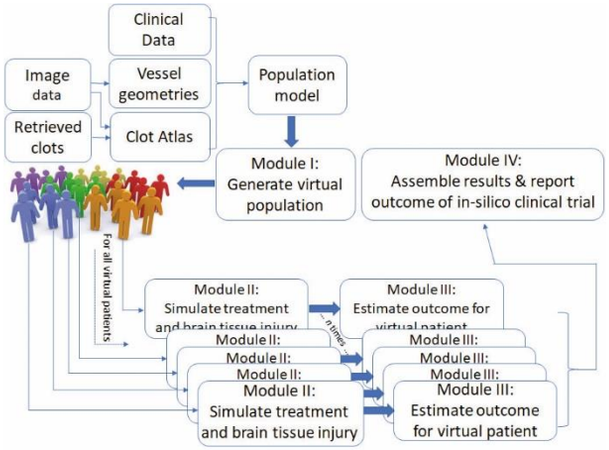
Our planned *in silico* clinical trials for acute ischemic stroke will thus consist of four main software Modules: one module containing the population model to generate virtual populations of stroke patients, one to simulate treatment and brain tissue injury, a third where the outcome for each individual virtual stroke patient is estimated, and the final module where all results will be assembled and the outcome reported.



More information:

INSIST; www.insist-h2020.eu

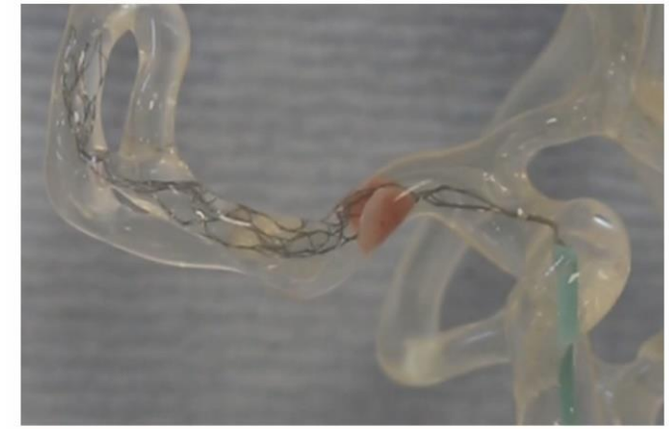
Project coordinator:
Prof. Dr. Charles Majoie, MD Professor of Neuroradiology, Department of Radiology and Nuclear Medicine, Amsterdam UMC, the Netherlands.
c.b.majoie@amc.uva.nl

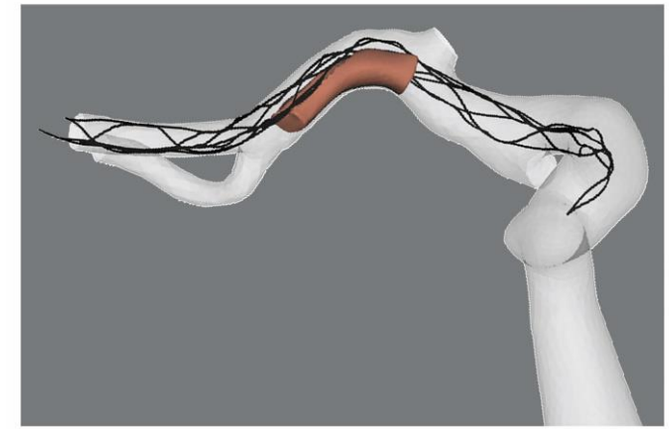
Project Manager:
Dr. Laurian Jongejan
L.zuidmeer@amc.uva.nl

The INSIST consortium

- Amsterdam UMC, the Netherlands
- University of Amsterdam, The Netherlands
- Erasmus Medical Center, the Netherlands
- KU Leuven, Belgium
- National University of Ireland Galway, Ireland
- University of Geneva, Switzerland
- Politecnico di Milano, Italy
- Cerenovus, Ireland
- University of Oxford, United Kingdom
- Lomonosov Moscow State University, Russia
- Institut de Recherches Internationales Servier, France

In Silico Clinical Trials for the Treatment of Acute Ischemic stroke





This project has received funding from the EU Horizon 2020 research and innovation programme (grant agreement No 777072).

Background

- Stroke is the number one cause of disability in the Western world and the 3rd most common cause of death.
- An estimated 1.3 million Europeans have a first stroke each year (on average every 25 seconds).
- This number is projected to rise to 1.5 million by 2025, largely due to the ageing population. One third of the patients with stroke will die and one third is left permanently disabled.
- 1 in 5 stroke survivors require long term institutional care.
- High societal costs: ~ €27 billion per year in Europe and another €11 billion per year for informal care provided by the patient's families.

Time is crucial in stroke.

Each hour without successful treatment, the brain loses as many neurons as it does in 3-4 years of aging. Therefore, the effectiveness of stroke treatment is strongly dependent on time to treatment.

Present

Choice of treatment is limited:

Until recently, thrombolysis with intravenous administration of alteplase was the only available treatment. Alteplase is a recombinant tissue plasminogen activator, which helps breaking down unwanted blood clots.

Now also intra-arterial thrombectomy, a minimally invasive procedure in which the obstructing thrombus is removed, is effective in patients with intracranial large artery occlusion.

However, despite the beneficial effect of thrombectomy, almost 2 out of 3 patients with an acute ischemic stroke have an unfavourable outcome and become functionally dependent.

Further improvement of medical devices and drugs for treatment is still urgently needed.

Future

Computer modelling plays an increasingly important role in research and development of new treatments. *In silico* models hold the promise that, in combination with patient models that accurately represent important patient characteristics, they can be used to set up *in silico* clinical trials in which "virtual" patients are treated with "virtual" treatments.

***In silico* clinical trials** can potentially reduce, refine, and partially replace human clinical trials.

Because *in silico* modelling allows early and fast hypothesis testing and supports trial design, the next generation clinical stroke trials can greatly benefit from *in silico* clinical stroke trials. This holds the promise that *in silico* models enable enhanced efficacy, cost reduction, and speed up the introduction of new therapies, devices, and medication for acute ischemic stroke.

INSIST objectives

- Generate virtual populations of stroke patients based on clinical, imaging, and histopathological data collected in large trials and registries (O1)
- Generate *in silico* models for the simulation of thrombosis and thrombolysis (O2), of intra-arterial thrombectomy (O3) and of microvascular perfusion and the death and healing of brain tissue (O4)
- Apply *in silico* stroke models to virtual populations of stroke patients with the goal to generate a full *in silico* stroke trial platform (O5).