



# STILETTO

The Stiletto project: The GNU Health Federation and  
Open Science in the context of international  
epidemiological and biomedical research

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# About me



[falcon@gnuhealth.org](mailto:falcon@gnuhealth.org)

Mastodon:

[@meanmicio@todon.eu](https://mastodon.social/@meanmicio)

## Academic & profession

- Physician
- Computer Scientist
- Genomics & Medical Genetics

## Social Medicine

- Founder of GNU Solidario
- Author of GNU Health
- Animal Rights

# About GNU Solidario



Non-for-profit organization

- Works globally
- Focused on Social Medicine
- Fights for the right of human and nonhuman animals
- The organization behind GNU Health
- Promotes Libre Software and Open Science

# Projects from GNU Solidario



Global**Exposome**







## Global**Exposome**

*Compassionate Science, Sustainable Planet*

# Exposome

## Exposome/ ('ɛkspəʊ,səʊm) /

“The cumulative measure of environmental influences and associated biological responses throughout the lifespan, including exposures from the environment, diet, behavior, and endogenous processes.”



# Building modern, empathetic societies for a sustainable planet

## Respect

Mother nature, animals  
(human and non-human)

## Education

People, patients, health prof,  
Politicians...



Global**Exposome**

*Compassionate Science, Sustainable Planet*

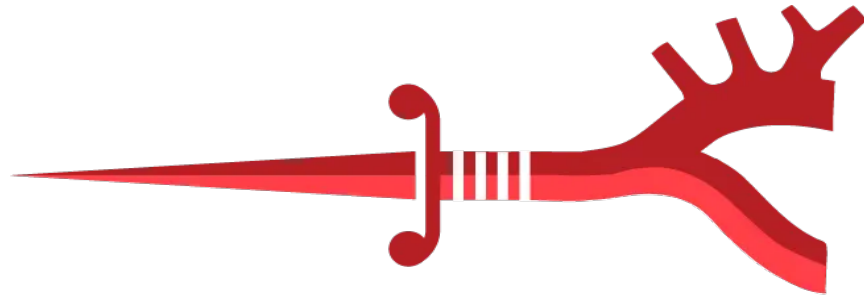
## Research

Medicine, exposomics,  
Agriculture,  
Social sciences,  
urbanism...

## Collaboration

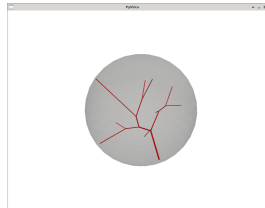
Open Science, Free Software,  
Local capacity building

# Stiletto Project components



# STILETTO

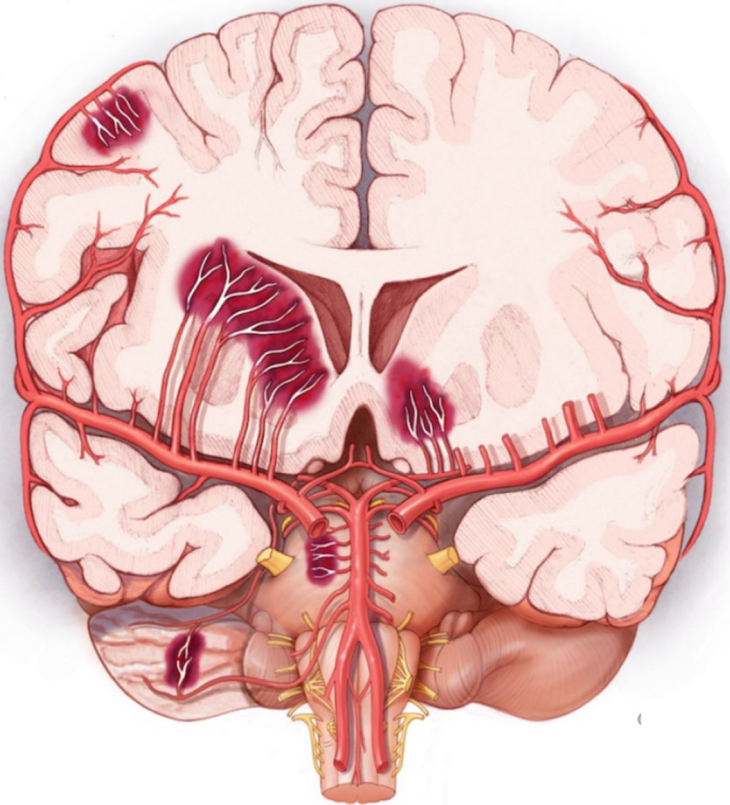
A computational model of the cerebral perforating arteries in health and disease



- Prospective, longitudinal, multicenter study
- Study of the role of the exposome in the etiology and progression of small vessel disease
- Relation among the exposome, genetics and pathology groups that made up cSVD
- Pave the way for future studies in polygenic factors in cSVD

- A computational model of the cerebral perforating arteries in health and disease
- Model and simulation of different scenarios of the perforating arteries and the Neurovascular Unit (NVU)

# Intro to the cerebral microcirculation



Credit: Mayo clinic foundation for medical illustration and Research

- Small vessels (micrometers, most  $< 500 \mu\text{m}$ )
- Brain parenchyma and subarachnoidal space
- Supply deep cerebral areas, including internal capsule, basal ganglia and thalamus.
- They play a critical role in motor, sensitive, cognitive and motional functions.
- Their malfunctioning leads to Cerebral small vessel disease (cSVD)

