Photoacoustic detection and monitoring of synovitis in finger joints with rheumatoid arthritis.

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-To determine the feasibility of detection of synovitis by photoacoustic imaging using three discrete wavelengths of pulsed light as an early indicator of the presence of RA.-To correlate the photoacoustic markers that are indicative for...

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

Summary

ID

NL-OMON43735

Source
ToetsingOnline

Brief title
Photoacoustic detection of rheumatoid arthritis.

Condition

- Autoimmune disorders

Synonym
Rheumatoid Arthritis

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Twente
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Photoacoustic tomograhpy, Rheumatoid arthritis, synovitis

Outcome measures

Primary outcome

The main study parameter/endpoint is the feasibility of finding structural markers for RA with photoacoustic imaging. These structural markers can, for a part, be compared with conventional methods such as physical examination and ultrasound imaging.

We expect to see the known physical differences (literature) that are encountered in RA such as edema, hypertrophy and a synovial membrane that is thickened and which has an increased vascularity.

Secondary outcome

From the obtained parameters of the fase 1 research we will define new specifications for a new generation of imaging device and improve the new image processing algorithms.

Study description

Background summary

Current methods to detect or diagnose rheumatoid arthritis (RA) are based on physical examination and ultrasound (US) imaging, while x-ray imaging and MRI imaging are used in problem-solving situations.
Physical examination is not sensitive enough for early stage diagnostics. US imaging is moderately sensitive to the synovium of the joint where the first changes are expected to be witnessed. These indicators are thickening of the synovial membrane, hypertrophy, edema (swelling) in the joint capsule and an increased blood volume. The latter is detectable using the power Doppler mode. However the technique suffers from subject-to-subject and inter-observer variation. X-ray imaging is limited to changes in bony structures, that occur

only after months to years of joint inflammation. MRI imaging is sensitive and specific, but requires contrast agents, is expensive and because of that relatively less accessible.
Photoacoustic imaging is a new modality that has the capacity to visualize blood vessels in soft tissue without the use of contrast agents. Pulsed light is absorbed by haemoglobin in blood which produces ultrasound by the photoacoustic effect. This ultrasound can be measured with high resolution ultrasound transducers. An increased density of blood vessels and/ or increased blood flow are hallmarks of joint inflammation which constitutes an early step in the progression of RA. Photoacoustic imaging promises visualization of synovial vascularity, since it reflects the presence of haemoglobin.
This method is expected to improve sensitivity and specificity of imaging in early arthritis. We will investigate the feasibility of using the method on a small population of patient volunteers.

Study objective

-To determine the feasibility of detection of synovitis by photoacoustic imaging using three discrete wavelengths of pulsed light as an early indicator of the presence of RA.
-To correlate the photoacoustic markers that are indicative for inflammation with conventional RA imaging modalities and clinical examination.
-To make/propose technological changes based on clinical experiences, and to use the results in the development of new generations of photoacoustic imaging devices that will be used in phase 2. (amendment)
-To find appropriate image analysis methods in order to get the best contrast and resolution within the investigated finger joint.

Study design

Two proximal interphanlengeal finger joints of a total of 30 patients and 20 healthy volunteers will be investigated by ultrasound imaging and photoacoustic imaging (three wavelengths). The total duration of the study is 2 years.

In phase 1, which will last for 1 to 3 months, 10 patients with highly inflamed PIP joints and 10 healthy volunteers are measured. Those measurements and results will be used for optimization of the measurement protocol and analysis algorithms that we use for the design and modification of the systems used in phase 2.

In phase 2, which will last till the end of 2015, new generations of imaging devices will be tested. Two new improved versions have been developed. Each of these versions requires 10 patients and 10 healthy subjects to test the main question of the research. This results in a total of 20 patients and 20 healthy subjects in phase 2.

A total of 30 patients and 30 healthy volunteers will be included in the whole project (fase1 +2)

Study burden and risks

The only burden for the patients is a 2 hour visit at the University of Twente. The rheumatologist will clinically investigate finger joints of the patient first. Followed by ultrasound and Doppler imaging of the finger joints (total 5-10 min).
The photoacoustic measurements will consist of two scans of approximately 15 minutes.

A thorough risk analysis was performed by the clinical physician and the medical instrumentation group of the ZGT.
The clinical physicians assessed the possible risks that are related to the use of laser sources. Based on their advice we improved the laser safety on several topics. All advices were included into the user protocol. The nominal ocular hazard distance (NOHD) and the hazard distance are taken into account. Additional warning signs were placed and the required safety level of the laser safety goggles is checked according to the most strict rules: EN 207. The EN 207 rules include a high optical density and a high damage threshold of the used safety glasses.

The medical instrumentation group looked into the electrical safety of the whole setup. No harm can be done to the patients because of the used isolation transformer which protects against current leakages. The isolation transformer does this by separating the setup from the grid main power. (IEC60601-1 en IEC60601-1-1)
Only after written permission from the Clinical physician and the medical instrumentation group we will be allowed to start with patient measurements.

Level of knowledge about mechanism of action
Due to light absorption, tissue experiences a temperature rise when exposed to laser light. To prevent tissue injury, the maximum permissible laser energy output is restricted to standards. These values are dependent on the used wavelength, beam geometry, scale and duration of measurement. This calculation is based on the following two conditions from the international standard IEC 60825-1,and the Dutch norm (Richtlijn) 2006/25/EG:

1. The exposure from any single pulse within a pulse train shall not exceed the MPE for a single pulse.
2. The average exposure for a complete pulse train of exposure duration T shall not exceed the MPE for a single pulse of exposure duration T.

Photoacoustics has been intensively investigated for medical purposes for the past decade. The most important risk factor is the used amount of light in from the laser source. International safety rules apply for all uses of laser light.

MPE levels for skin and eyes were carefully defined for medical use.
During the experiments of this research the used laser will not exceed not exceed the MPE levels for the skin. Safety measures have been taken in the user protocol to ensure the safety of both user and patient.

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

* Men and women of 18 years and older that are fully competent to give informed consent first phase:
* Patients with at least one proximal interphalangeal joint with clinically evident inflammation, significant joint effusion, hypertrophy (referred by their rheumatologist) and a postive power Doppler score.

Exclusion criteria

* Patients with a cardiovascular disease
* Patients with bloody discharge, ulcers or wounds on the hands.
* Patients with a history of non-RA related injuries/ surgeries in the joints of interest.
* Patients lacking a good general health.
* Patients who suffer from tremors.
* Patients who are incompetent to give informed consent

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-07-2013
Enrollment:	50
Type:	Actual

Ethics review

Approved WMO Date:	29-04-2013
Application type:	First submission
Review commission:	METC Twente (Enschede)
Approved WMO Date:	04-09-2014

Application type:	Amendment
Review commission:	METC Twente (Enschede)
Approved WMO Date:	27-09-2016
Application type:	Amendment
Review commission:	METC Twente (Enschede)

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	NL42249.044.12