C4BIO : REPRODUCTIBILITÉ & CARACTÉRISATION DES TISSUS BIOLOGIQUES

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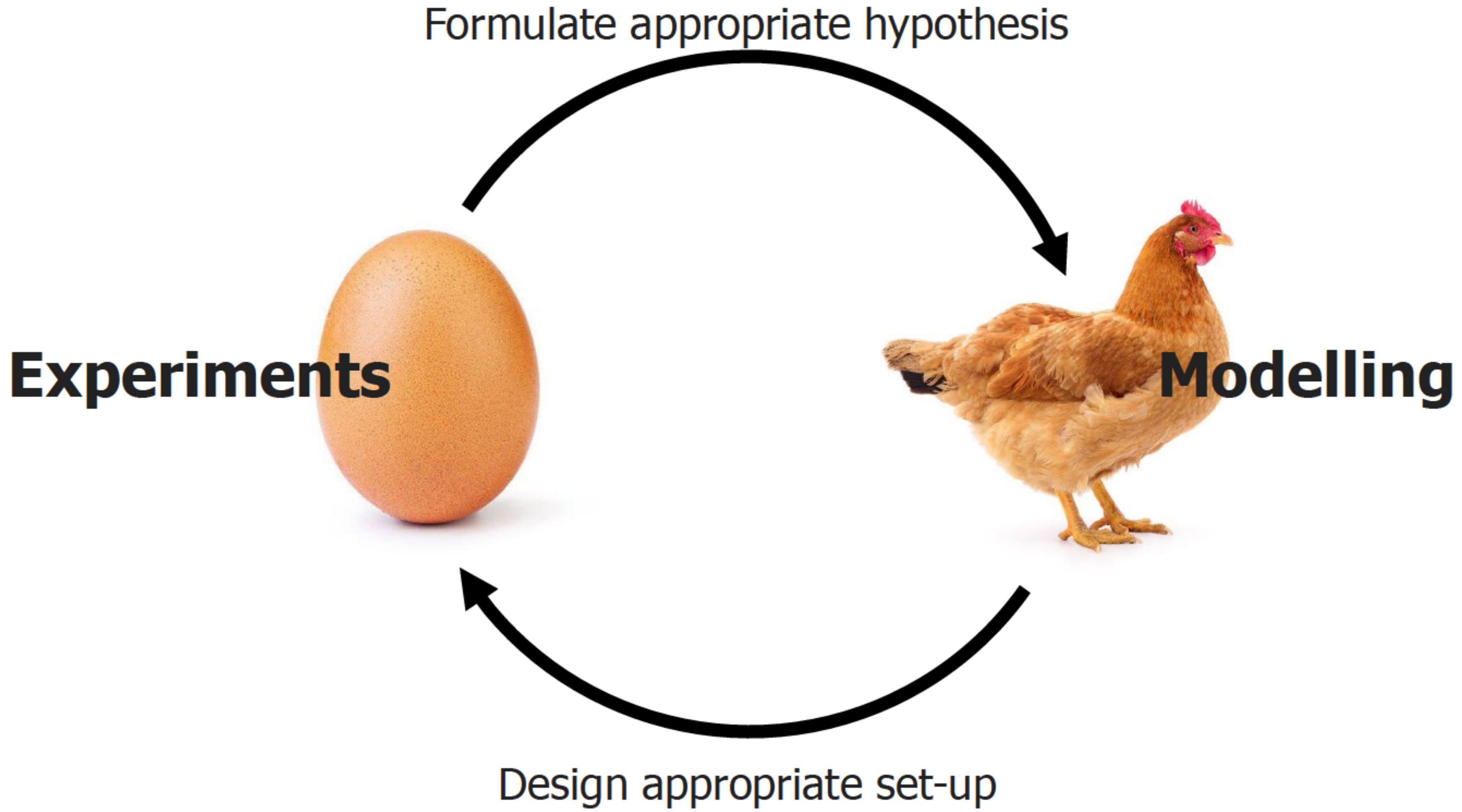
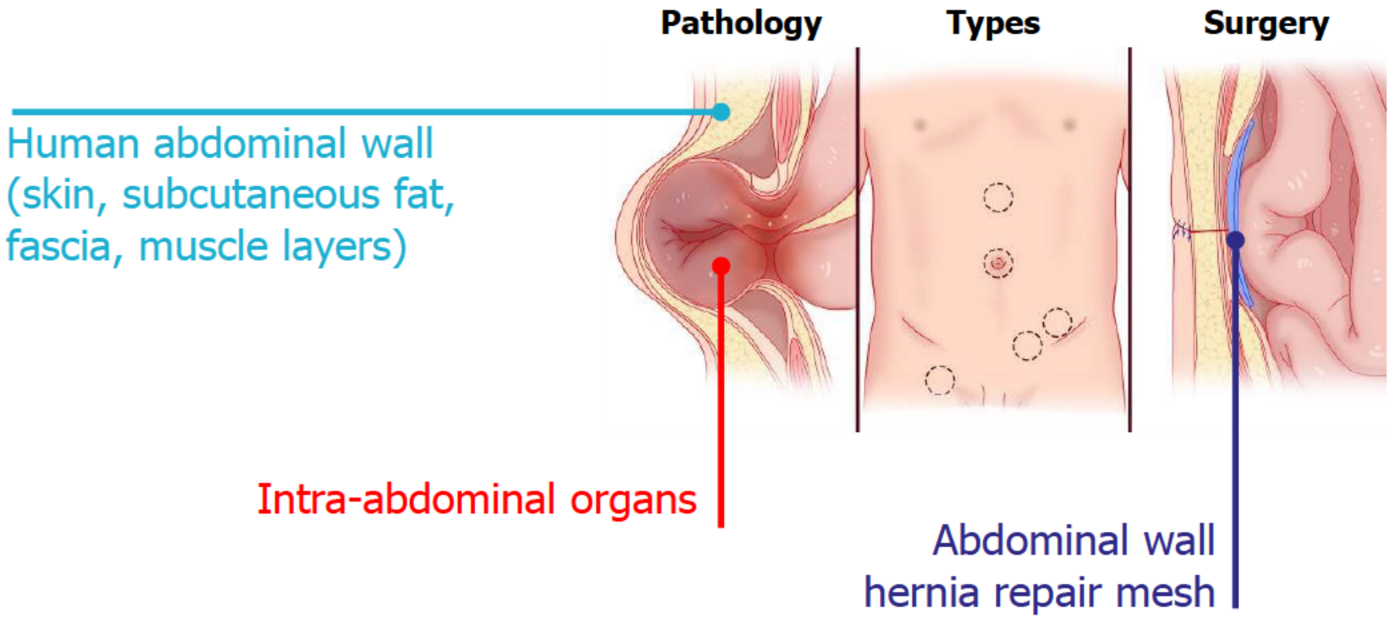
EXPERIMENTS FOR/FROM MODELLING?