# Stroke and small vessel disease in numbers



12.2 Million new cases / year  
(1 every 3 seconds)  
Ischemic: 88% / Hemorrhagic: 12%  
**cSVD: approx 3 M**



100 M live with stroke sequelae  
**1 of 4 persons will suffer a stroke**  
In 2035 incidence will increase 35%



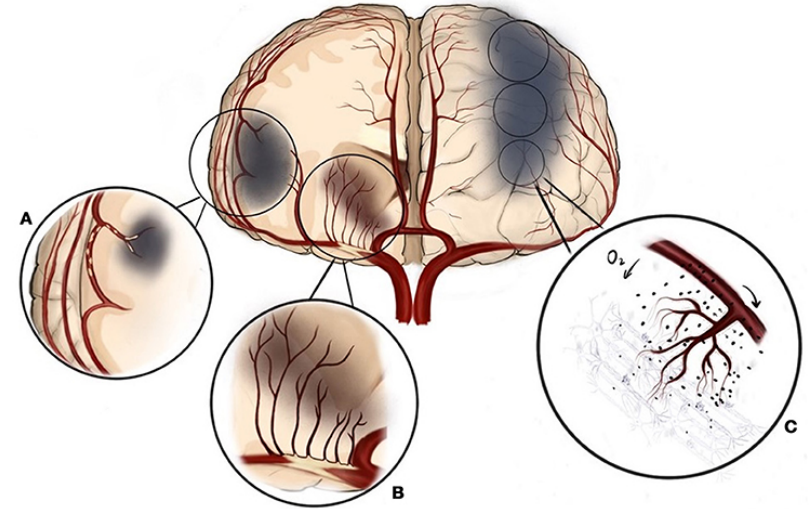
Second cause of death  
**Leading cause of permanent disability**



USD 452 billions global cost



**cSVD**  
25% stroke cases  
**Causes the 45% dementia cases**



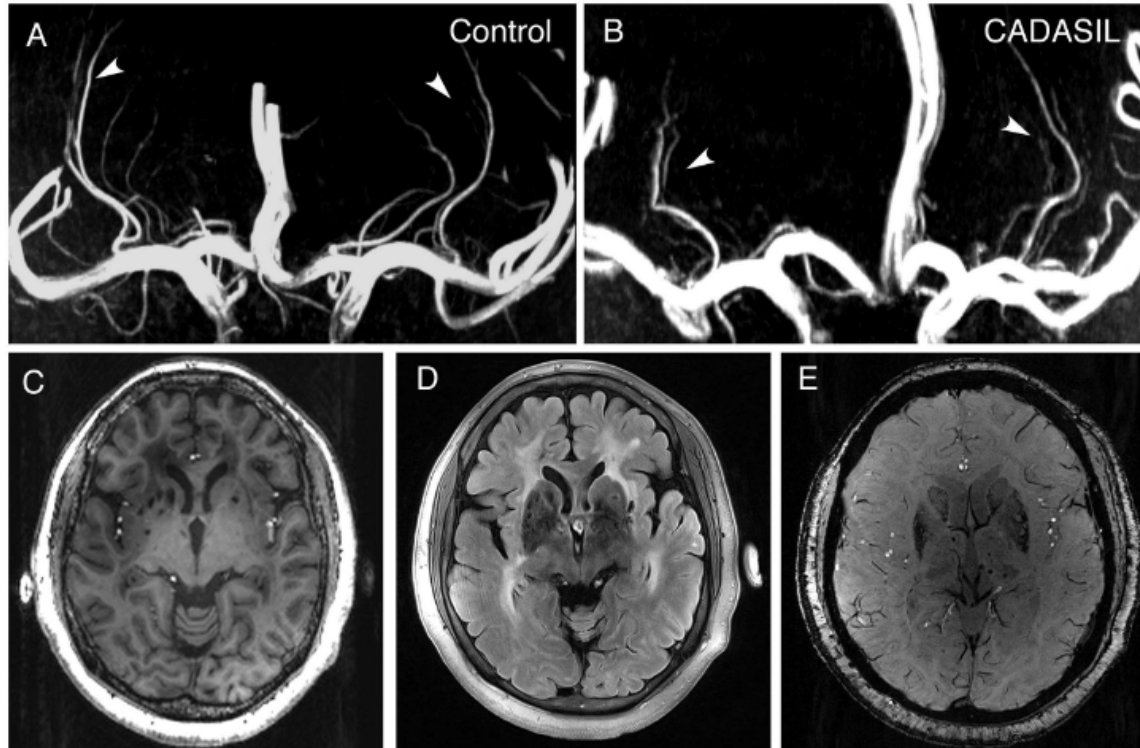
Front. Neurol., 21 August 2018  
Sec. Endovascular and Interventional Neurology

Sources: World Stroke Organization (2022) / CDC / SAFE Europe

# Cerebral small Vessel disease (cSVD) - Classification

CSVD types		
Type 1	Atherosclerosis (“sporadic”)	Hypertension, diabetes, hyperlipidemia
Type 2	Cerebral Amyloid Angiopathy	
Type 3	Monogenic	CADASIL (notch3), CARASIL (HTRA1), MELAS, Fabry's disease,..
Type 4	Inflammatory / immuno-mediated	Wegner granulomatosis, Churg-Strauss, connective tissue vasculitis (Lupus, Sjögren, sclerodermia, rheumatoid vasculitis..), microscopic polyangiitis, IgA vasculitis (Henoch-Schönlein purpura)
Type 5	Venous collagenosis	
Type 6	Others	Post-radiation angiopathy, non-amyloid microvasculature degeneration in Alzheimer disease

