Generation of data and related technologies: sensing, OoC, microfluidic collectors, ….

Adrian Ionescu (EPFL)

EDITH

Outline

- Data generators in Digital Twins Roadmaps
- CfT: 1st International Synposium on Digital Twins
- Examples of sensing and OoC technologies in Digipredict FET proactive project
- Biomarkers in biofluids: the interstitial fluid (ISF) use case
- Future development trends

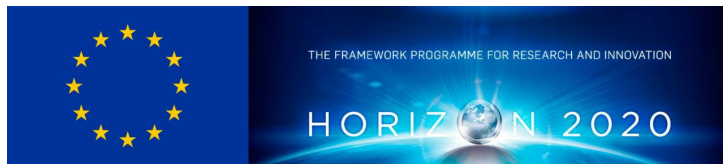Ecosystem for Digital Twins in Healthcare

Data generators in DTs Roadmaps

Joint action of FET Proactive Projects, requested by the EiC:

- DIGIPREDICT
- Neurotwin
- OPTOMICS
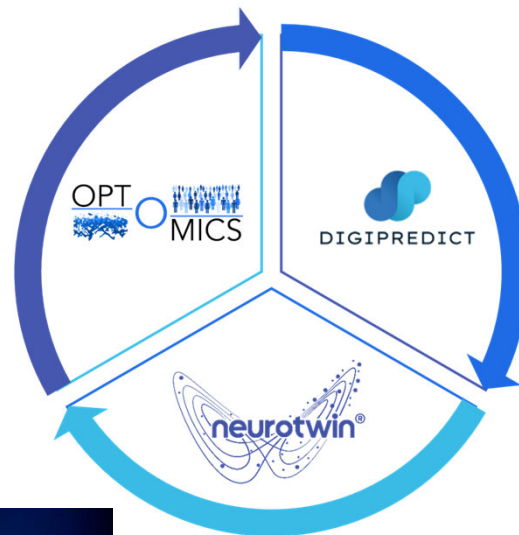
- Timely → Unify Digital Healthcare in Europe
- Expected benefits
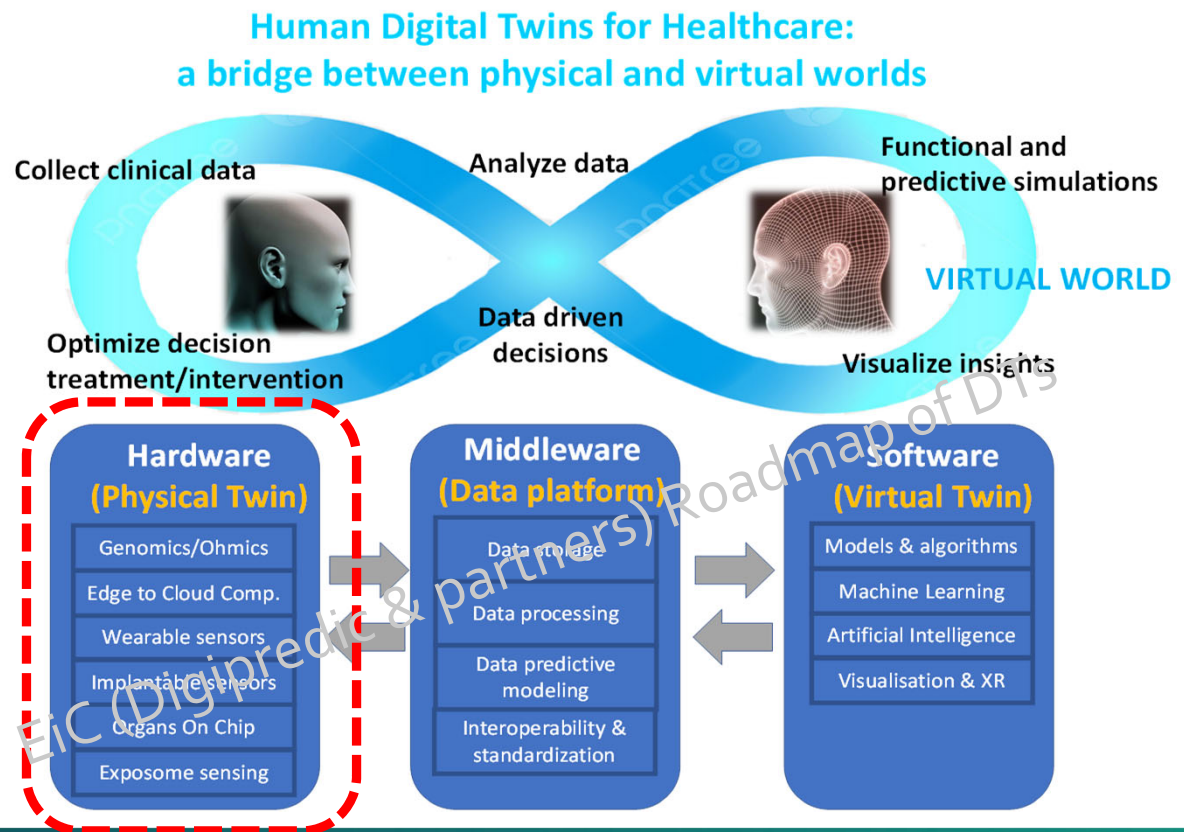- Impacts
- Ethical Considerations

