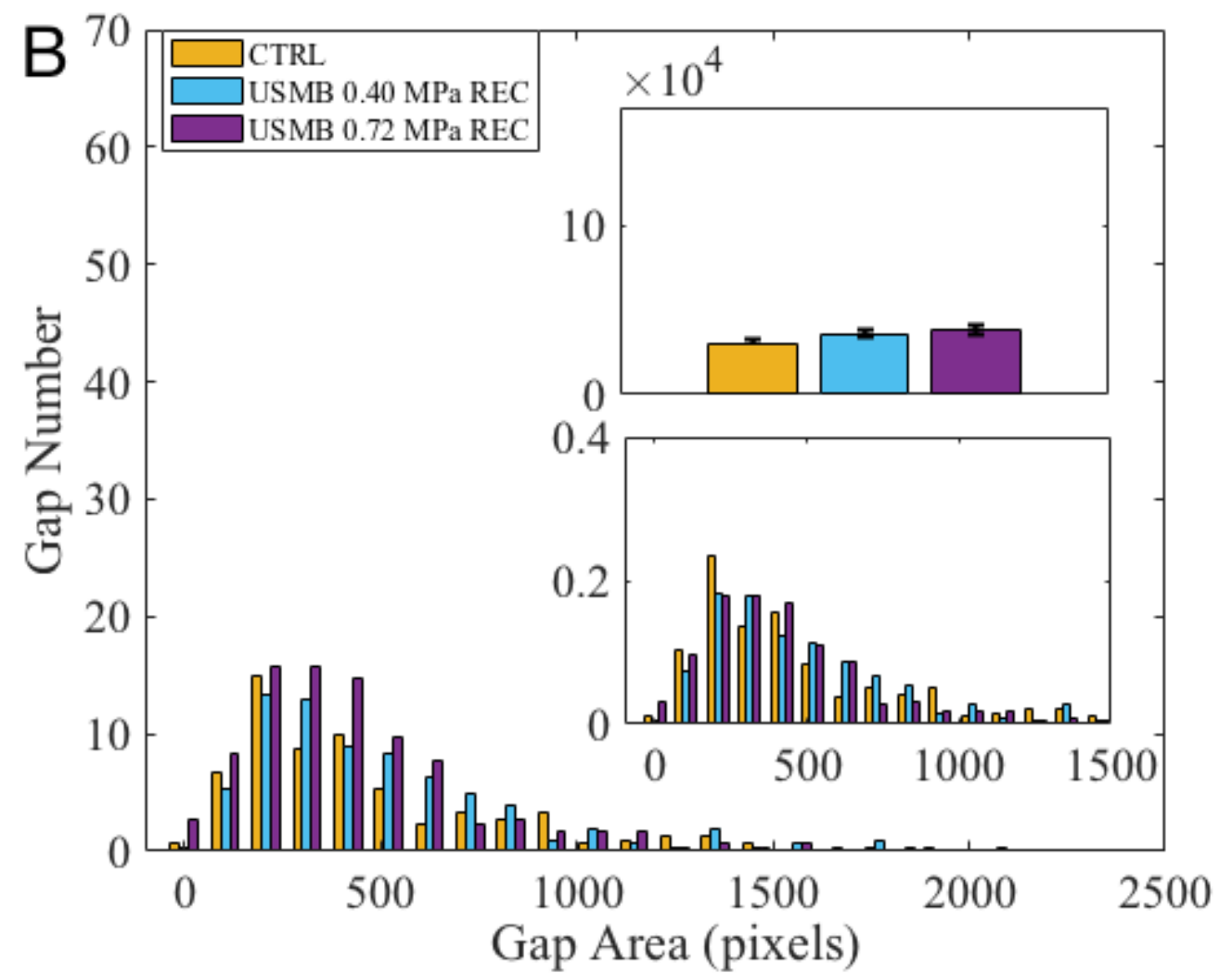


# Effect of Irradiation Pressure

Under Irradiation



Recovery After 45min



# Widening the Scientific Interests

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- Reversible Cavitation-Induced Junctional Opening in an Artificial Endothelial Layer, Small 2019.
- A Microfluidic Platform for Cavitation-Enhanced Drug Delivery, Micromachines 2021.
- The on-a-chip cross talk between cancer and immune system in the era of immunotherapy”, Lab on a Chip 2021.
- A T-Junction device allowing for two simultaneous orthogonal views: application to bubble formation and break-up, Microfluidics and Nanofluidics 2018.
- Perspectives on Cavitation Enhanced Endothelial Layer Permeability, Colloids and Interfaces B: biointerfaces 2018.
- Invited contribution on Cavitation Enhanced Drug Delivery, Pharmaceuticals, 2022.



# How to Sell It?

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- Ready-to-use platform for endothelial permeability studies of different drugs (pharmaceutical industry):
    - Reproduction of physiological conditions
    - Reduced use of animals in experimentation
    - Lower cost
  - Framework to develop drug delivery protocols (including cavitation-enhanced approaches)
- \* Challenge: Making a user friendly, stand-alone system

IRBM Pomezia



In Vitro Blood-Brain Barrier Model (BBB)

CL2NS@Sapienza (IIT)



**MicroFlu Lab**

# Follow-up

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- IIT - Brain-Blood Barrier
- Temple Philadelphia - Artificial Blood Vessel
- ISS - Dendritic Cell Mobility and Extravasation
- ISS - Reprogramming of patient fibroblasts into neurons



# Writing the Proposal and the Budget

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You know very well how to do it!

# External Support

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An external consultant was asked to take care of the following:

- Market Analysis and Technology Positioning
- Commercialization and Exploitation
- Intellectual Property Right and Freedom to Operate
- Potential Competitors
- Fundraising Strategies and Potential Partnerships

\* Discussion with Irene Giardina, as previous awardee, was extremely useful to plan this part



# Advisory Board

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A group of experts forming the Advisory Board will represent the standpoint of several stakeholders involved in the research on drug delivery.

A representative of the Ethic Committee of the host institution will be asked to participate the Board.

We already have letters expressing the interest of getting directly involved in the development of INVICTUS from IRBM, a worldwide company engaged in drug discovery and delivery, and CLNS, a research centre focused on developing technological innovation for neurodegenerative disorders, hereditary and nervous system disfunction.

# Ethical Issues

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## \* Ethical Issues may be formidable

They come in different forms, when humans and other animals are involved (you may imagine how complex the matter is from the number of pages to fill in the PoC form)

In my case, two problems arose:

1. We were using HUVECs (human umbilical vein endothelial cells) purchased by a company. Although the company provided all the needed documentation, the project run the risk of being stopped until further approval
2. Use of tissues from patients was initially (and unconsciously) envisaged. In agreement with the ERC officers, we eventually decided to drop that part.

\* Due presumably to my fault, I was unable to internal support to solve the issue.  
I only understood that an Ethical Committee exists and meets once every 6 months (‘)



# Final Comments on PoC

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## Positive aspects

- Opportunity for opening new (complementary) research lines
- Fostering young researchers in confining/interdisciplinary fields
- Getting in touch with companies

## A less positive aspect

- Emphasis on market placement may be misplaced: most often tech-transfer is difficult
  - i) Low TRL - often zero.
  - ii) Incomplete knowledge/understanding of leading technologies in the field
  - iii) Incomplete knowledge of the potential market/inability to identify the most appropriate application
  - iv) Difficulty in identifying funding mechanism
  - v) Researchers may not really desire to invest time/talent

Thank you for attending

Good Luck!