Value of MRI - DWI in Assessment of Disease Activity in pulmonary parenchymatous lokalization of Sarcoidosis

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Primary Objectives: 1. Is it feasible to visualize active inflammation in patients with pulmonary sarcoidosis by using Diffusion Weighted Imaging when compared to 18F-FDG PET?Secondary Objectives: 1. Is it feasible to visualize lymph node…

Ethical review	Approved WMO
Status	Pending
Health condition type	Lower respiratory tract disorders (excl obstruction and infection)
Study type	Observational invasive

Summary

ID

NL-OMON37541

Source
ToetsingOnline

Brief title
MRI-DWI in Assessment of Activity of Sarcoidosis / MAAS

Condition

- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
Sarcoidosis

Research involving
Human

Sponsors and support

Primary sponsor: Sint Antonius Ziekenhuis

Source(s) of monetary or material Support: subsidie onderzoeksfonds Sint Antonius Ziekenhuis

Intervention

Keyword: Activity, DWI, Sarcoidosis

Outcome measures

Primary outcome

Presence of active inflammation in the pulmonary parenchyma as assessed by DWI,

compared to the gold standard using a qualitative assessment (positive or

negative for presence of disease activity).

Secondary outcome

Pulmonary parenchymatous lesions:

- ADC values (MRI: DWI)

- Contrast ratio consolidation / paraspinal muscle (MRI: STIR)

- SUV max (FDG-PET)

- enhancement characteristics

Mediastinal and hilar lymph nodes:

- Presence of disease activity in mediastinal and hilar lymph nodes as assessed

by DWI

- ADC value (MRI: DWI)

- Correlation of contrast ratio consolidation / paraspinal muscle (MRI: STIR).

- SUV max (FDG-PET)

Evaluation of false positive and false negative results.

Study description

Background summary

Sarcoidosis is an idiopathic, inflammatory disease characterized by the formation of non-caseous granulomas. In about two-thirds of patients there is a spontaneous remission of the disease, whereas 10-30% of patients experience a chronic or progressive course.
In symptomatic patients with a new presentation of sarcoidosis and the presence of typical intrathoracic abnormalities on imaging and/or biopsy, there is no doubt regarding the presence of active disease. However, in sarcoidosis patients with chronic pulmonary consolidations and persisting symptoms, the assessment of disease activity is more difficult as symptoms of dyspnoea and fatigue are aspecific and may be caused by old fibrotic changes as well as by ongoing, active inflammation. A gold standard for identification of active inflammation is currently lacking. According to the ATS/ERS/WASOG consensus report 1 active disease is defined as clinical symptoms w/wo active formation of granulomas w/wo immunological biomarkers w/wo progression to fibrosis and is thus based on the combination of clinical markers, biochemical markers, pulmonary function, imaging and/or histopathology.
The presence or absence of active disease has important therapeutic implications, because active inflammation can be treated with immune suppressive therapy (prednisone, infliximab) whereas chronic fibrosis is treated with supportive care. The ability to assess disease activity allows selective administration of immune suppressive therapy (TNFα inhibitors) and response monitoring during therapy.

Recent studies show that 18F-FDG PET is able to detect active inflammation within chronic pulmonary consolidations in patients with sarcoidosis.2,3 In newly diagnosed patients, Keijsers et al found a sensitivity of 97% of 18F-FDG PET in identifying sarcoidosis activity. 3 In a systematic review of Treglia et al regarding the emerging role of 18F-FDG PET as a marker of disease activity, two important conclusions were: 1) 18F-FDG PET seems to be a very useful molecular imaging method in assessing disease activity, in staging and identifying occult sites, and in monitoring treatment response in patients with sarcoidosis and 2) 18F-FDG PET shows a better diagnostic accuracy compared to 67Ga scintigraphy in patients with sarcoidosis, based on the higher sensitivity.4 Milman et al. have shown that disease activity, as shown by 18F-FDG PET uptake, decreased during treatment with TNFα inhibition (adalimumab) compared to pre-treatment FDG uptake.8

An important drawback of 18F-FDG PET is the radiation burden. The effective dose is estimated to be 4,4 mSv for PET alone, 13,5 mSv for combined PET / non-diagnostic CT and 14 to 25 mSv for combined FDG PET / diagnostic CT (depending on scan parameters).9, 10 For a combined FDG PET / diagnostic CT

study, the lifetime attributable risk of cancer incidence was estimated 0.231 to 0.514% for a 20-year old female and 0.163 to 0.323% in a 20-year old male. Because sarcoidosis patients are usually young or middle aged adults, a non-radiation emitting study such as MRI would be preferred to assess and monitor sarcoidosis activity.