RESPONSE TO HEALTHCARE NEEDS

Proactive Care	Reactive Care
✓ Reduce/remove disease risk	✚ Screening for disease
✓ Strong lifestyle execution	✚ Less lifestyle execution
✓ Decreased cost	✚ Increased cost
✓ Pre-disease intervention	✚ Post-disease treatment
✓ Deterrent, precautionary	✚ Remedial, counteractive
✓ Preventive, protective	✚ Palliative, urgent care

THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION

HORIZON 2020

Ecosystem for Digital Twins in Healthcare

EUROoCS 8/11/2023

EiC DT Roadmap to be released in April 2024

Key components to build DTs for healthcare

- Data
- Models
- Infrastructure
- Clinical settings and validations
- Regulatory and ethics framework
- Healthcare economic models and sustainability

Human Digital Twins for Healthcare: a bridge between physical and virtual worlds

Collect clinical data

Analyze data

Functional and predictive simulations

VIRTUAL WORLD

Optimize decision treatment/intervention

Data driven decisions

Visualize insights

Hardware (Physical Twin)
- Genomics/Ohmics
- Edge to Cloud Comp.
- Wearable sensors
- Implantable sensors
- Organs On Chip
- Exposome sensing

Middleware (Data platform)
- Data storage
- Data processing
- Data predictive modeling
- Interoperability & standardization

Software (Virtual Twin)
- Models & algorithms
- Machine Learning
- Artificial Intelligence
- Visualisation & XR

EiC (Digipredic & partners) Roadmap of DTs

Implementation of an Inclusive Roadmap

https://digitaltwin4health2024.eu/

EDITH leaders and partners involved/invited.

Digital Twins are making possible a revolution in human model development by leveraging data from multi-omics analyses, medical and imaging data, environmental and life style big data that are continuously updated by a multitude of biosensors at an unprecedented scale. With these complex data sets, first of their kind(s) Human Digital Twins can be personalized and used to prevent and cure each one's own disease(s). The Symposium is calling for contributions across the following scientific, translational and policy-making pillars:

- Emerging technologies for Digital Twins
- Designing and building data and models repositories
- Development, testing and implementation of IT platform architectures combining computational advances, cybersecurity, cloud services and edge infrastructure
- Clinical Translation – Industrial Uptake, including standardization and interoperability
- Ethical considerations and Societal Adoption
- Transformational Vision – Policy Creation and Implementation towards Proactive Healthcare

World-class research and innovation will be presented at topic-oriented sessions and problem-driven workshops. High quality abstracts from enthusiastic students and young scientists will be presented in a specially designed, interactive poster session. As the Symposium's central activity, a specially designated forum with high level European Commission and European Parliament representation will provide the floor for productive dialogue and policy making.

The Symposium envisions contributions to Digital Twins Roadmaps towards exploitation of most technologies to realize, validate and use such personalized Human Digital Twins in advanced clinical setups.