# Radiological Markers in cSVD

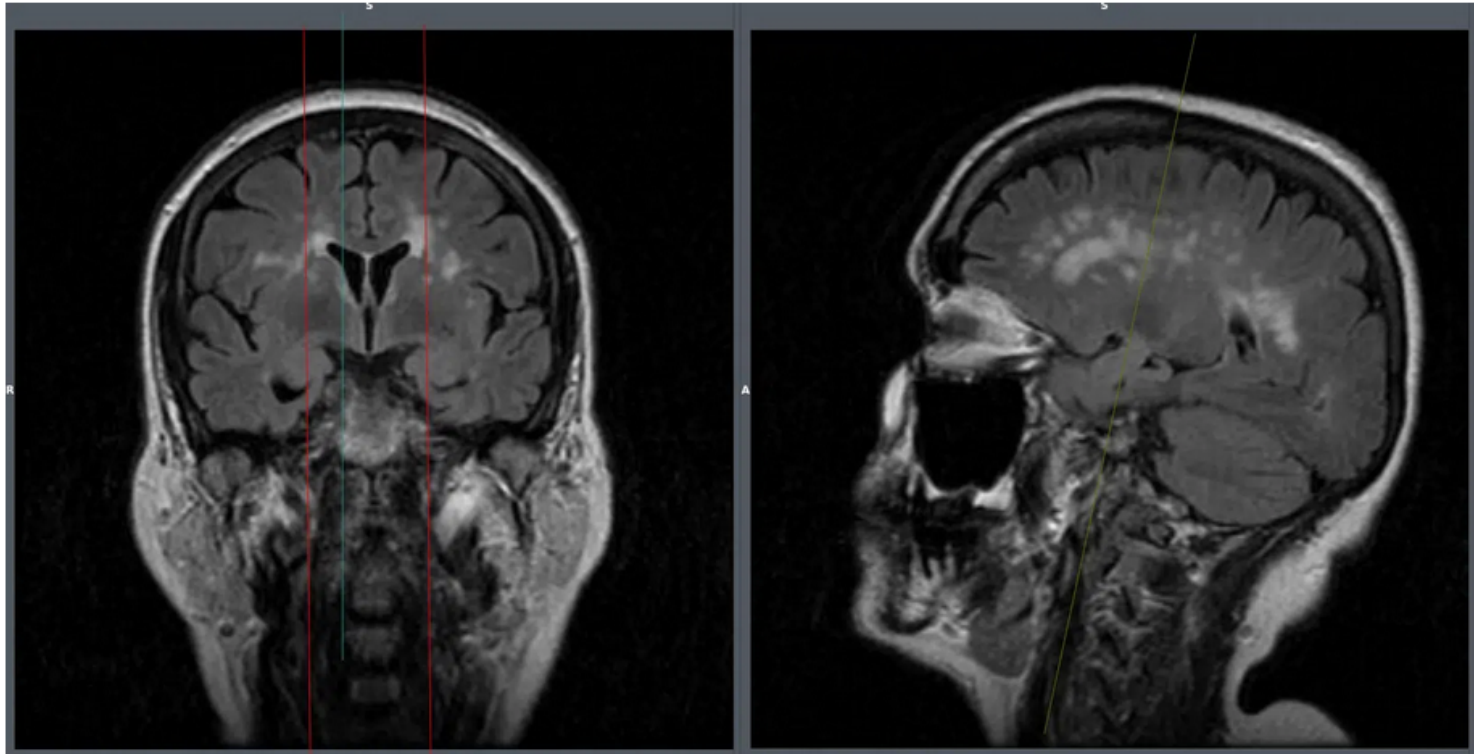


- Main markers
  - Leukoaraiosis / WMH
  - Microbleeds
  - Lacunar infarcts
  - Increased perivascular space (basal ganglia)
  - Cerebral atrophy (loss of volume)

Fuente: Lenticulostriate Arteries and Basal Ganglia Changes in Cerebral Autosomal Dominant Arteriopathy With Subcortical Infarcts and Leukoencephalopathy, a High-Field MRI Study  
Front. Neurol., 09 August 2019 (Sec. Applied Neuroimaging)  
Volume 10 - 2019 | <https://doi.org/10.3389/fneur.2019.00870>



# cSVD monogenic (CADASIL)



Magnetic Resonance showing multiple lesions in white cerebral white matter in a patient with CADASIL

© 2024 CC BY-SA Dr. Luis Falcón

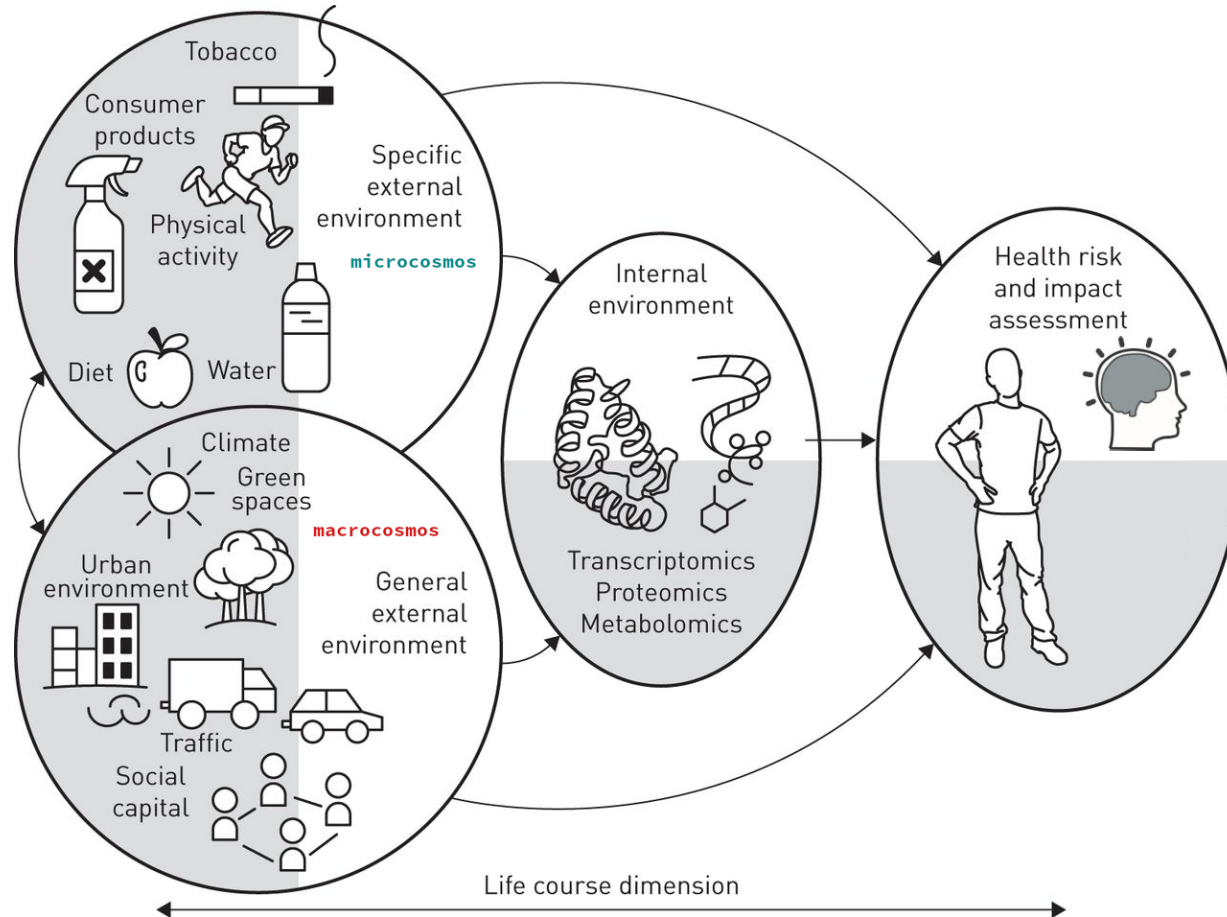
# Sporadic cSVD



Magnetic Resonance from an elderly patient showing white matter hyperintensities and brain atrophy compatible with small vessel disease