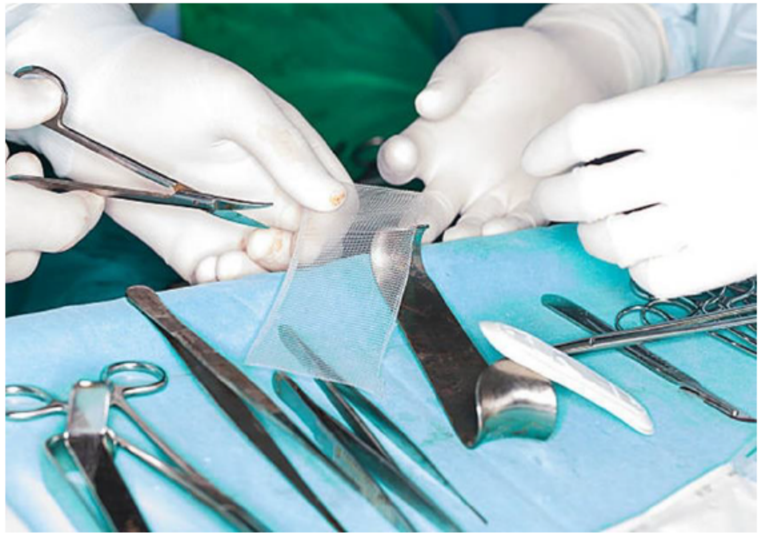


SURGICAL PROCEDURE TO REPAIR ABDOMINAL WALL HERNIA

+20 million hernias operated per annum globally
The 2nd pathology of consultation in general surgery



Mesh: 90% of the surgeries
- synthetic (absorbable, non-abs.),
- animal tissue (porcine or bovine)



Source: FDA

Saiding et al., 2023, Abdominal wall hernia repair: from prosthetic meshes to smart materials
Najm et al., 2023, A Review of Abdominal Meshes for Hernia Repair—Current Status and Emerging Solutions

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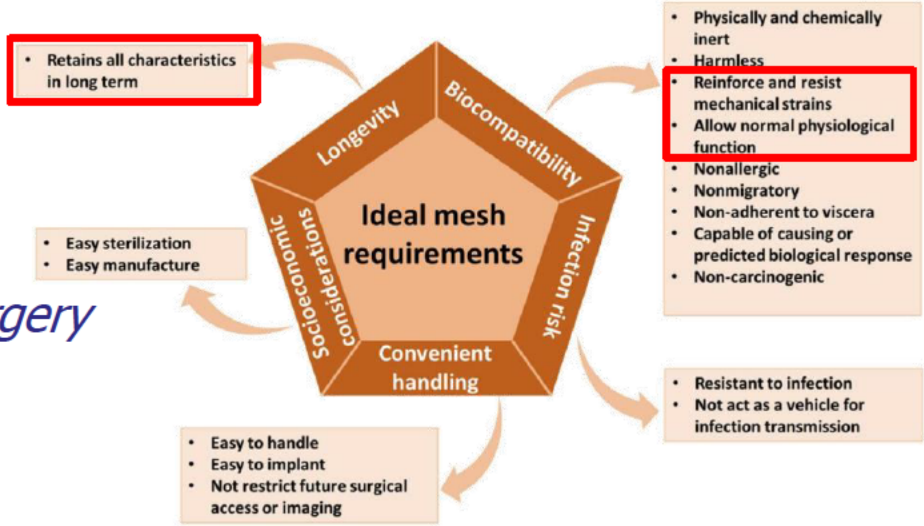
LONG TERM FOLLOW-UP

"Pain, infection, hernia recurrence, scar-like tissue that sticks tissues together (adhesion), obstruction, bleeding, mesh migration etc." (source: FDA)