Chairs: Andreani D. Odysseos (EPOS-Iasis, Cyprus) and Adrian Ionescu (EPFL,

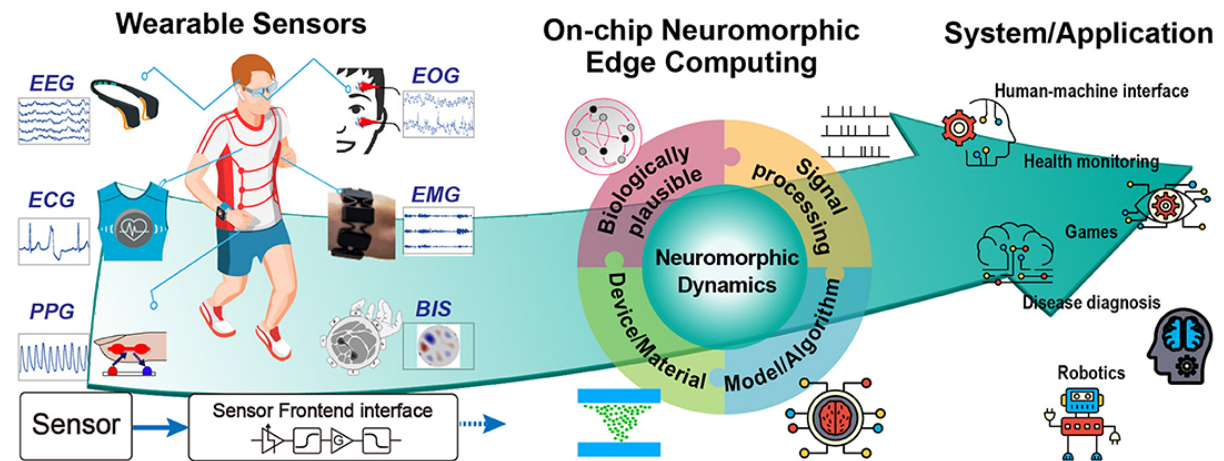# Edge technologies for data collection in Digital Twins

- **Requirements**
  - Real-time
  - Energy efficient
  - Physical footprint
  - Robustness
  - Security and privacy
- **Functions**
  - Sense
  - Extract
  - Classify
  - Reason and decide
  - Act
- **How? Think future platforms:**
  - CPU &digital accelerators
  - In-memory
  - In-sensor

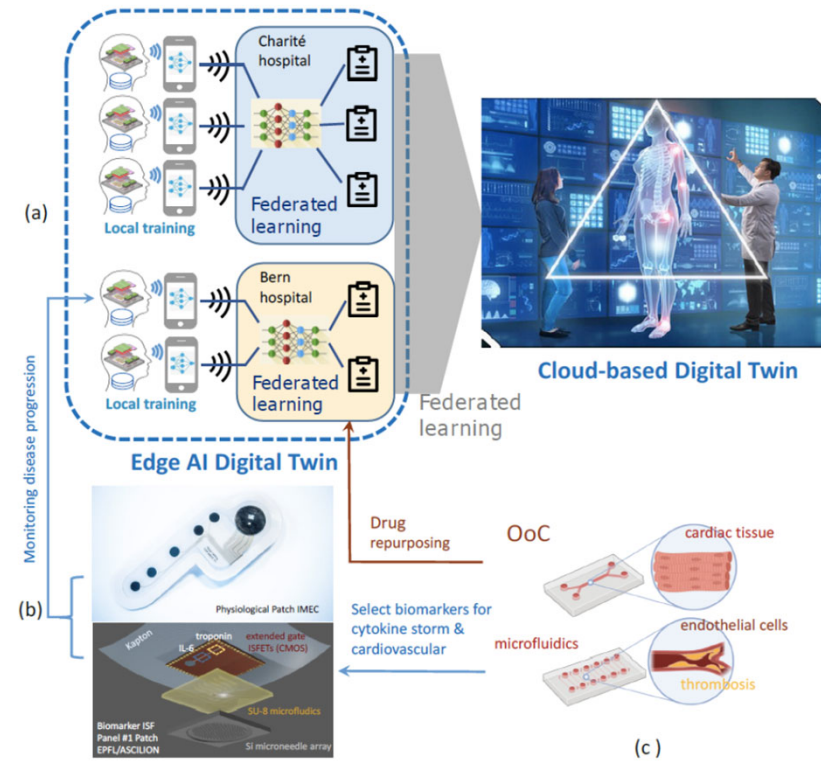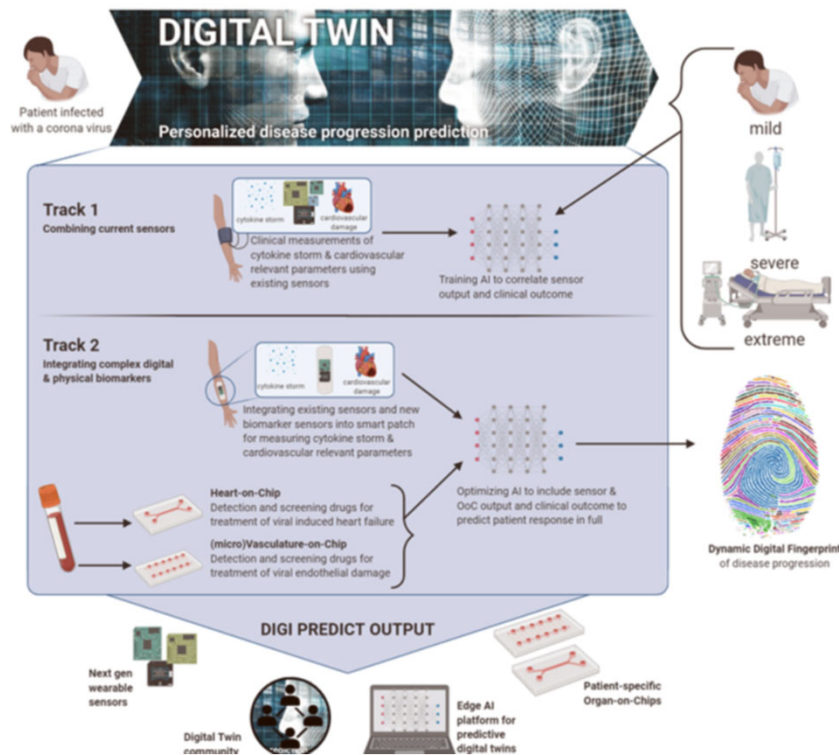
E. Covi et al., Front. Neurosci., May 2021.