© 2024 CC BY-SA Dr. Luis Falcón

# Exposome, macrocosmos, microcosmos & cSVD



Adapted from  
<https://publications.ersnet.org/content/errev/25/140/124>

# Some variables

## Macro

- Pollution (PM2.5)
- Socioeconomic Status
- Urbanization degree  
"Operating Sectors"  
(GNU Health)
- Living and sanitary conditions

## Micro

- Diet
- Psycho-social stress
- Physical activity
- Alcohol
- Smoking

WHR /  
BMI

Inflammation  
biomarkers  
IL6, fibrinogen, hs-  
PCR...

Arterial  
pressure

Sex

Pathology  
group  
Sporadic,  
genetic,  
autoimmune..

Polygenic  
Risk Score  
PRS-cSVD

Age

WMH

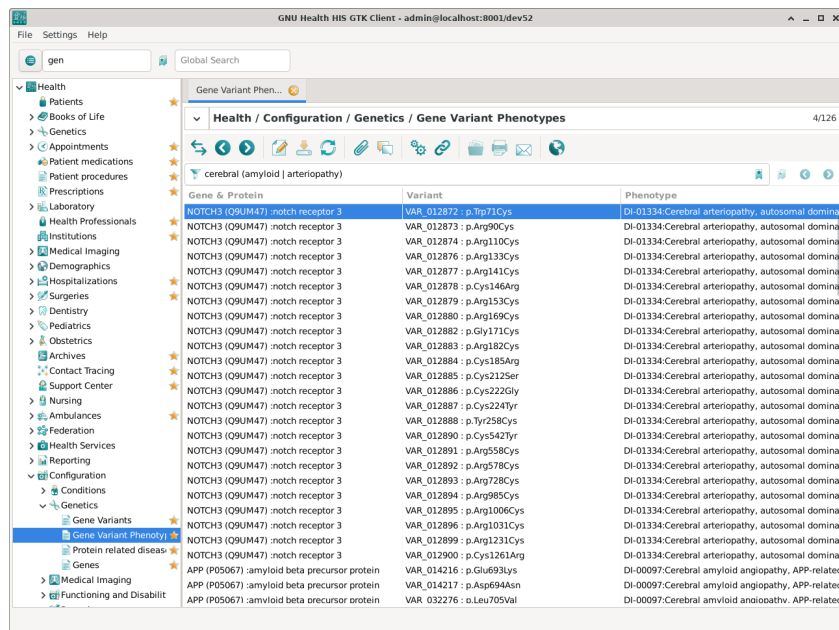
tCSVD score  
(Microbleeds, WMH,  
lacunes, perivascular  
space)

effects

Cerebral  
Volume /  
atrophy

Cognitive  
status

# Data collection: The GNU Health ecosystem



MoH / Analytics

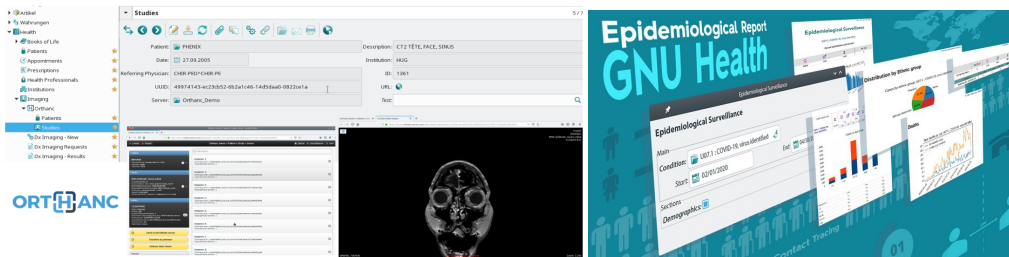
Hospital Management  
ERP

Electronic Health  
Record

Demographics /  
Social Medicine

- Demographic information
- Social Medicine
- Lifestyle
- Domiciliary Units / urbanism degree
- Clinical history / variables of interest
- Medical Imaging / Radiology
- Laboratory / biochemistry
- Genetics (phenotypes, natural variants, family history)
- ICD-11
- Data anonymization
- Reporting

GNUHealth



# GNU Health Information System



# Collecting and aggregating data from participating entities: Federated Health Network & Information System



Nodes

Message Server

Information System

Participating  
centers  
("nodes")





# Collecting and updating information from MyGNUHealth PHR

## Research

GNU Health - admin@localhost/genetics - Administrator - GNU SOLIDARIO HTAL (Euro)

Variant Phenotypes 17 / 40

BRCA1

Gene & Protein	Variant	Phenotype
BRCA1 (P38398): breast cancer 1, early onset	VAR_007778: p.Thr1025Ile	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_007781: p.Val1047Ala	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_007782: p.Pro1150Ser	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_007796: p.Ala1170Glu	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_007799: p.Met1173Arg	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020679: p.Glu101Lys	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020680: p.Glu23Lys	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020683: p.Asp749Tyr	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020690: p.Ser1187Ile	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020691: p.Gln1200His	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020692: p.Arg1204Ile	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020693: p.Lys1207Asn	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020695: p.Ser1217Tyr	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_063212: p.Met1173Lys	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_075666: p.Arg1699Trp	DI-02602:Breast cancer
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_020896: p.Pro47Ala	DI-02602:Breast cancer
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_020900: p.Met299Ile	DI-02602:Breast cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_007757: p.Cys61Gly	DI-01655:Ovarian cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020702: p.Cys1697Arg	DI-01655:Ovarian cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_075666: p.Arg1699Trp	DI-01655:Ovarian cancer
BRCA1 (P38398): breast cancer 1, early onset	VAR_020679: p.Glu101Lys	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020680: p.Glu23Lys	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020690: p.Ser1187Ile	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020691: p.Gln1200His	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020695: p.Ser1217Tyr	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020696: p.Phe1226Leu	DI-01559:Breast-ovarian ca
BRCA1 (P38398): breast cancer 1, early onset	VAR_020697: p.Arg1243Gly	DI-01559:Breast-ovarian ca
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_023700: p.Gln255His	DI-01603:Fanconi anemia c
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_023702: p.Ala349Pro	DI-01603:Fanconi anemia c
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_023703: p.Trp647Cys	DI-01603:Fanconi anemia c
BRIP1 (Q98X63): BRCA1 interacting protein C-t	VAR_023704: p.Arg707Cys	DI-01603:Fanconi anemia c