Patients with a reoperation within 10 years of surgery: 1/5 in 2003, 1/6 in 2023

Underestimated: not all recurrences undergo reoperation

➔ **Outcomes have only marginally improved in 20 years**

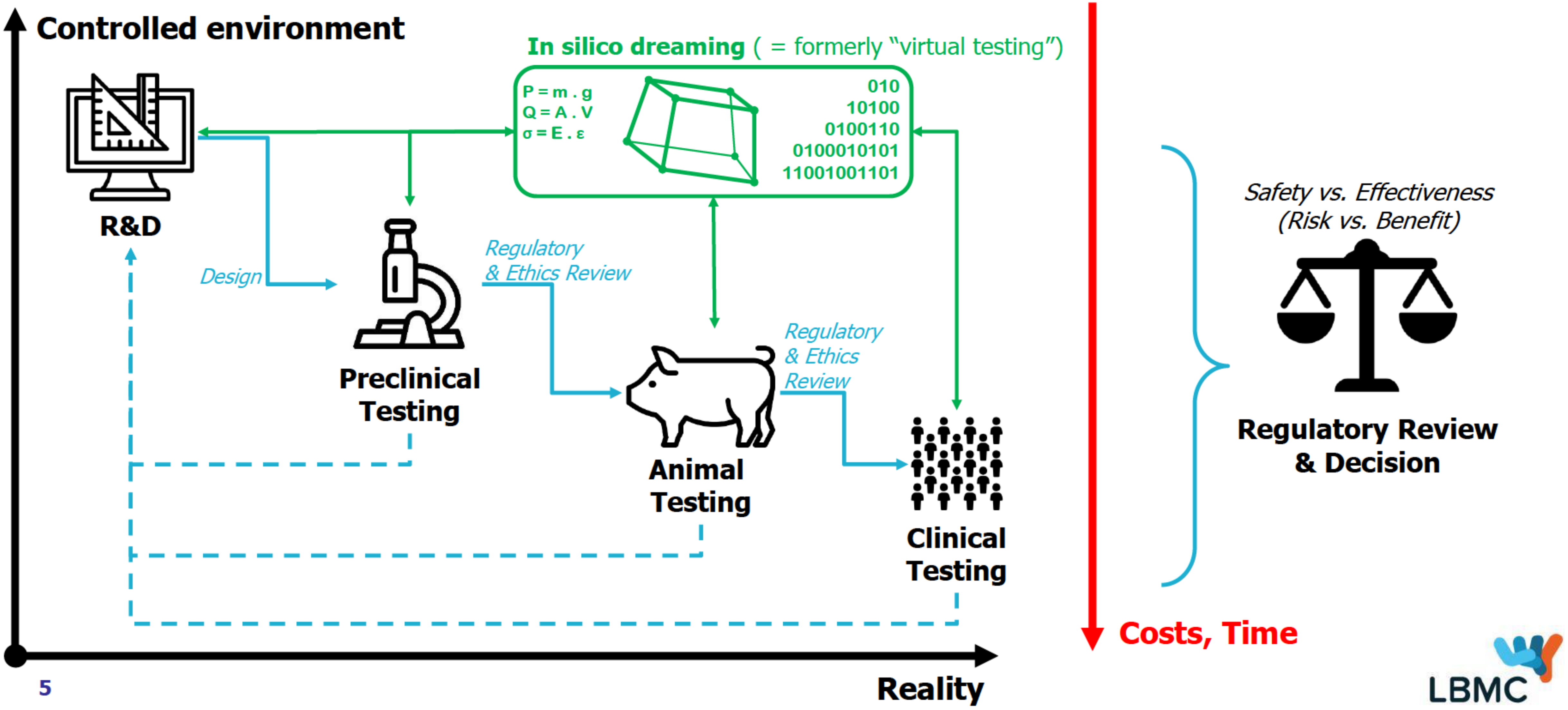


Research Topic on "Mesh-related complications" in *Frontiers in Surgery*

- Not all meshes are equal: ~~one unique ideal mesh~~
- Not all people are equal: ~~one unique mid patient~~

➔ **Considering both the patient-specific abdominal wall and the dedicated mesh repair**

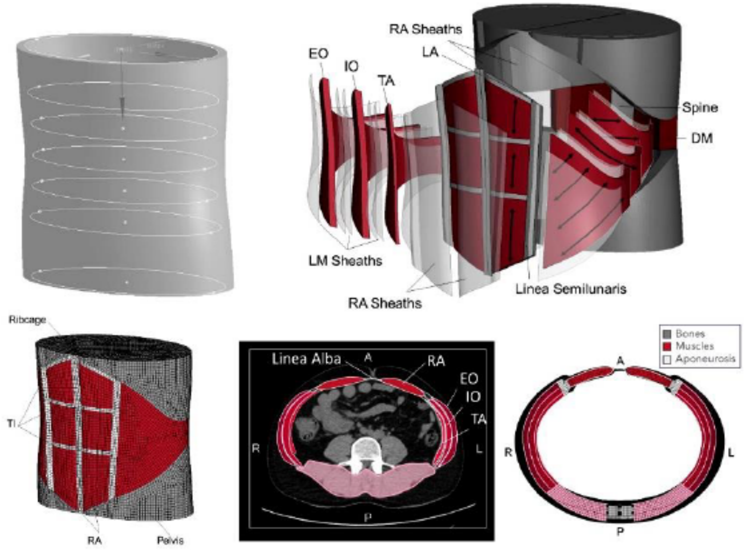
REGULATORY SCIENCE OF THE MEDICAL DEVICE INDUSTRY



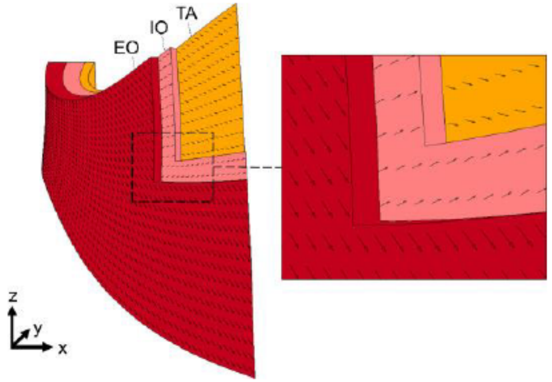
Podwojewski, 2012, Caractérisation biomécanique globale de la paroi abdominale saine, lésée et réparée : de l'ex vivo à l'in vivo
Jourdan et al., 2024, Numerical investigation of a finite element abdominal wall model during breathing and muscular contraction

MODELING HUMAN FOR MEDICAL DEVICES

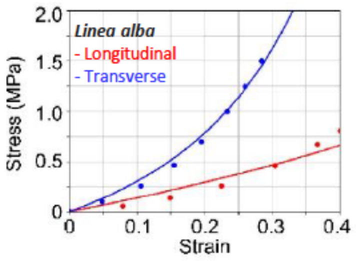
Abdominal wall FE model



Active muscle model

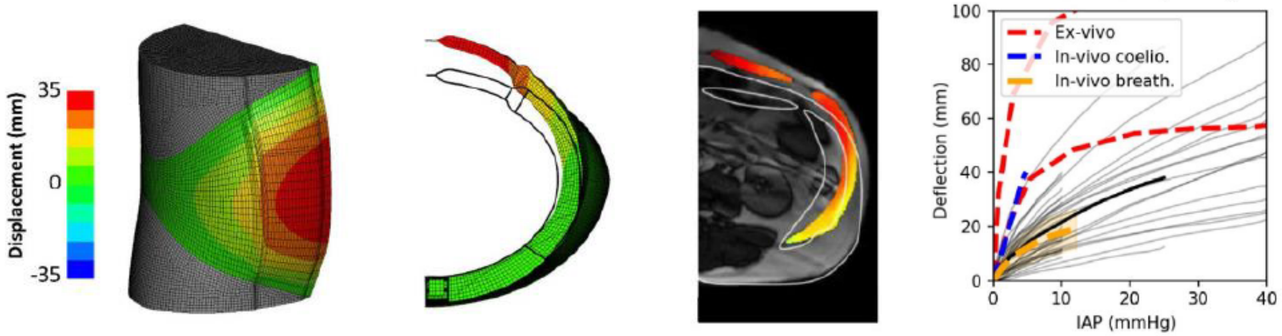


Material law fitting parameters (calibration against dedicated experiments)

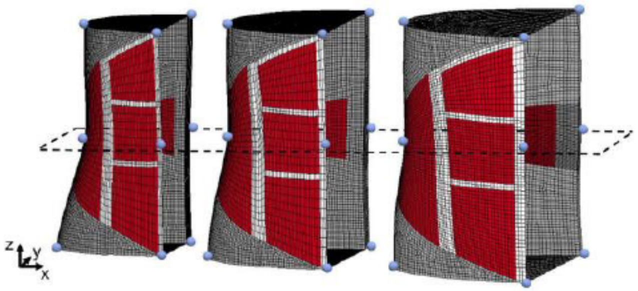


Connective tissues	Source	Mooney-Rivlin			
		C_1 (Pa)	C_2 (Pa)	C_3 (Pa)	C_4
Linea Alba	[28]	190,000	1001	280,000	4
Anterior Rectus Sheath		300,000	1001	245,000	6
Posterior Rectus Sheath		120,000	50,000	500,000	7.3
Linea Semilunaris	NA	1000	1001	1,000,000	6.0
Muscles (Passive)		Holzapfel-Gasser-Ogden			
		μ_1 (Pa)	α_1	k_{11} (Pa)	k_{21}
Rectus Abdominis	[48]	3000	5.5	45,000	0.01
External Oblique		4000	5.5	12,000	1.1
Internal Oblique		8000	4	15,000	0.01
Transversus Abdominis		6000	5	60,000	0.01