Exposome: a measure of the environment's impact on health.

A.M. Io

Example 1: vital sign, OoC and dynamic biomarker data integration in hospital setups

Ecosystem for Digital Twins in Healthcare

Example 2: Data complexity in cancer & role of DT

Disease complexity in the 21st century with a focus on cancer (similar complexities apply to other translational domains) and the role that a citizen-centric Digital Twin can play in the future.
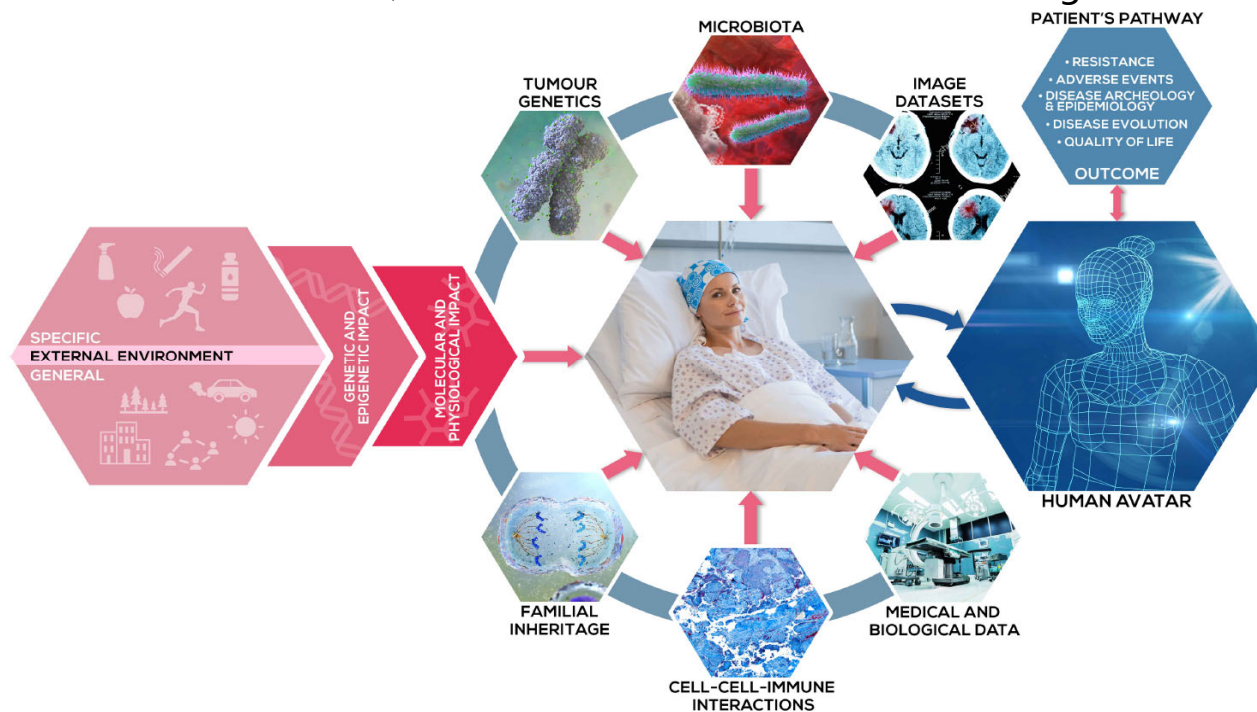