Connected

GNU Health 2.0rc1

HOME Menu

26 9 2023 12 35

Genotyping test

Domain & Context medical genetics

rs397508635	CFTR	P13569
p.Ser13Phe	VAR_000101	LP/P

Cystic fibrosis (CF) [MIM:219700]

pecific natural variant information by entering the reference seq ID . Once it finds a match on the information is automatically shown. Some of the information shown contains the gene symbol, acid change, natural variant ID, the category (likely benign or pathogenic) and the MIM identifier.

Relevance important Private page: ☒

Save

GNU Health 2.0rc1

HOME Menu

Personal key

Sign in

MyGNUHealth  
The GNU Health Personal Health Record



# Work with the GNU Health installed base



The Stiletto project: The GNU Health Federation and Open Science in the context of international epidemiological and biomedical research

# Work with the GNU Health installed base



HEADQUARTERS



HEALTH INSTITUTIONS



ACADEMIC INSTITUTIONS



REGIONAL OFFICES



ANIMAL RIGHTS



HUMANITARIAN MISSIONS

The Stiletto project: The GNU Health Federation and Open Science in the context of international epidemiological and biomedical research

Luis Falcón

# ... and Academic institutions / the GNU Health Alliance

## HST.936: Global Health Informatics to Improve Quality of Care

The 2015 iteration of our course will focus on Public Health Emergencies and Humanitarian Crises.

Classes begin: February 6, 2015  
Fridays 9am - 11am ET (GMT -5)  
Room: 09-057



**GNUHealth**  
**ALLIANCE**  
OF ACADEMIC AND RESEARCH INSTITUTIONS



Leibniz  
Universität  
Hannover



# ... and medical & surgical partners

## Collaboration



# Genomics and Medical Genetics

## Collaboration

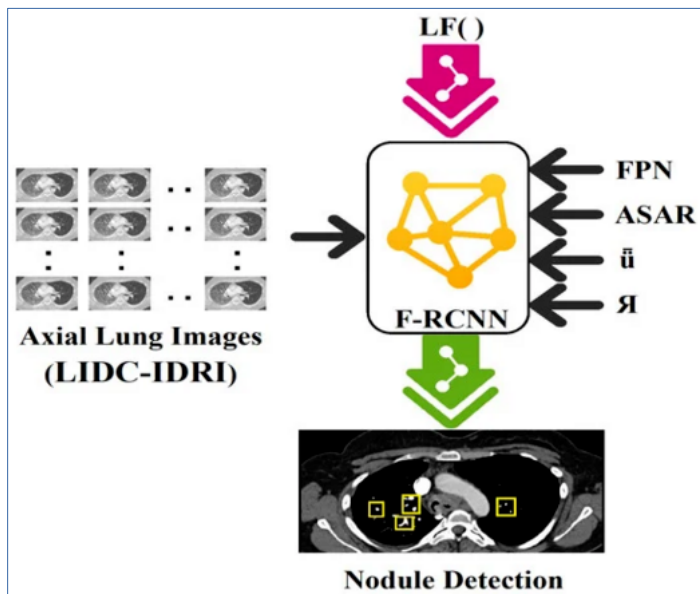
The screenshot displays the GNU Health HIS GTK Client interface. The window title is "GNU Health HIS GTK Client - admin@localhost:8001/gh44to50". The interface includes a sidebar with a tree view of medical categories such as Patients, Appointments, Prescriptions, Health Professionals, Institutions, Laboratory, Medical Imaging, Demographics, Books of Life, Genetics, Surgeries, Hospitalizations, Pediatrics, Obstetrics, Nursing, Health Services, Reporting, Configuration, Conditions, Procedures, Institutions, Laboratory, Medicaments, and Genetics. The main panel is titled "Health / Configuration / Genetics / Natural Variants" and shows details for a specific variant: FTId: VAR\_007799, Gene: BRCA1 (P38398) :BRCA1 DNA repair associa, AA Change: p.Met1775Arg, dbSNP: rs41293463, and Significance: LP/P: Likely pathogenic or pathogenic. Below this, there are sections for "Phenotypes / Diseases" (DI-02602:Breast cancer) and "Gene & Protein" (BRCA1 (P38398) :BRCA1 DNA repair associated). A PyMOL viewer is embedded in the interface, showing a 3D ribbon diagram of the BRCA1 protein structure. The viewer includes a toolbar with buttons for Stop, Play, and MClear, and a status bar at the bottom.

**Open Science:** Using GNU Health in the context of a BRCA1 gene mutation and the structural representation of its protein BRCA1-M1775R ("PDB source: 1N50 *Structural consequences of a cancer-causing BRCA1-BRCT missense mutation*") with PyMOL.



