Ga-68-DOTA-(RGD)2 PET/CT: imaging angiogenesis in patients with low-flow vascular malformations

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The primary objective of this study is to measure whether αvβ3 integrin expression and tracer uptake values of 68Ga-DOTA-(RGD)2 change in patients with (recurrent) low-flow vascular malformations after embolization therapy.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Cardiac and vascular disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON44225

Source
ToetsingOnline

Brief title
Ga-68-DOTA-RGD2 PET/CT in low-flow vascular malformations

Condition

- Cardiac and vascular disorders congenital

Synonym
low-flow vascular malformation, lymphatic malformation, venous malformation

Research involving
Human

Sponsors and support

Primary sponsor: Radiologie en Nucleaire Geneeskunde
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: alpha-v-beta-3 integrin, Feasibility study, Low-flow vascular malformations, Lymphatic malformations, PET imaging, Venous malformations

Outcome measures

Primary outcome

The main study parameter is the tracer uptake (68Ga-DOTA-(RGD)2) in the

low-flow vascular malformation, as quantified by PET/CT. The tracer uptake is

calculated as the ratio of the tissue radioactivity concentration c (MBq/kg)

and the injected activity (MBq), divided by the body weight (kg):

SUV=c/(injected activity/weight). SUV data will be presented as mean and

standard deviations.

Secondary outcome

The additional study parameter is the lesion-to-background ratio (LBR).

Study description

Background summary

Vascular malformations are congenital anomalies of the vascular or lymphatic system. These malformations can be classified as low-flow and high-flow according to their hemodynamic characteristics. Arteriovenous malformations (AVM) are high-flow due to the arterial blood flow pattern. Venous malformations (VM) and lymphatic malformations (LM) are low-flow lesions. This study focuses on low-flow vascular malformations.
With increasing age and length of the patient, the vascular malformation grows as well, and shows no tendency towards spontaneous involution. Lesion-related complications include pain, swelling, infections, hemorrhage or functional concerns depending on the location of the vascular malformation. In order to prevent lesion-related complications and to reduce the size of the lesion, treatment is often indicated. Management options include surgery and embolization therapy. Embolization therapy is favorable, but the treatment plan is complex and invasive with multiple embolizations and thorough follow-up. Moreover, recurrence or and residue with persisting complaints is common.

The exact mechanism of recurrence of a vascular malformation is still unknown. However, angiogenesis and vasculogenesis are considered to play an important role in formation and growth of vascular malformations. With recent progress in molecular imaging, angiogenesis can be imaged using a non-invasive 68Ga-DOTA-(RGD)2 PET/CT scan. 68Ga-DOTA-(RGD)2 is a radiolabeled RGD-based peptide that binds to αvβ3 integrin, which is expressed on newly-formed blood vessels. After injection of 68Ga-DOTA-(RGD)2, the localization of the vascular malformation can be imaged and uptake values can be measured. Assessment of the uptake values and the dynamics in αvβ3 integrin expression after embolization therapy might result in adapted management, considering a combination of embolization therapy with angiogenesis inhibitors.

Study objective

The primary objective of this study is to measure whether αvβ3 integrin expression and tracer uptake values of 68Ga-DOTA-(RGD)2 change in patients with (recurrent) low-flow vascular malformations after embolization therapy.

Study design

In this pilot study, included patients will undergo a 68Ga-DOTA-(RGD)2 PET/CT scan twice. A 10-minutes static PET/CT scan is performed 60 minutes after intravenously injection of 68Ga-DOTA-(RGD)2 (100-200 MBq, 70 µg peptide). This procedure will be repeated after multiple embolization procedures or after the last treatment in case of complete radiological response or relief of symptoms.

Study burden and risks

In each patient, one blood sample will be taken to determine whether liver- and kidney functions are within the normal range. This venous blood sampling will be performed during the screening procedure, which will preferably be scheduled during a regular hospital visit and otherwise will be performed by the general practitioner. In addition, the patient will come to the hospital for the PET/CT procedure. During this visit, a history on general condition will be taken and a venous cannula will be placed for injection of the radiolabeled peptide.
The risks associated with the radiolabeled peptide injection are low. Toxicity tests have been performed in mice and no adverse reactions were seen. Placement of the venous cannula can cause local bruising.
The combination of 68Ga-DOTA-(RGD)2 and the low-dose CT will cause a radiation dose equivalent of 4.7-5.2 mSv to the patient, depending on the location of the vascular malformation that will be imaged. During normal work-up (standard of care) patients receive a radiation dose between 1.5 mSv and 200 mSv, depending on the location of the vascular malformation that is treated (radiation dose of an embolisation of a vascular malformation in the lower and upper extremities is approximately 1.5 mSv, the radiation dose during treatment of a vascular malformation in the abdomen is between 11-200 mSv, depending on the extent of

the lesion). The addition of the 68Ga-DOTA-(RGD)2 PET/CT scan will therefore not cause a change in risk: patients with a vascular malformation in the lower and upper extremities will still be in category IIb, patients with a vascular malformation in the abdomen are in category III as defined by the International Commission on Radiation Protection (ICRP).
Diagnostics and treatment of the subject are not influenced by the outcome of this study and therefore the patient will not directly benefit from participation in this study. However, imaging angiogenesis could contribute to improved understanding of the pathophysiology of low-flow vascular malformations and therefore has potential to improve treatment options.

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

- Patients with a low-flow vascular malformation, who are scheduled for embolization therapy;- More than or equal to 18 years of age;- Ability to provide written informed consent

Exclusion criteria

• Contra-indication for PET/CT: Pregnancy, Breast-feeding, Severe claustrophobia;• Impaired renal function: Creatinine clearance <= 60 mL/min according to The Cockcroft-Gault equation;• Impaired liver function: ALAT, ASAT >= 3x ULN or Total bilirubin >= 2x ULN ;• Other serious illness

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-10-2018
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	nvt
Generic name:	Ga-68-DOTA-RGD2

Ethics review

Approved WMO Date:	07-12-2017
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-03-2018
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	05-04-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	03-10-2018
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2017-003666-27-NL
CCMO	NL63173.091.17