New EiC Project
Real Care!

How my digital twin helped me survive cancer…

- https://www.siemens-healthineers.com/perspectives/digital-twin-cancer

Hi guys, it's Anna 😊. After being quiet for a while, I feel like writing to you again to tell you about what's been happening over the past few weeks. Hopefully writing about my illness won't just help me, but also other patients out there who are experiencing similar things.

My doctors recently found several liver metastases that needed urgent treatment. **The weird thing is, I wasn't feeling ill or anything**.

I just received a call from my health coach a couple of weeks ago asking me to come in to have an ultrasound. Turns out, it was my "digital self" who triggered the call
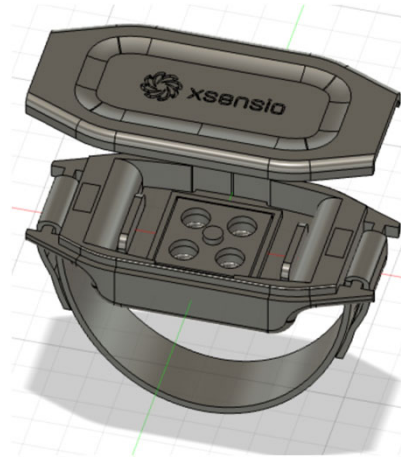

Genomics

Vital signs

Social determinants

Behavioral

Lab data
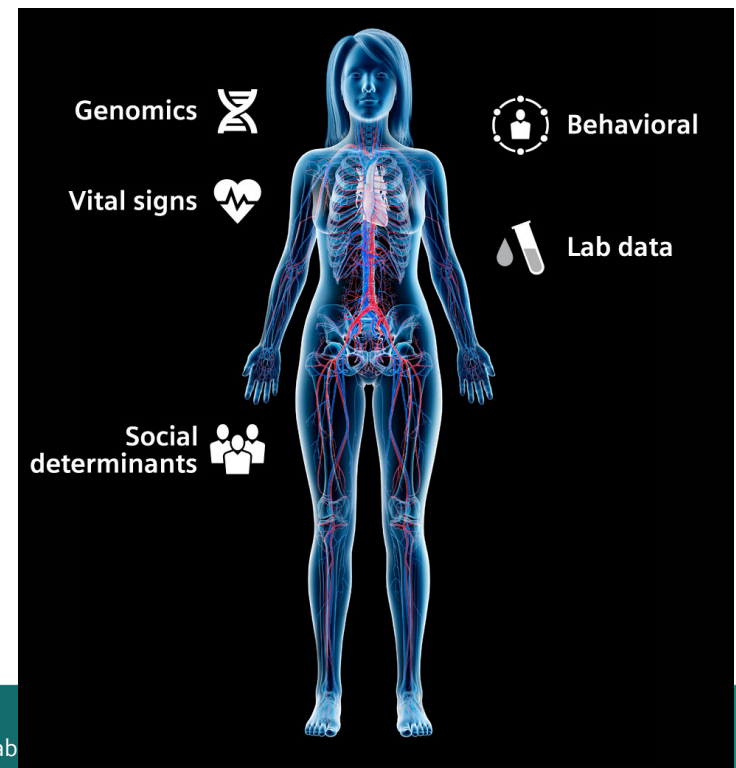
Investigational studides for biomarker discovery in biofluids

- Challenge: very little know-how on biomarkers and their dynamics in other fluids than blood (gold standard).