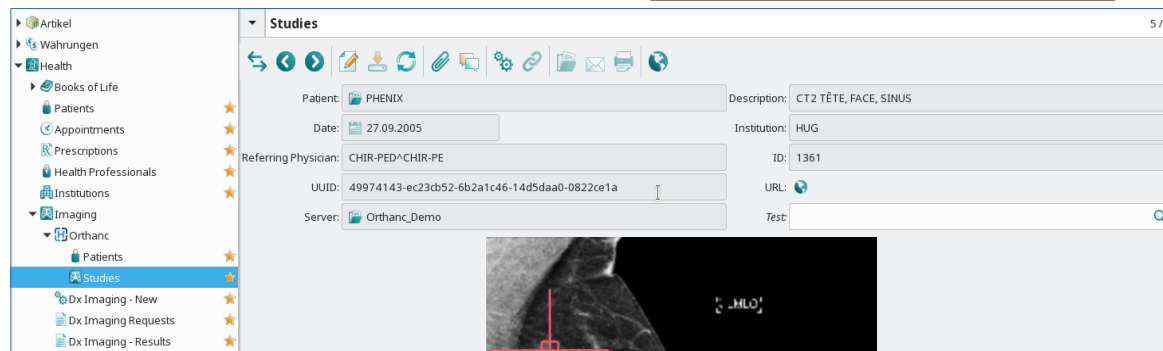
# Medical Imaging & Orthanc

## Collaboration

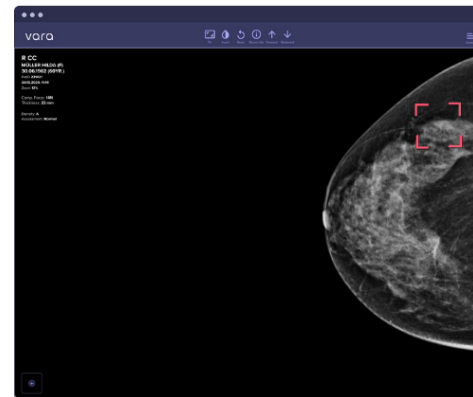


GNU Health used in "Early Detection of Lung Nodules Using a Revolutionized Deep Learning Model"

Some examples of use cases of GNU Health and Orthanc for the early detection of **breast** and **lung cancer**

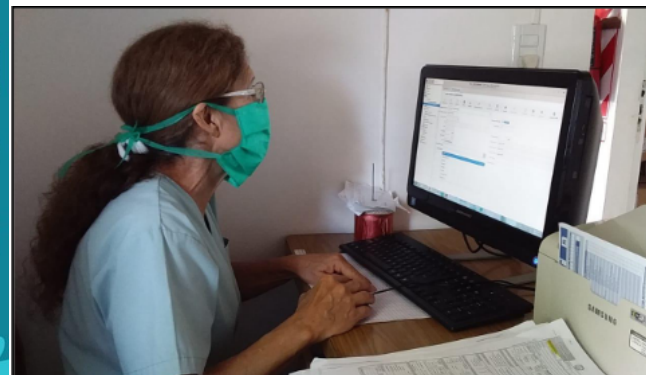
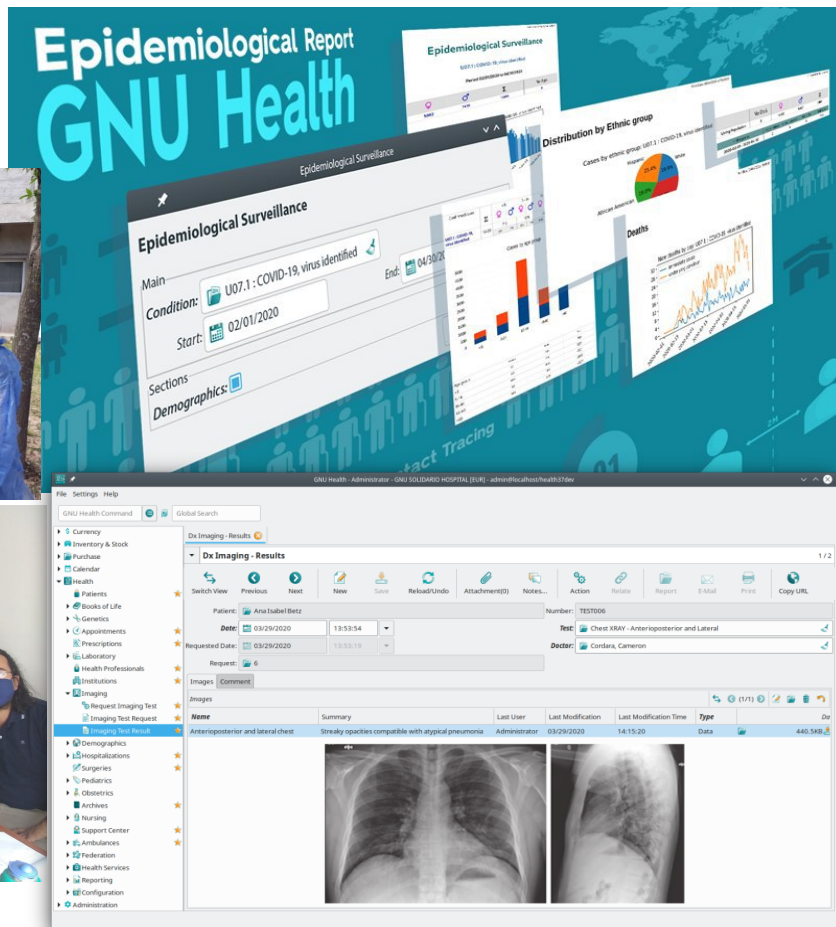