Diffusion weighted MR imaging visualizes the movement of water molecules within biological tissues. The ability of water molecules to diffuse is dependent on the characteristics of the particular tissue they reside in. The presence of intracellular organelles, macromolecules, and integrity of cell membranes cause diffusion of intracellular water molecules to be more restricted than that of water molecules in the extracellular space. The degree of diffusion restriction of water molecules is an intrinsic tissue property, and is reflected in the signal intensity on DWI. Diffusion can be quantified by calculating the apparent diffusion coefficient (ADC value). DWI has an important, established role in the detection of acute cerebral ischemia, in abdominal MRI, and in imaging of pancoast tumours. Its use in thoracic and oncological imaging is growing. Studies have shown diffusion weighted imaging (DWI) valuable in differentiating between benign and malignant pulmonary nodules and lymph nodes, and between lung carcinoma and post obstructive atelectasis 5,11. Furthermore, (whole-body) MRI with DWI can be used for N- and M-staging in patients with non-small cell lung cancer, and a number of studies have shown an accuracy comparable to FDG-PET 6,7. Currently, the value of DWI in sarcoidosis (or any other interstitial lung disease) has not yet been investigated.

In areas with active inflammation, cellularity is higher than in fibrotic regions, which means that the ratio between the intra- and extracellular compartment is larger in inflammation compared to fibrosis. The diffusion of water molecules will be more restricted in inflamed areas than in fibrosis.

Our hypothesis is that it is feasible to detect active inflammation with DWI in patients with a new presentation of sarcoidosis and to differentiate active inflammation from fibrosis in patients with chronic pulmonary infiltrates (compared to 18F-FDG PET). We also believe it is feasible to detect intrathoracic lymph node localizations of sarcoidosis.

Most pathologic processes, such as tumor and inflammation, lead to an increase in T1 and T2 relaxation times. Fibrosis causes shortening of T2. The imaging sequense STIR TSE (short T1 inversion recovery turbo spin-echo) is very sensitive to changes in T1 and T2. Recent studies have shown STIR to be more sensitive than DWI in detecting pulmonary malignancies and in differentiating different subtypes of adenocarcinoma.12 In a large, prospective cohort, Ohno et al. found STIR imaging more sensitive and accurate than DWI and integrated 18F-FDG PET-CT in the N-stage assessment of patients with NSCLC.13
In our protocol, we have added a STIR TSE sequence to investigate whether it is possible to differentiate between inflammation and fibrosis based on

differences in T1 and T2 relaxation times.

Study objective

Primary Objectives:
1. Is it feasible to visualize active inflammation in patients with pulmonary sarcoidosis by using Diffusion Weighted Imaging when compared to 18F-FDG PET?

Secondary Objectives:
1. Is it feasible to visualize lymph node localisation of sarcoidosis by using Diffusion Weighted Imaging when compared to 18F-FDG PET?
2. Is there a relationship between the contrast ratio of parenchymatous sarcoidosis on STIR and metabolic activity as assessed by 18F-FDG PET?
3. Is there a relationship between enhancement of parenchymatous sarcoidosis on MRI and metabolic activity as assessed by 18F-FDG PET?

Study design

This is an observational (pilot) study in sarcoidosis patients who undergo a 18F-FDG PET scan for detection of active inflammation.
The proportion of active inflammation found with 18F-FDG PET and DWI will form the basis for a sample size calculation needed for a larger validation study.

Patients with a new presentation of pulmonary localized sarcoidosis are included (n=10), as well as patients with chronic pulmonary infiltrates secondary to active inflammation or fibrosis (n=10).
MRI with DWI is added to the regular work-up of these patients, which includes laboratory investigation, pulmonary function tests, a CT scan of the chest and a 18F-FDG-PET scan.

Study burden and risks

Burden: MRI scan of the thorax (duration 45 minutes).

The risk is equal to that of a regular MRI scan with intravenous contrast and relates to the presence of a strong magnetic field.
Patients will be asked to fill in the regular contra-indication form prior to the MRI scan. Prior to the MRI scan renal function will be assessed.

There is no direct personal benefit for participants.
If results are favourable, we expect a benefit for sarcoidosis patients as a group, because then an non-radiation examination would make detection and monitoring of sarcoidosis activity possible.

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

sarcoidosis with a pulmonary (parenchymatous) localisation

Exclusion criteria

- Asymptomatic patient
- Co-existing pulmonary or medastinal pathology (malignancy, pneumonia)
- Contra-indications for MRI, for example:
* MRI incompatible pacemaker
* MRI incompatible insulin pump or nerve stimulator
* MRI incompatible prosthetic heart valve
* vascular clips

* ossicular chain prosthesis
- Doubt regarding the diagnosis of sarcoidosis
- Immune suppressive therapy
- Renal insufficiency (glomerular infiltration rate < 60 ml/min)
- Pregnancy or breast feeding

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2012
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	14-08-2012
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	NL38882.100.12