- Carried out as an EPFL-Xsensio collaboration and within EDITH

- Focus on interstitial fluid (ISF)
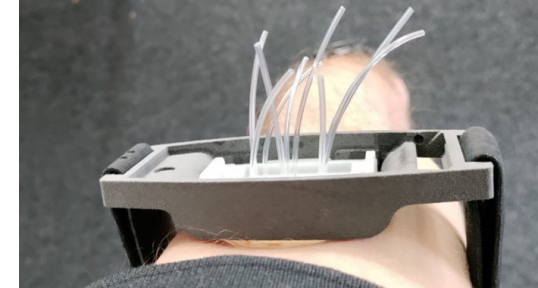
- No new sensors used, only lab analysis

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in Healthcare

ISF screening: Study design

EPFL/Xsensio internal study :

- **20 participants** with over **55 biomarkers** being screened in **ISF and blood**.

- ISF and blood collection on 20 healthy subjects. **The ISF collector is applied for 1 hour on the triceps.** Capillary blood is collected at the beginning of the ISF collection (~50ul)

- Skin damage was assessed by a dermatologist for 6 subjects, 24hours after collection. Subject fully recovered; **no skin damage was observable**.
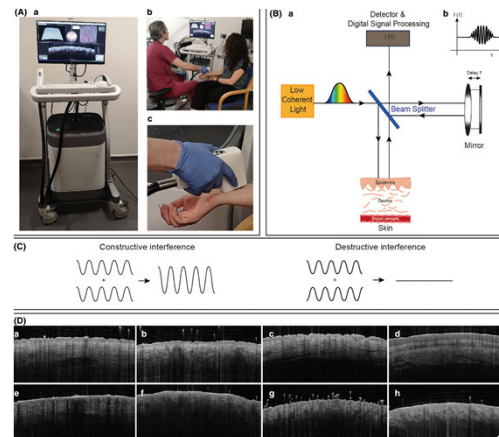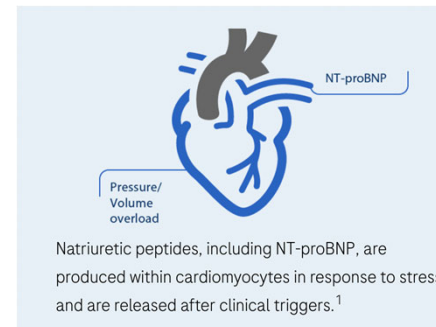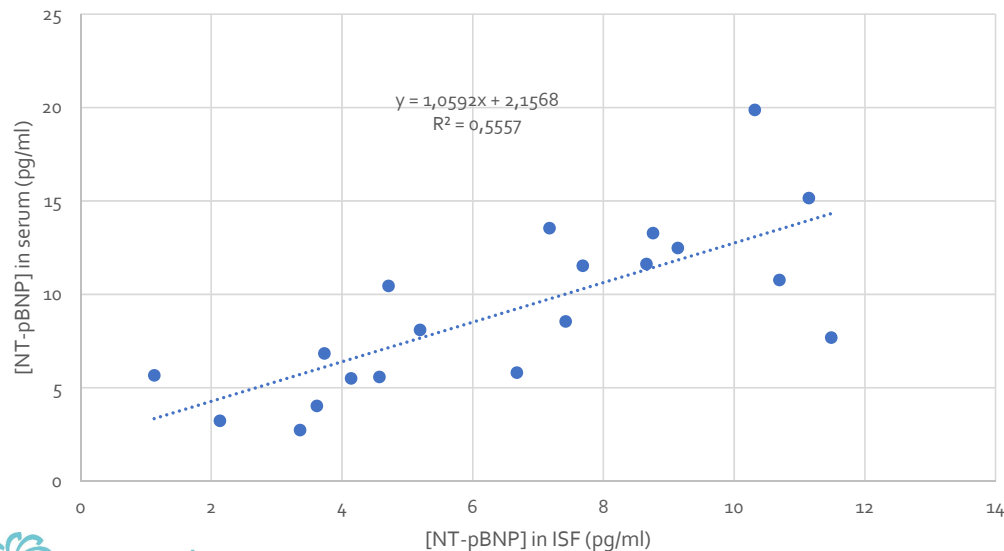

Total protein content, Lactate, IgG, Albumin, NT-pBNP, Cholesterol and a panel of inflammatory proteins

NT-pBNP levels comparison :

- We have demonstrated that NT-pBNP was present in ISF at levels similar than in serum.

- Strong association (r = 0.74) between ISF level and serum level.

