Do metals released from implanted medical devices reach the brain?

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Primary ObjectiveThe aim of this clinical part of the Body Barrier project is to produce data from metals that pass the mucosa-blood barrier and/or the blood-CFS barrier. The clinical data will be used to validate the multi-organ-on-chip platform to...

Ethical review	Approved WMO
Status	Pending
Health condition type	-
Study type	Observational invasive

Summary

ID

NL-OMON57587

Source
ToetsingOnline

Brief title
Brainmetals

Synonym
not applicable

Health condition

om dierproeven te vervangen met een 'organ-on-chip' platform

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit van Amsterdam
Source(s) of monetary or material Support: TTW #19247: BodyBarrier

Intervention

Keyword: Blood-Brain Barrier, Medical Devices, Mucosa-Blood Barrier, Organ on chip

Outcome measures

Primary outcome

Blood and CSF handling and analysis (ACTA),(month 1-12): Blood (60) and CSF(41) samples will be analysed to determine the concentrations of the metals using ICP-MS, and compared with metals in dental and medical implants using ACTA*s micro-sampling techniques, EDAX and SEM.

Correlation of clinical data with results obtained from the Body Barriers platform (ACTA),(month 12-48): Determination of whether metals observed in blood also pass the in vitro mucosa blood barrier into the microfluidics compartment of the TissUse bioreactor chip. Determination of whether metals observed in CSF are also detected passing the BBB of the Body Barriers platform thus coming into contact with brain organoids

Deliverables/Milestones:

Completed analysis of metals in dental medical devices and correlation to blood & CSF (month 12)

Correlation of clinical data with Body Barriers (month 48)

Secondary outcome

As a *by-product*, information is obtained about which metals from dental and medical devices can be found in the peripheral blood and/or cerebrospinal fluid (CSF).

Study description

Background summary

This project is part of the NWO project **Body Barriers**. The whole project aims to develop a next generation *organ-on-chip* (OoC) platform that mimics the functions of two of our important body barriers (i.e. mucosa-blood barrier and blood-brain-interface, the blood-brain barrier resp. blood-CFS barrier) and to establish Proof of Concept (POC) testing with metal leachables derived from (dental) medical devices.
There is a wealth of data showing that some metals can pass the (oral) mucosal barriers as well as the blood-brain-interface, such as mercury and nickel, and so do metals leaching from medical devices (3-7). Metals and accumulation thereof in the brain may induce oxidative stress, inflammation and mitochondrial dysfunction, leading to neuronal dysfunction and consequent neurodegeneration, as seen in Alzheimer*s disease, multiple sclerosis or amyotrophic lateral sclerosis (ALS) (1,2). Our recent pilot data now indicates that in the cerebrospinal fluid (CSF) of patients with Alzheimer*s disease, enhanced levels of nickel and titanium compared to controls were detected, indicating that such metals indeed penetrate the brain and may be associated with neurodegeneration.

Study objective

Primary Objective
The aim of this clinical part of the Body Barrier project is to produce data from metals that pass the mucosa-blood barrier and/or the blood-CFS barrier. The clinical data will be used to validate the multi-organ-on-chip platform to be developed in the Body barriers project .

Secondary Objective
As a *by-product*, information is obtained about which metals from dental and medical devices can be found in the peripheral blood and/or cerebrospinal fluid (CSF).

Study design

Observational study

Test groups
Patients referred to the Spaarne Gasthuis who will undergo orthopaedic surgery (hip or knee implants), where spinal anaesthesia is indicated, will be asked to participate in this study after they have been extensively informed about the purpose of the study and the consequences for themselves.

Specific actions during the research
After inclusion and informed consent of patients, before undergoing the surgical treatment, participants are invited for a consultation on ACTA. During the consultation, an extensive medical and dental anamnesis will be taken, in which an inventory is made of any medical devices applied in the mouth and any medical devices present in the body. A micro-sample is optionally taken from the metal-containing medical devices present in the mouth to evaluate the metal composition. When dental implants have been applied and the patient does not have an implant passport, the oral-implantologist will be contacted to find out the brand and type of implant.
As part of the spinal anesthesia a small amount of CFS is aspirated to ensure the needle tip has reached the spinal space.In this study (approx. 3 ml CFS will be retracted and kept for this study. In addition, as part of the anesthetic preparation, a small ampoule of blood (3-5 ml EDTA whole blood) may be collected and used for further analysis in this study. Sample collection will be done by Spaarne Gasthuis.

Study burden and risks

The extra burden for the patients only concerns the extra visit to ACTA

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients whose orthopedic surgery is planned and where it is decided to use spinal anesthesia will be informed by the attending orthopedist in Spaarne Gasthuis that they can participate in this study. They will be given the information letter.
If they indicate an interest in participating in this study, their pre-surgery anesthesia consultation will be combined with a consultation with the ACTA researcher (at the Spaarne Gasthuis location). They will also be sent a bottle to take morning urine. The researcher will give a verbal explanation of the study, answer any questions and, if the patient wishes to participate, will also perform an oral examination. The follow-up, collection of CSF and blood will be performed during surgery.

Exclusion criteria

Age under 18 or above 80
Legally incompetent adults

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-03-2025

Enrollment:	50
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO Date:	12-05-2025
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL82256.018.24