ORT<sup>H</sup>ANC



# GNU Health in pandemic context

## Collaboration



# Mental Health and its socioeconomic determinants

Collaboration



Facultad de Ingeniería UNER PRESENTACIÓN DE AVANCES

**PROYECTO TECNOLÓGICO PARA LA INCLUSIÓN SOCIAL**

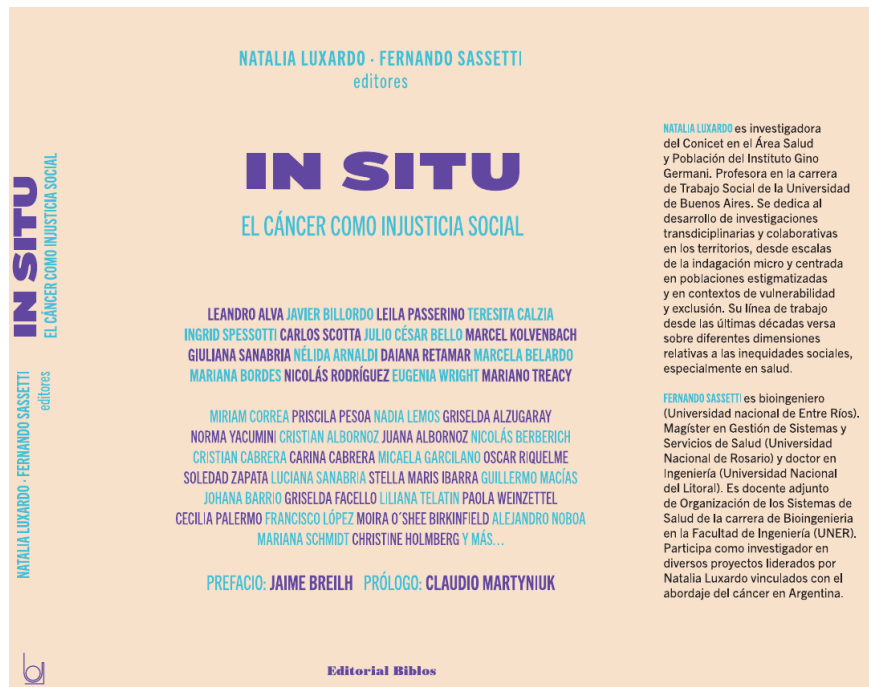
Salud mental comunitaria - tecnología para la organización de redes de cuidados en la zona oeste de la ciudad de Paraná (Entre Ríos)

**Viernes 24 de mayo**  
A las 16:00 | Esc. de Gestión Social  
Pablo de Tarso (Ceferino Namuncura 1451)

Organiza: Cátedra de Salud Pública  
Actividad abierta a la comunidad



# Learn from previous research projects related to Social Medicine



Dra. Natalia Luxardo  
Univ Buenos Aires  
CONICET



Dr. Fernando Sassetti  
Univ Entre Ríos  
Cátedra Salud Pública

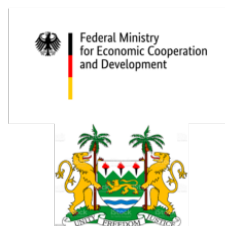


**GNU Health** was used to collect and process the demographic, clinical, epidemiological and socio-sanitary information from the participating centers

# 100% Free Software and Open Science



Digital  
Public  
Goods  
Alliance



python

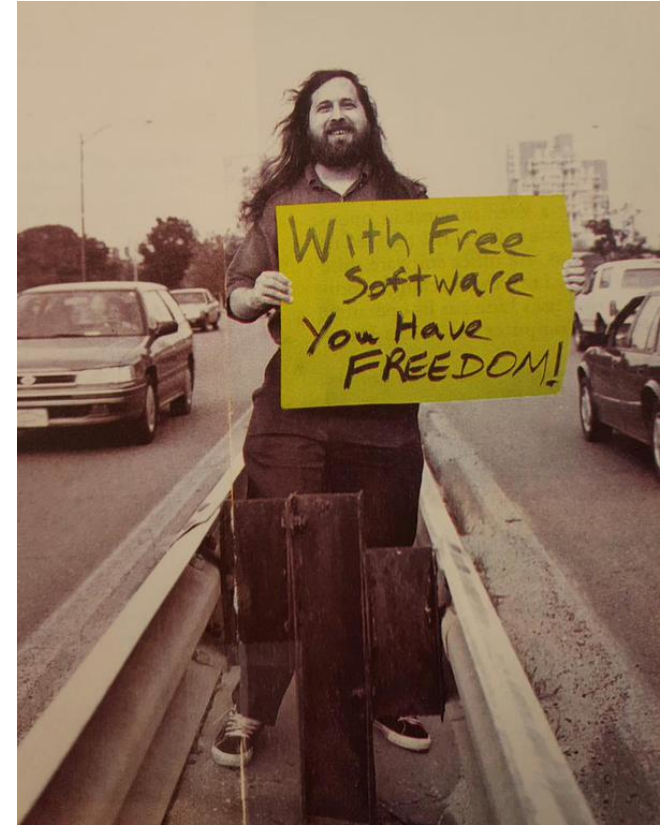


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# We are Free/Libre Software, not “open source”

- Free/Libre software is a philosophy and movement (free culture & science)
- It's about collaboration, solidarity, equity and privacy
- Big tech companies have taken over part of the movement, making “open source” their business.
- The term “Free Software” respects RMS (father of the movement) will and the organizations behind the movement.