Simulated outcomes against experimental data (evaluation)

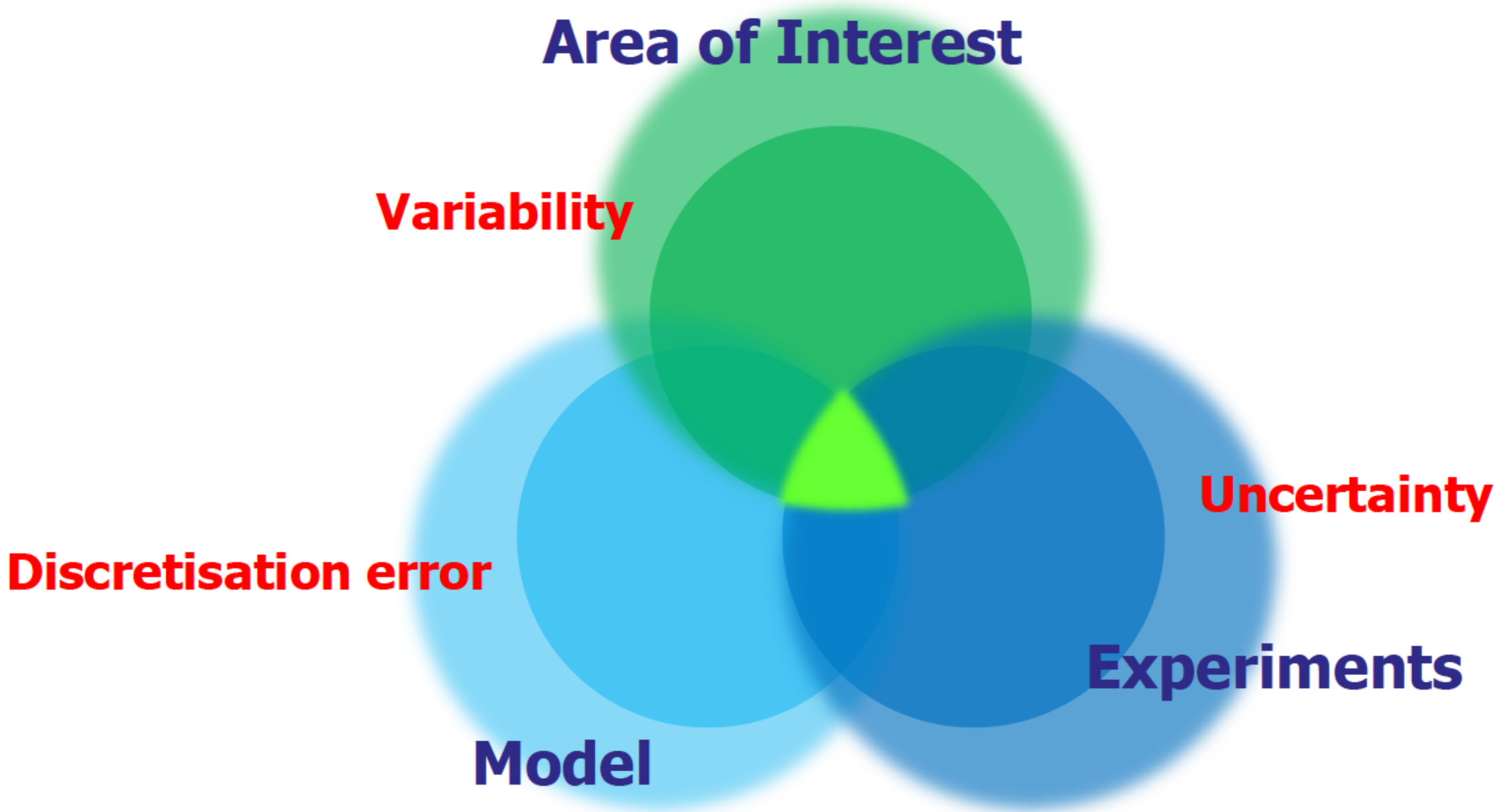


Various BMI (variability)



➔ +15 years of research efforts: ready for MD certification?

MODEL CREDIBILITY



→ **Verification & Validation (& Uncertainty Quantification) plans**

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MAJOR CHANGES IN STANDARDS FOR MEDICAL DEVICES

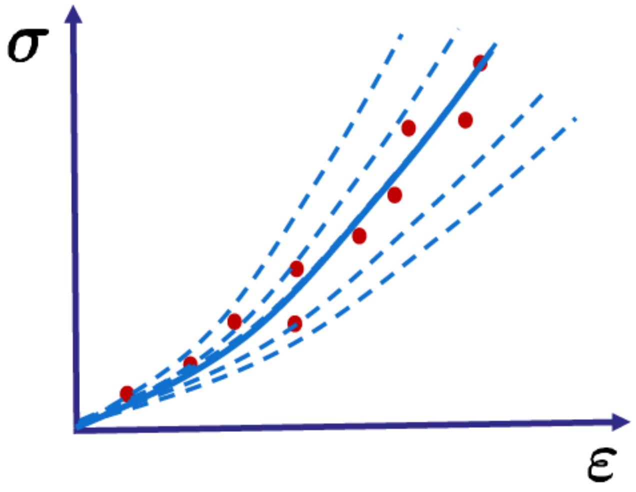
ASME Technical standard "**Assessing Credibility of Computational Modeling through Verification and Validation: Application to Medical Devices**", ASME VV-40, 2018.

FDA draft guidance "**Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions**", FDA-2021-D-0980, Dec 2021.

U.S. Food and Drug Administration

FDA's Model calibration **evidence:**

"**Comparison** of model results with the same **data used to calibrate model parameters**."



- **FDA:** how **credible** is the model?
- **Modellers:** how can we **trust** the data?
- **Experimenters:** better **quality** data?