Natriuretic peptides, including NT-proBNP, are produced within cardiomyocytes in response to stress, and are released after clinical triggers.[1]

Diagnosis of Heart Failure in non Acute setting

NT-proBNP cut-offs

<125 pg/ml	>125 pg/ml
HF unlikely	HF likely. consider confounding factors

Blood and ISF NT-pBNP levels comparison

$y = 1{,}0592x + 2{,}1568$
$R^2 = 0{,}5557$

● > 40 ans   ● < 40 ans

● Male   ● Female

xsensio
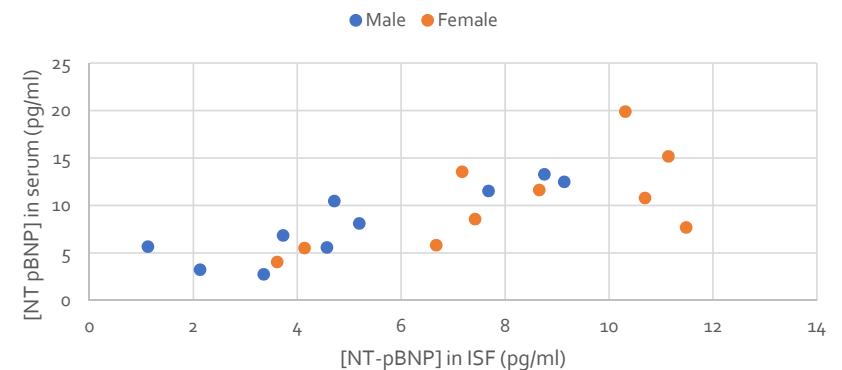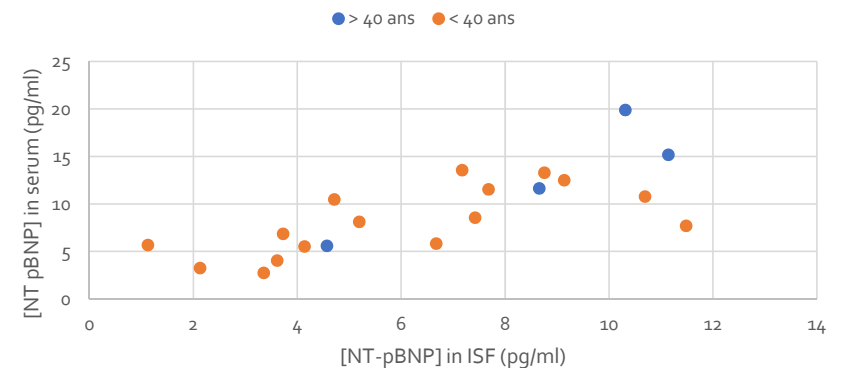
Correlation summary O-link

Correlation coefficient summary ISF vs Serum

	CRP	IFNG	SAA	CSF3	NT-pBNP	VCAM	CCL19	CXCL19	ICAM	IL33	IL15	CCl7	IL17F	FLT3LG	CSF2	CCL8	TGFA
Pearson's r	0,95	0,93	0,92	0,79	0,74	0,74	0,74	0,70	0,56	0,55	0,55	0,55	0,53	0,50	0,49	0,47	-0,48

