Fluoride PET-CT imaging for the detection of bone formation in (very) early and preclinical spondyloarthritis.

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To investigate if subjects with an increased risk of developing spondyloarthritis have evidence of bone formation on [18F] Fluoride PET-CT.

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

Summary

ID

NL-OMON55045

Source
ToetsingOnline

Brief title
[18F]Fluoride PET in pre-SpA

Condition

- Joint disorders

Synonym
arthritis of the back, Spondyloarthritis

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Jan van Breemen instituut

Intervention

Keyword: Imaging, PET, Spondyloarthritis

Outcome measures

Primary outcome

Our main endpoint is [18F]Fluoride uptake present in the sternum, spine and SI joints on whole body PET-CT scans in 10 participants with sacroiliitis on MRI and 10 participants without sacroiliitis on MRI of the Pre-Spa cohort. Both percentage of participants with any PET-positive lesion as well as dichotomous scores of lesions and cumulative scores per participant will be described.

Secondary outcome

Comparison of clinical features between individuals with [18F] PET positive lesion and those with negative [18F]PET-CT at baseline and follow up following the Pre-Spa Study protocol until five years after start of the study.

Evaluate if presence of [18F]Fluoride PET-lesions is related to molecular features (e.g. gene expression or serum biomarker).

Study description

Background summary

Axial spondyloarthritis (axSpA) is a chronic inflammatory arthritis with a prevalence of 0,5-1% in Western countries. The disease starts in young adults, mainly males, between the age of 20-40 years and is characterized by inflammation and new bone formation with structural damage of the spine. This results in pain and limited mobility of the spine with a high impact on functioning in daily life. The disease entity comprises both non-radiographic axSpA where no structural changes are seen on conventional imaging as well as radiographic axSpA also referred to as ankylosing spondylitis where structural lesions of the spine or sacroiliac joints are present. Despite recent advances in therapeutic options for axSpA it is still not possible to sufficiently

control inflammation in all patients, as only 60- 70% of the patients respond of whom 30% only partially. Disease remission is only achieved in about 20% of the patients. In addition, so far no effects on halting new bone formation have been shown. This results in functional impairment and loss of quality of life for most axSpA patients.

Possibly this limited efficacy can be explained by: 1.Available treatments are not aimed at the right targets to stop inflammation and new bone formation. 2.The diagnostic delay disables us to initiate treatment early enough to halt the chronic autonomous inflammation and new bone formation sufficiently.

To target inflammation and new bone formation more successfully it is essential to increase the insight into the pathogenic processes that initiate and drive inflammation and new bone formation in axSpA, and make an earlier diagnosis.

Both inflammation and new bone formation can be visualized by various imaging modalities. Active inflammatory lesions of the spine and SI joints can be seen on MRI. We have previously shown that with [18F]Fluoride PET-CT it is possible to study the active process of new bone formation. This is in contrast to X-rays of the spine or SI joints with which only end stage destruction can be visualized. It was confirmed by histology that [18F]Fluoride PET-CT lesions in ankylosing spondylitis patients represent active local osteoid formation, representative of new bone formation, and that these lesions are responsive to TNF treatment. This underlines that [18F]Fluoride PET-CT is a robust method to evaluate bone bone formation in axSpA patients.

In axial spondyloarthritis it is hypothesized that molecular processes that trigger inflammation and new bone formation are initiated even before the disease becomes clinically manifest This phase is called the pre-clinical phase.
First-degree relative (FDR) of axSpA patients have an increased risk of developing disease compared to the general population. Familial studies showed that the recurrence risk of AS in HLA-B27 positive FDRs of AS is 20%. When including early (pre-radiographic) disease stages of SpA, this recurrence risk in HLA-B27 positive FDRs of axial SpA is approximately 30-40%. We have previously shown that indeed subclinical signs of spondyloarthritis can be observed in upto 25% of these at risk FDR of HLA-B27+ axSpA patients. Interim analysis of 1 year follow up in 123 FDR showed that 6% developed clinically manifest disease in the first year. These data indicate that there is a high incidence of pre-SpA in these FDRs and that disease incidence is much higher than in the general population which thus supports the rational of studying this population at risk.

Of importance, pwe have shown in healthy first-degree relatives (FDRs) of HLA-B27+ xSpA patients at risk of developing AxSpA, that 20% had sacroiliitis on MRI of the SI-joints (but no clinical diagnosis of AxSpA). Underlining that in at risk individuals already imaging abnormalities suggestive of

(subclinical) inflammation can be observed. So far, no data on new bone formation in at risk individuals is available.

Study objective

To investigate if subjects with an increased risk of developing spondyloarthritis have evidence of bone formation on [18F] Fluoride PET-CT.

Study design

A cross-sectional, monocenter PET study in 20 patients with an increased risk of developing axial spondyloarthritis.

Study burden and risks

The total radiation burden will be about 4.0 mSv.

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

- First degree relative of HLA-B27 positive AxSpA patients
- Age between 18 and 40 years at time of inclusion
- Able and willing to give written informed consent
- 10 participants with an MRI highly suggestive of SpA according to the ASAS definition at baseline
- 10 patients without an MRI highly suggestive of SpA according to the ASAS definition at baseline

Exclusion criteria

- Patients already diagnosed with spondyloarthritis
- Individuals with concomitant conditions which may impact participation to the study or interpretation of the data, such as:
- Individuals that have an arthritic disease, other than SpA
- Individuals that have a diagnosed condition with back pain other than SpA (e.g. diagnosed intervertebral disc degenration)
- Individuals with communication problems
- Individuals with psychiatric diseases
- Individuals with drug abuse
- Individuals with a life expectancy less than 5 years
- Individuals who are pregnant or have a positive hcg urine test
- Individuals who are breastfeeding
- Individuals who have received treatment with any investigational drug within previous 3 months
- Individuals who already received a research related radiation burden (cumulative > 5 mSv) in the year before inclusion
- Other conditions by judgement of the physician

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):	01-02-2021
Enrollment:	20
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	[18F]Fluoride
Generic name:	[18F]Fluoride

Ethics review

Approved WMO Date:	09-10-2020
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	05-03-2021
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
EudraCT	EUCTR2020-001422-62-NL
CCMO	NL73580.018.20