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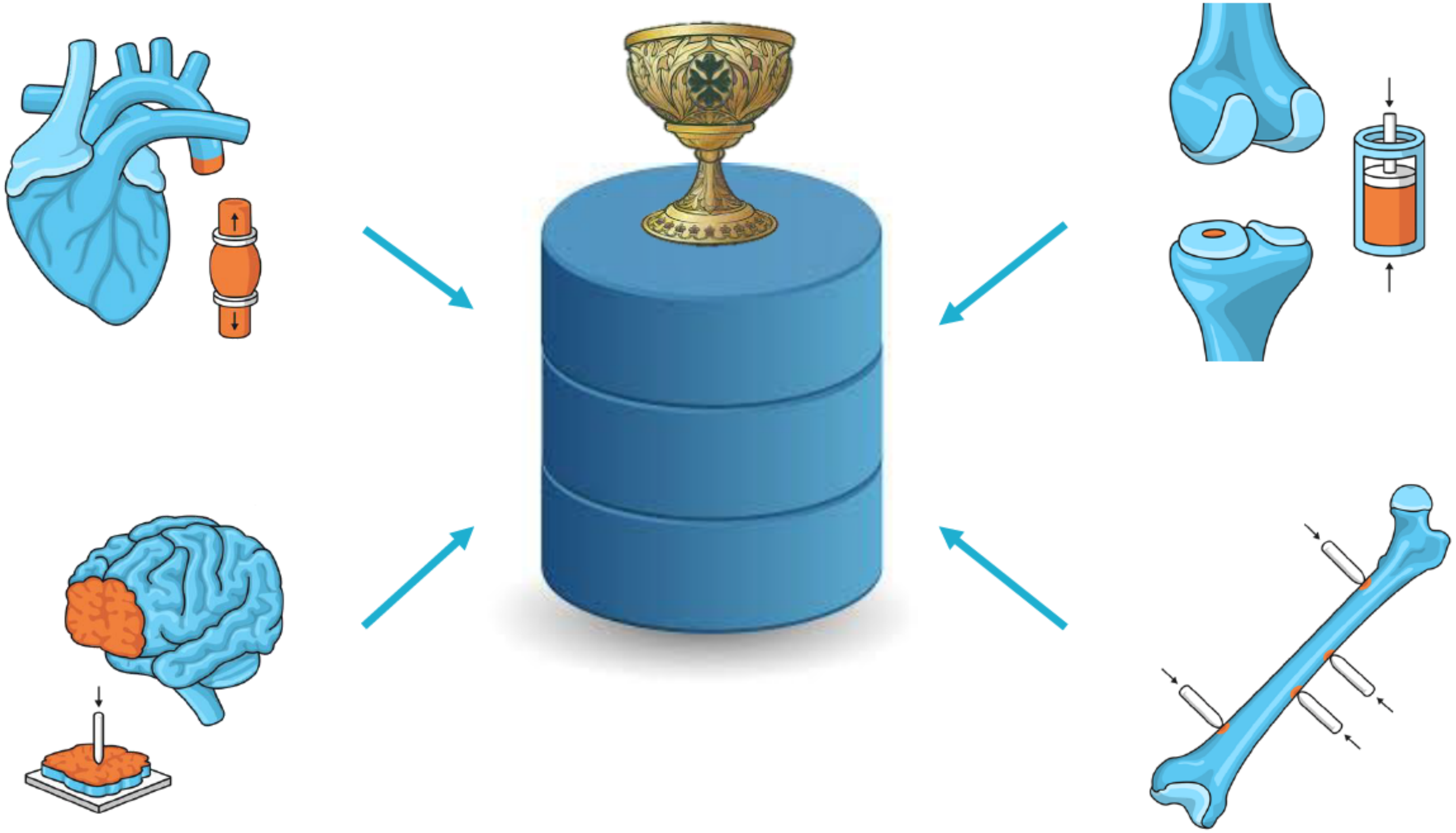
BUILDING A ‘CREDIBLE’ INTERNATIONAL DATABASE OF TISSUE PROPERTIES



Mechanical properties from mechanical tests available for almost all tissues

Strength of Biological Materials. Hiroshi Yamada, 1970.

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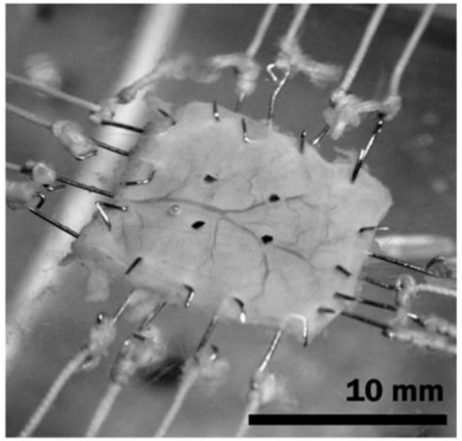
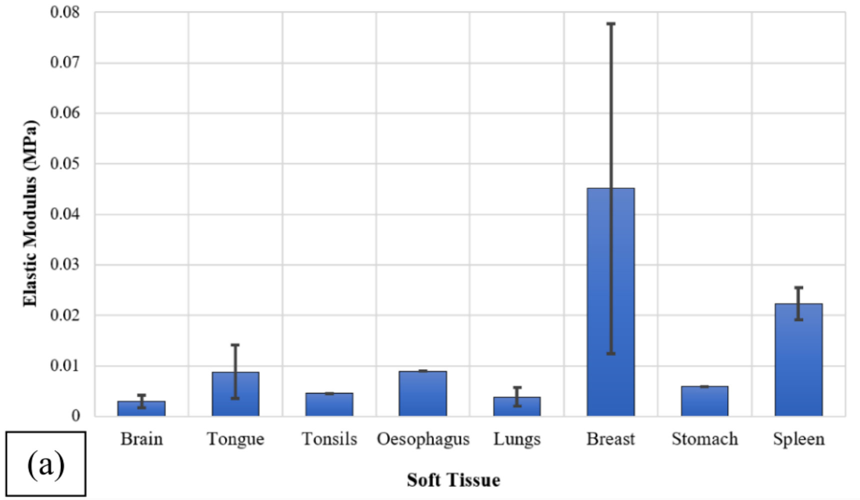
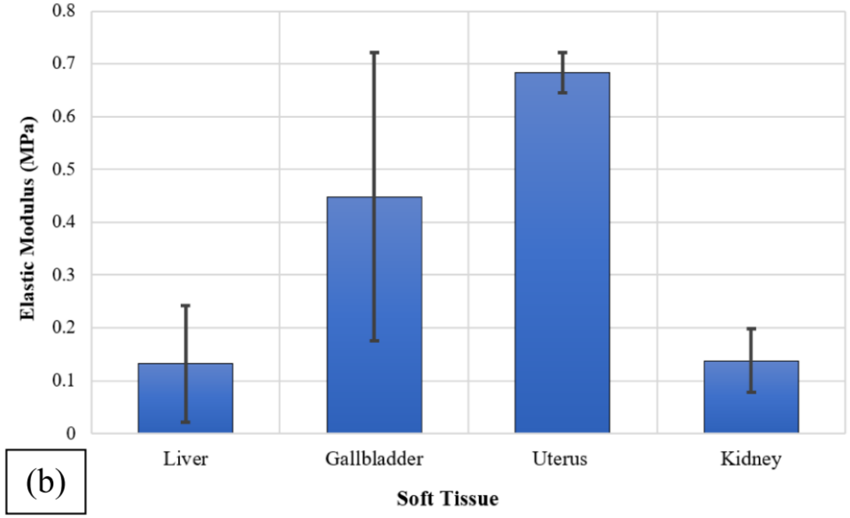
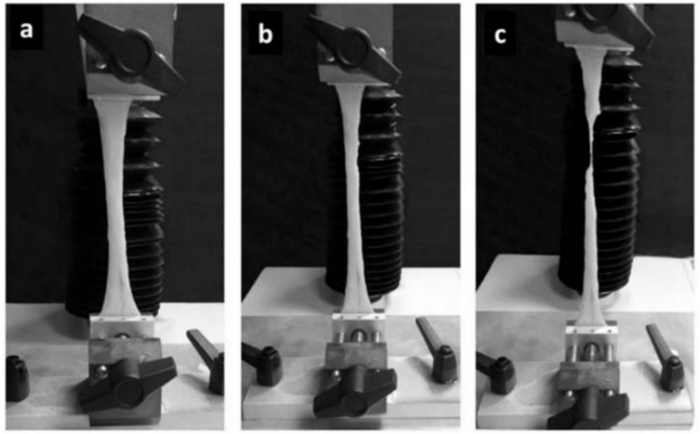
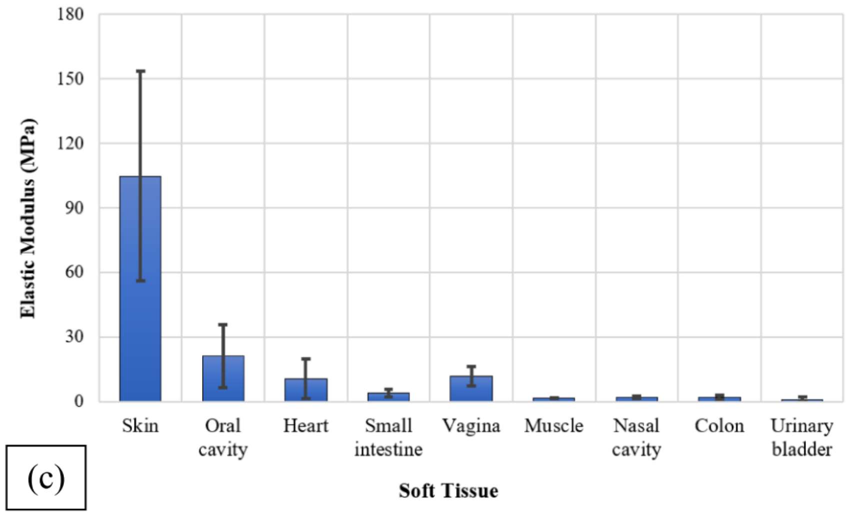
MECHANICAL PROPERTIES OF WHOLE-BODY SOFT HUMAN TISSUES: A REVIEW. *SINGH AND CHANDA, 2021.*