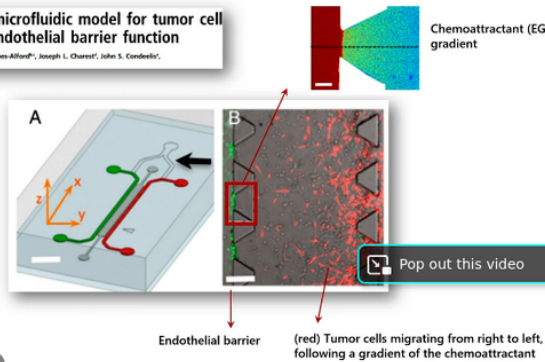
# Human-relevant, cruelty free research

## Organ-on-a-chip



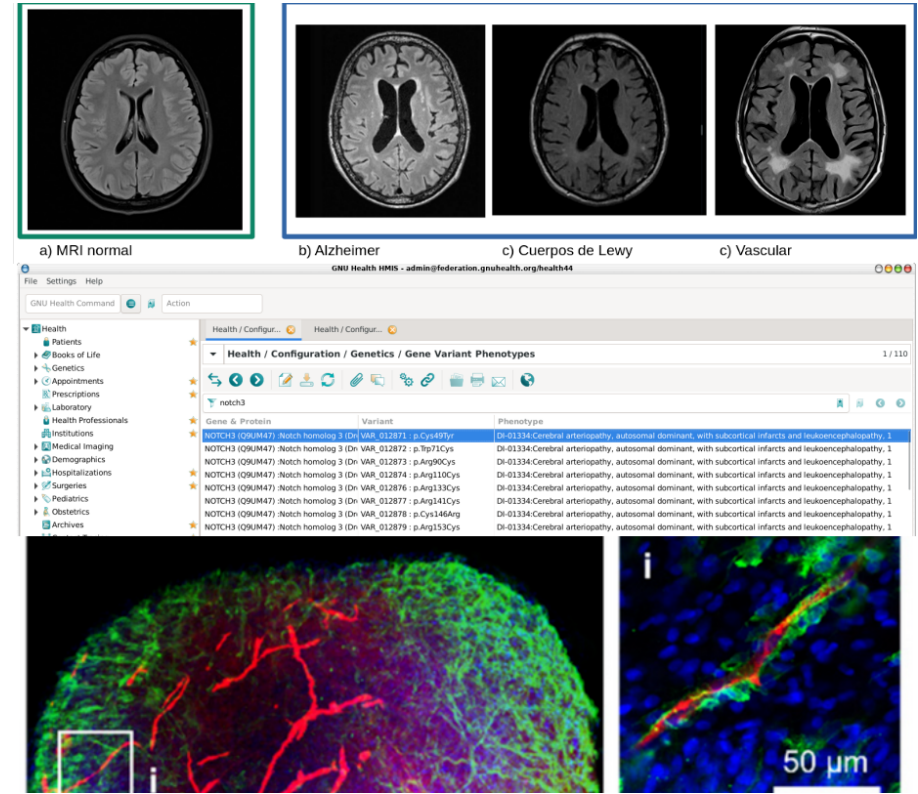
### Three-dimensional microfluidic model for tumor cell intravasation and endothelial barrier function

Ioanna K. Zervantonaki<sup>1</sup>, Shaomei K. Hughes-Alford<sup>2</sup>, Joseph L. Charest<sup>1</sup>, John S. Condeelis<sup>1</sup>, Frank B. Gerlter<sup>1</sup>, and Roger D. Kamm<sup>1,3</sup>



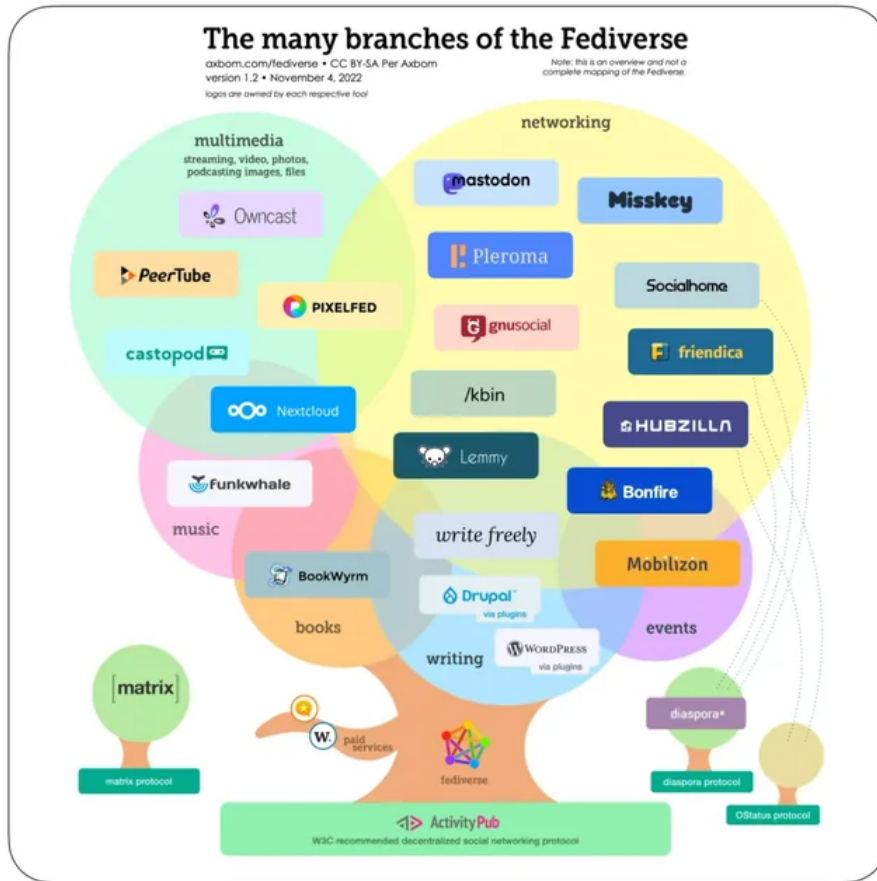
[Link to paper](#)

Zervantonaki, I. K., Hughes-Alford, S. K., Charest, J. L., Condeelis, J. S., Gerlter, F. B., & Kamm, R. D. (2012). Three-dimensional microfluidic model for tumor cell intravasation and endothelial



# Meet and Join us at the Fediverse

## Collaboration



## GNU Health

<https://mastodon.social/@gnuhealth>

## GNU Solidario

<https://mastodon.social/@gnusolidario>



# Respect: “*First, do no harm*”

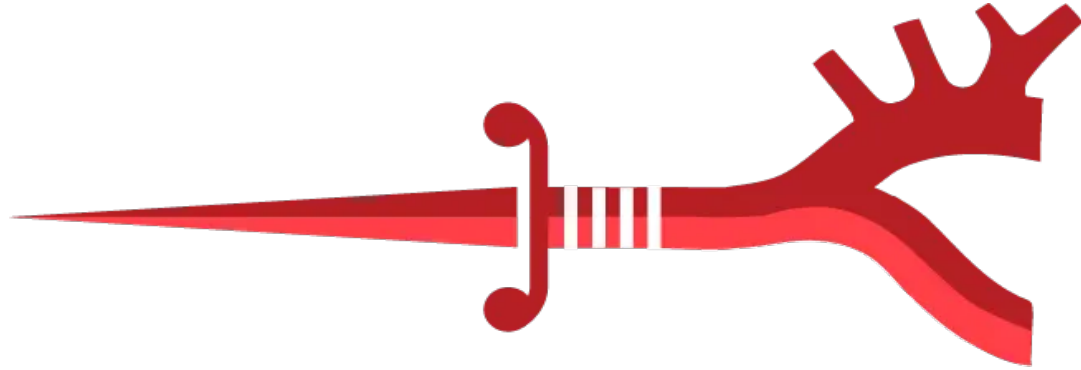
*Primum non nocere*

## Respect

Mother nature, animals  
(human and non-human)



Thank you!



# STILETTO

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[falcon@gnuhealth.org](mailto:falcon@gnuhealth.org)