Very strong association   *Strong association*   *Moderate association*
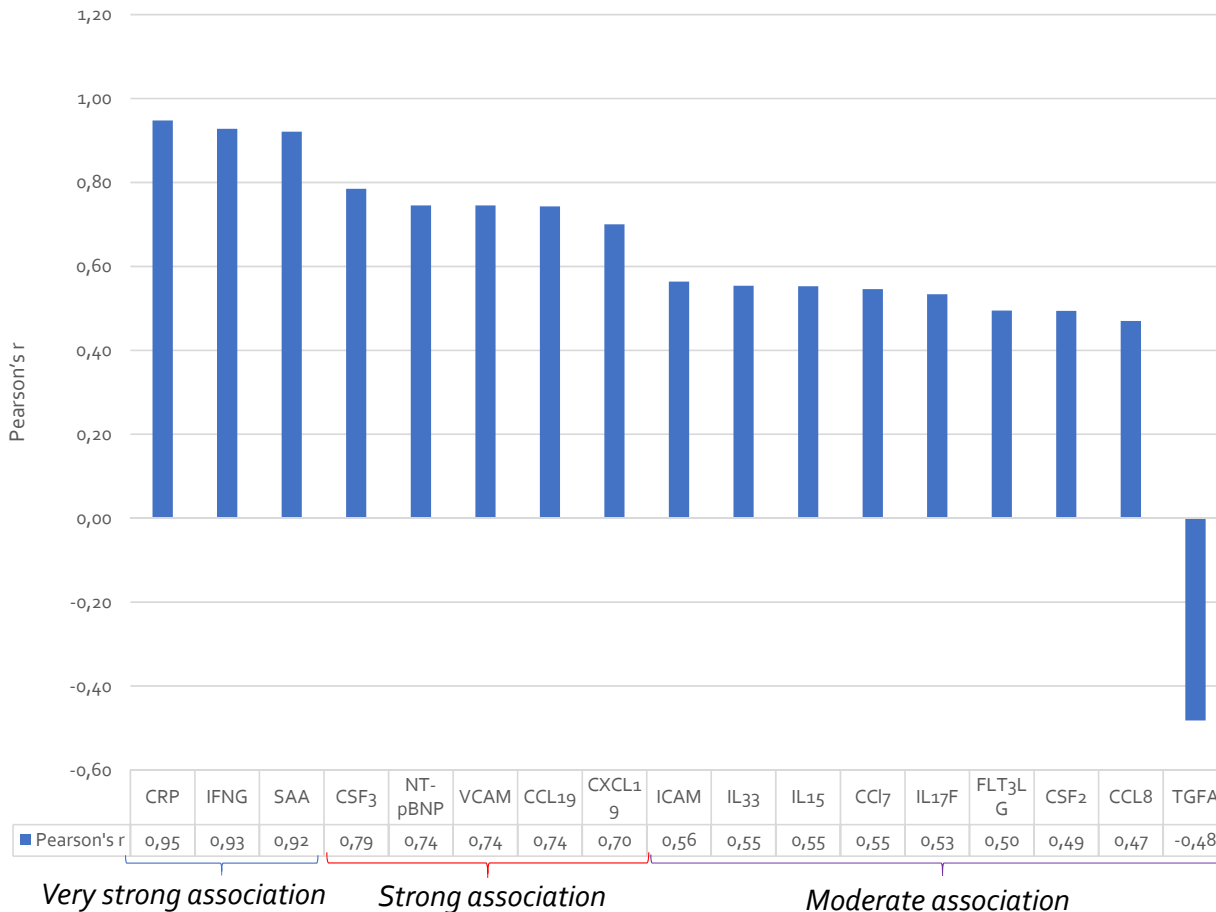
- In total, **17 markers were statistically associated** between ISF and blood.

- The correlation here is "**static**" we would need to see the dynamics : "Does the evolution in ISF correlates with the evolution in blood ?"

Correlation Coefficient (r)	Description (Rough Guideline)
+1.0	Perfect positive + association
+0.8 to 1.0	Very strong + association
+0.6 to 0.8	Strong + association
+0.4 to 0.6	Moderate + association
+0.2 to 0.4	Weak + association
0.0 to +0.2	Very weak + or no association
0.0 to -0.2	Very weak - or no association
-0.2 to – 0.4	Weak - association
-0.4 to -0.6	Moderate - association
-0.6 to -0.8	Strong - association
-0.8 to -1.0	Very strong - association
-1.0	Perfect negative association

- The Pearson's corelation and the p_values are calculated given the null hypothesis (Ho) : « The slope of the regression line is zero »

xsensio

Future development trends of data-driven DT includes

- **Maturity, integration and adoption of related technologies** - The implementation of DT technology relies on industrial information systems, IoT sensors, artificial intelligence, big data, and other technologies. In sensing and OoC the maturity of the technologies is very heterogeneous.

- **Discovery studies of biomarkers and their dynamics can precede and specify further sensors developments** – OoC can play an important role.

- **The evaluation criteria for DTs should be more rigorous -** systems that evaluate the degree of development of existing DTs and clarify the direction of DT construction to guide upgrading and optimization, especially in healthcare applications, are still lacking.

- **Improvements and validations of data generation technologies and models in clinical settings driven by well-identified use-cases -** long process, requiring large amount of resources multidisciplinary teams → EDITH EU platform as enabler.

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http://www.edith-csa.eu

Deliverables available under tab 'dissemination/material'

Indication of interest via de contact form on site