"No one believes in simulation, except those who do them

Everyone believes in experiments, except those who do them"

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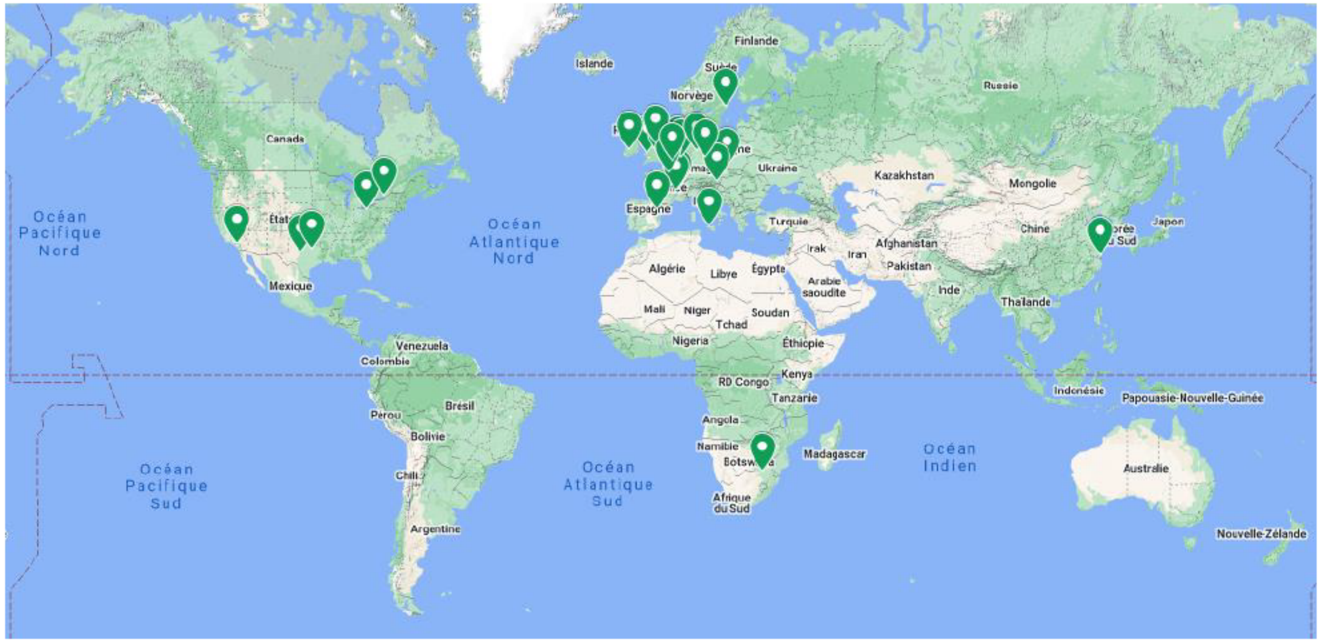
2020: A CONSORTIUM OF ACADEMICS AND INDUSTRIALS

VPH Institute
Building the Virtual Physiological Human

Avicenna Alliance
Association for Predictive Medicine

https://c4bio.eu/

FIBER KU LEUVEN



27 academics + industrials + standards bodies (ISO & ASME)

Johnson & Johnson | stryker | Ansys | Boston Scientific | Medtronic | Leartiker POLYMERS TECHNOLOGY | materialise

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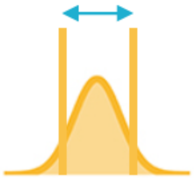
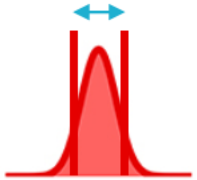
C4BIO: COMMUNITY CHALLENGE TOWARDS CONSENSUS ON CHARACTERIZATION OF BIOLOGICAL TISSUE

1. **Quantify the variability**
   among different research groups:
   testing using participants' own methodology



