The impact of clot composition on its mechanical properties

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Primary Objective: We want to develop a model that predicts the propensity of thrombi to fracture depending on their composition, structure, and heterogeneity. We will develop methods to create both homogeneous and heterogeneous thrombus analogs to...

Ethical review	Not approved
Status	Will not start
Health condition type	Embolism and thrombosis
Study type	Observational invasive

Summary

ID

NL-OMON51109

Source
ToetsingOnline

Brief title
Clot composition and mechanical properties

Condition

- Embolism and thrombosis

Synonym
stroke

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: blood clot, composition, mechanical properties

Outcome measures

Primary outcome

Blood from healthy volunteers will be used as a source for red blood cells, platelets, immune cells, fibrinogen, plasma. Using these components, we will optimize to generate clot analogues of various composition for mechanical testing and imaging. The main study endpoints will be to establish and quantify the relationship between clot composition -for both homogeneous and heterogeneous clost- and the -global and local- mechanical properties and imaging features.

Secondary outcome

Not applicable.

Study description

Background summary

Stroke is the second leading cause of death worldwide1. Recently, randomised controlled trials aiming at revascularisation demonstrated the efficacy of intra-arterial treatment to remove the occluding thrombus2. Unfortunately, complete revascularisation is still achieved in less than half of cases and 20-30% of thrombi cannot be retrieved at all3. Moreover, the treatment carries the risk of inducing thrombus fragmentation and distal embolization4. To improve procedural success rates, we need to understand how thrombi fracture in response to mechanical deformations during retrieval. It is extremely challenging to determine this experimentally as both the time point and the location at which soft matter fracture initiates are unpredictable. While a handful of recent studies have conducted macroscopic fracture of simplified fibrin gels5 and thrombus analogs with differing haematocrit6, the micro-structure of the thrombus at the fracture point and how it changes during fracture has yet to be studied. This is particularly pressing because thrombi

between patients are heterogeneous in structure, molecular and cellular composition7. Thus, fracture occurs differently for different thrombi. The central question we address here is how the micro-structure of different thrombi affect the macroscopic fracture mechanics leading thrombus formation and embolization. To investigate this is a systematic manner, we need to generate clots made from fresh human blood.

Study objective

Primary Objective: We want to develop a model that predicts the propensity of thrombi to fracture depending on their composition, structure, and heterogeneity. We will develop methods to create both homogeneous and heterogeneous thrombus analogs to better mimic real thrombi, and evaluate their mechanical properties using various platforms.

Study design

This is fundamental research, using blood from healthy volunteers. Blood from healthy volunteers is regularly needed for the coming 4 years (approximately once every two weeks). The blood will be used as a source for fibrinogen, red blood cells, immune cells, platelets and plasma to optimize methods and to investigate the effect of clot composition on the mechanical properties. For example, the impact of platelet induced clot contraction on clot stiffness will be measured using unconfined compression experiments. Furthermore, we aim to quantify the effect of fibrinogen content on clot properties. Both will be linked to pre-clinical imaging to translate these findings for treatment optimization.

Study burden and risks

The procedure involves standard blood withdrawal, very much comparable to the standard procedure when you would be a blood donor. The procedure will be carried out by qualified personnel in a safe environment. There is no additional risk associated with this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Subjects should sign up voluntarily
- Subjects should be healthy
- Subjects should be between 18 and 70 years old
- Subjects should give written informed consent

Exclusion criteria

- Subjects with diseases known to affect coagulation (e.g. cancer, diabetes, cardiovascular disease)
- Subjects using medication interfering with coagulation

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	25
Type:	Anticipated

Ethics review

Not approved

Date:	13-01-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL76853.078.21