Initial Immune Response to New Biomaterials

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Cardiac valve disorders
Study type	Observational non invasive

Summary

ID

NL-OMON42385

Source
ToetsingOnline

Brief title
Immune Response to Biomaterials

Condition

- Cardiac valve disorders

Synonym
Heart valve prosthesis, New heart valves

Research involving
Human

Sponsors and support

Primary sponsor: Technische Universiteit Eindhoven
Source(s) of monetary or material Support: European Seventh Framework Programme: Acronyme LifeValve (GA 242008)

Intervention

Keyword: Biomaterials, Immune Response

Outcome measures

Primary outcome

The endpoint for the volunteer to participate in the study will be directly

after the blood collection is completed.

The main study parameters will be:

• Cellular Infiltration

Secondary outcome

• Cytokine release profile

• Gene expression profile

Study description

Background summary

Annually 60.000 patients in Europe only are born with congenital heart failure. These young patients have to go trough multiple reoperations, since the current available valve prostheses cannot accommodate for growth. This leads to increasing risks of morbidity and mortality.
Tissue engineering holds great promise to overcome these limitations. Over more than 15 years, the Eindhoven University of Technology and the Zurich University Hospital made great progress in the development of decellularized tissue engineered heart valves (DTEHVs) in order to develop living valvular prostheses that allow for growth. These DTHEVs are based on vascular-derived cells seeded into biodegradable synthetic polymer scaffolds. Recently, we completed our first long term in vivo follow up in sheep, in which it was shown that these valves show rapid host cell repopulation. In addition, the DTEHVs demonstrated an increase in extracellular matrix content over time, indicative for regenerative and growth potential. These results are very promising and have never been observed with any other type of valve prosthesis.

Study objective

The exact mechanism behind the observed fast recellularization of the DTEHV constructs is still unknown. A reasonable explanation might be that scaffold remnants inside the tissue-engineered constructs recruit the circulating blood cells. In order to investigate this mechanism, an advanced in vitro flow setup was developed to mimic native-like in vivo conditions in terms of flow and pressure. Herein, a biomaterial of interest can be subjected to human circulating blood-derived cells. Since it is not yet known whether the interaction of the blood cells with the scaffold remnants is favorable, we will investigate the response of these circulating cells to assess if their response is targeted more towards degeneration or regeneration. For this first pilot study we would like to address the following questions:

• Do the scaffold remnants in tissue-engineered constructs recruit blood-derived cells?
• Is there a different infiltration profile between certain blood-derived cell subsets?
• Is the initial immune response to the biomaterial representing a degenerative or regenerative response?

In the absence of useful literature information on the subject to perform a power size calculation, we will start with a pilot study to validate the setup and to assess valuable initial outcomes. To minimize the load on the volunteers and taking into account the limited availability of DTEHV biomaterial, we will start with a total of n=4 volunteers. These will be healthy male volunteers in the age between 25 and 35.

Study design

At the day of the experiment, 50 ml of blood will be collected from a volunteer via a single venous puncture after the volunteer had given us his consent. After blood collection, the volunteer will no longer participate in the study. The collected blood will be used immediately for the in vitro experiments. Subsets of blood cells will be separated via density gradient spinning. The two obtained subsets (the granulocyte and agranulocyte cell fraction) will be separated. These subsets will be stained with a live cell staining, after which the subpopulations will be mixed again. These stained cells will be used in the in vitro experimental set up.

A sample of the stained cell population will be taken prior to exposure to the biomaterial as a control sample, representative for time point 0. Subsequently, the stained cells are exposed to the biomaterials in the flow-setup. In total, 4 individual flow systems are available for simultaneous use. Each system will contain a different type of biomaterial. We have a scaffold-based sample, a scaffold-based sample with tissue, and a non-scaffold based sample with tissue.

As a control group we have a test setup without a biomaterial. Each of the setups will contain the same amount of blood from the same donor (7.5 ml each).

The analyses that will be performed on the circulating cell samples will be flow cytometry, ELISA and qPCR to assess the composition and response of the circulating cells to the biomaterials. During the in vitro experiment, samples will be collected for analyses every hour. After a total of 5 hours, the experiment will be terminated. The biomaterials will be processed for qPCR, fluorescence microscopy and SEM analyses to assess the response of the infiltrated cells into the biomaterials.

Study burden and risks

The physical load on the volunteers is low. Just one single vena puncture. The associated risks are low and the total amount of collected blood is small (50 ml)

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

• Male persons
• Feeling physically healthy, defined as not having fever or flu-like symptoms.

Exclusion criteria

• Known infectious / genetic diseases, which could affect the immune system

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	15-09-2015
Enrollment:	4
Type:	Actual

Ethics review

Approved WMO

Date:	23-07-2015
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	NL53574.100.15