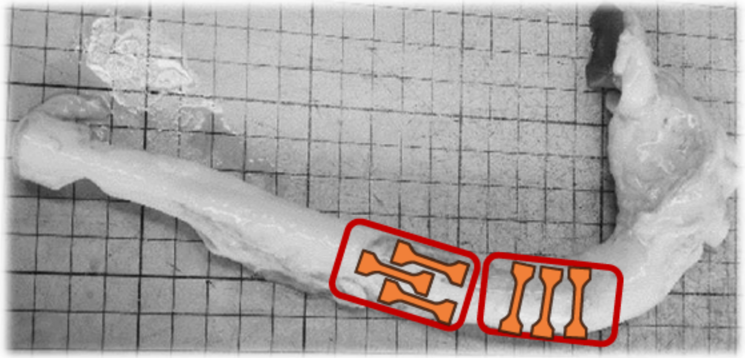
2. **Standardize the approach**
   by defining consensus methodology
   between participants

3. **Evaluate standardized approach**
   by retesting using consensus methodology



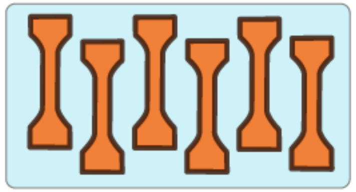
4. **Make the outcome publicly available**
   results & consensus methodology

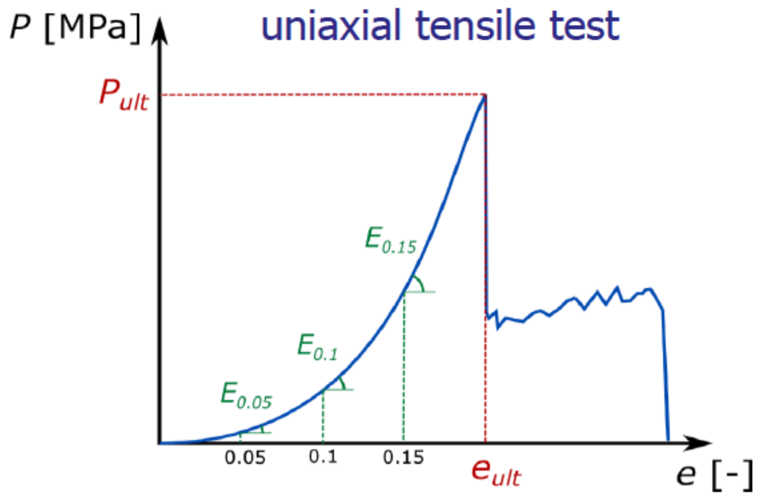
➢ **Initial focus:** mechanical properties of the aorta



materialise

Leartiker POLYMERS TECHNOLOGY





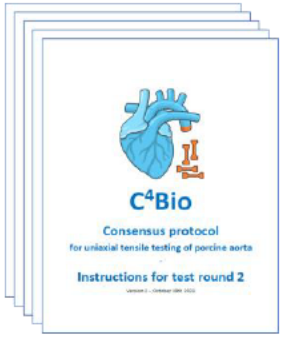
ROUND 1: PILOT CAMPAIGN

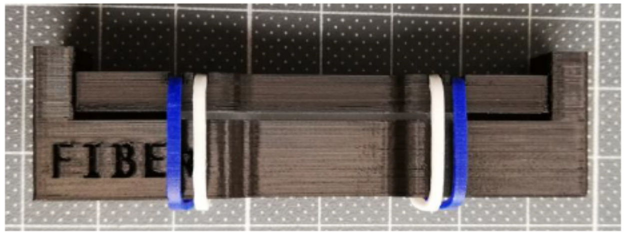
Maximal force
- Biological: 2N - 35N
- Synthetic: 0,5N - 10N

Maximal strain
- Biological: 30% - 140%
- Synthetic: 70% - 2000%

- Wide range of protocols (from the set-up to the post-processing)
- Large variability on synthetic samples' outcomes
- Larger variability for biological samples
- Results very sensitive to geometrical uncertainty (if width <3,8mm)

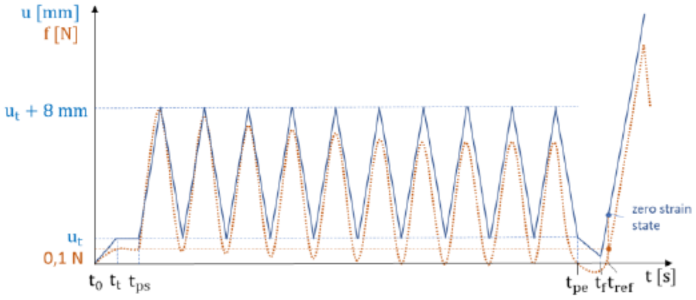
ROUND 2: TOWARDS A CONSENSUS PROTOCOL





Width and thickness: digital measurement

+ DIC or marker tracking



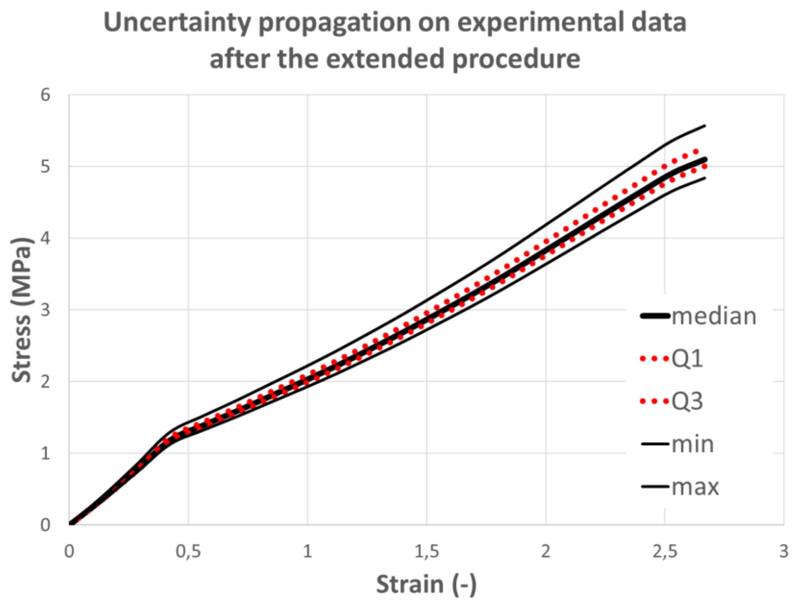
➔ Still a variability in the dimensions of the samples

- Image quality
- Human errors
- Image interpretation

ROUND 2: MECHANICAL BEHAVIOR

➔ Still a variability in the mechanical behavior between teams

ROUND 1 VS. ROUND 2



- Less outliers in Round 2
- Variability decreasing for the area, the strain energy, the inter-groups results.
- The uncertainty related to the sample's dimensions does not explain the variability
- **Source of discrepancy: understanding and respecting guidelines!**

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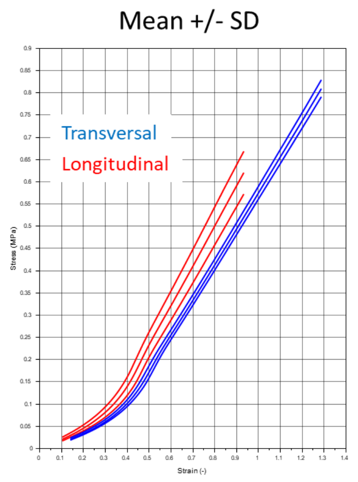
ROUND 3: ON-GOING



- ✓ Identification of a synthetic material that mimics soft tissue mechanical behavior
- ✓ Automating the measurement of dimensions (image processing)
- ✓ Exchanges between teams to assist during experiments.
- Dedicated experiments: 2D vs. 3D DIC, initial pre-strain etc.
- Variability analysis based on modelling (analytics and FEM)
- Online app. including a verification of the protocol when uploading data

What we learnt:

- Trust no one: *errare humanum est*
- Perform yourself the experiments you have designed,
- At first, use your own experimental data for your model to understand what you have missed.

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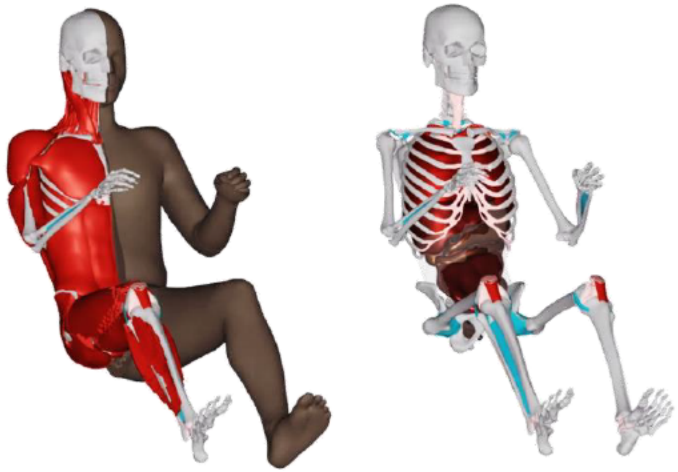
« ET POURTANT, ELLE TOURNE ! »

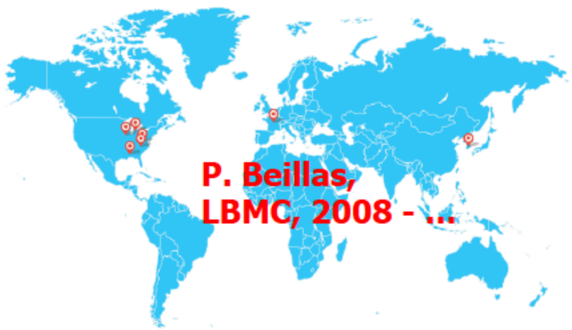
GHBMC
Global Human Body Models Consortium

Uncertainty about materials not always a barrier for modelling:
it will depend on the level of observation!



GHBMC M50-O https://www.elemance.com/

HONDA NISSAN gm HYUNDAI Renault Group STELLANTIS



Commercial FEM of the whole human body for industries

(automotive, sports, aerospace, healthcare, military…)

100ms of simulation → ~10h of computation using 48 cores

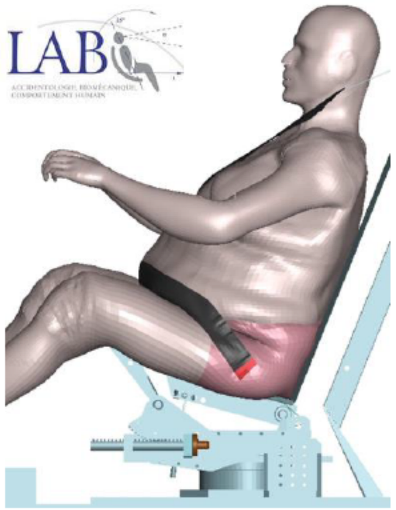
+200 scenarios of validation regarding experimental data

Abdomen: +20 full body setups, +50 on isolated organs

✓ **Captures most existing biomechanical knowledge of human impact response**

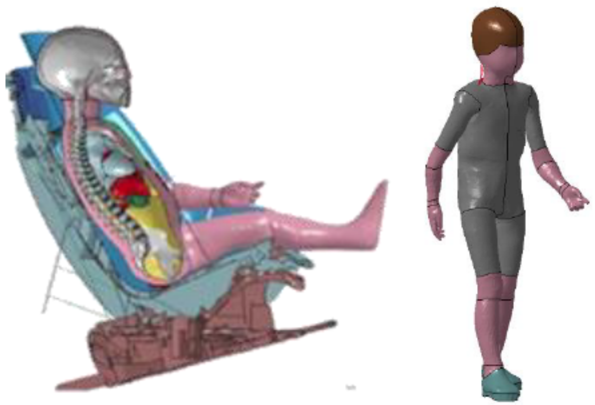
→ **+ 15 years of financial/research efforts coupling both industrials and academics**

WHAT IS A CREDIBLE FE MODEL FOR INJURY ASSESSMENT?



GHBMC: widely accepted by the community

- Continuous improvement and updates (v6.1), several solvers ➔ **cover current needs**
- PIPER: an open-source **framework for posing and personalizing models**
- Strong Verification plan, built by the users ➔ **runnability**
- Strong Validation plan with dedicated experiments, built with the users ➔ **credibility**



Opensource alternatives to fill a gap (provided with validation plans ➔ **reproducibility**):

- VIVA+ (LGPL v3) for a simplified representation (in progress), PIPER Child (GPLv3)

➔ A **coordinated approach** between **experiments and modelling**, **developers and users** (i.e. industrials)

CONCLUSION

Experimental data from biological tissue:

- a requirement driven by the normative Medical Device aspects
- a need of technical standards / guidelines to reduce the inter-operator uncertainty and improve the credibility
- C4Bio: a collective international effort based on a open Grand Challenge involving both academics and industrials

But credible experimental data are not enough to make a model credible

- An integrated approach to design both appropriate experiments and modelling
- Enough information shared to simulate experiments: useful for calibration, evaluation, validation

Industrials are focused on products, with a common need for human modelling: common efforts

Experiments are not cutting-edge science, but are still crucial for modelling, and require funding!

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VPH Institute
Building the Virtual Physiological Human

Avicenna Alliance
Association for Predictive Medicine

Thank you for your attention

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