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# BMJ Open

## Identification of anatomic risk factors for acute coronary events by Optical Coherence Tomography in patients with myocardial infarction and residual non-flow limiting lesions: Rationale and design of the PECTUS-obs study.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048994
Article Type:	Protocol
Date Submitted by the Author:	12-Jan-2021
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Keywords:	Coronary heart disease < CARDIOLOGY, Coronary intervention < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

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4 1 **Identification of anatomic risk factors for acute coronary events by**  
5 2 **Optical Coherence Tomography in patients with myocardial**  
6 3 **infarction and residual non-flow limiting lesions: Rationale and**  
7 4 **design of the PECTUS-obs study.**  
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31 *Word count*

32 2650

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34 *Keywords*

35 Myocardial Infarction (MI), Non-culprit Lesion, Fractional Flow Reserve (FFR), Optical Coherence

36 Tomography (OCT), Vulnerable Plaque

37

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45

## 46 **Abstract**

### 47 **Introduction**

48 In patients with myocardial infarction, the decision to treat a non-culprit lesion is generally based on  
49 its physiological significance. However, deferral of revascularization based on non-ischemic fractional  
50 flow reserve (FFR) values in these patients results in less favorable outcomes compared to patients  
51 with stable coronary artery disease (CAD), potentially caused by vulnerable non-culprit lesions.  
52 Intravascular optical coherence tomography (OCT) imaging allows for in vivo morphological  
53 assessment of plaque 'vulnerability', and might aid in the detection of FFR-negative lesions at high  
54 risk for recurrent events.

### 55 **Methods and analysis**

56 The PECTUS-obs study is an international multicenter prospective observational study that aims to  
57 relate OCT-derived vulnerable plaque characteristics of non-flow limiting, non-culprit lesions to  
58 clinical outcome in patients with myocardial infarction. A total of 438 patients presenting with  
59 myocardial infarction (STEMI and NSTEMI) will undergo OCT-imaging of any FFR-negative non-culprit  
60 lesion for detection of plaque vulnerability. The primary study endpoint is a composite of Major  
61 Adverse Cardiovascular Events (all-cause mortality, non-fatal myocardial infarction, or unplanned  
62 revascularization) at 2-year follow-up. Secondary endpoints will be the same composite at 1- and 5-  
63 year follow-up, target vessel failure, target vessel revascularization, target lesion failure and target  
64 lesion revascularization.

### 65 **Ethics and dissemination**

66 This study has been approved by the Medical Ethics Committee of the region Arnhem-Nijmegen. The  
67 results of this study will be disseminated in a main paper and additional papers with subgroup  
68 analyses.

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3 69 **Registered under NCT03857971 on 28-02-2019**  
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9 **Strengths and limitations of this study**

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11 72 • The PECTUS-obs is the first prospective study to assess the incremental value of OCT imaging  
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13 73 of FFR-deferred non-culprit lesions in patients presenting with MI.  
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15 74 • OCT is the only imaging modality with a spatial resolution high enough to truly measure  
16  
17 75 fibrous cap thickness, the plaque feature most associated with adverse events.  
18  
19 76 • In PECTUS-obs, OCT imaging will only be performed at baseline. However, any new MI or  
20  
21 77 revascularization will be allocated to a specific coronary vessel and lesion by comparison of  
22  
23 78 the baseline and follow-up angiograms.  
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25 79 • If intracoronary imaging with OCT is able to identify lesions associated with worse outcome,  
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27 80 this might warrant studies on focal or pharmacological intervention of OCT-determined  
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29 81 vulnerable plaques.  
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## 85 Introduction

86 In patients presenting with myocardial infarction (MI), percutaneous coronary intervention (PCI) of  
87 the culprit lesion is the standard method of treatment. [1] A high percentage of these patients have  
88 additional lesions at different sites in the coronary arteries, not responsible for the acute event. The  
89 optimal treatment of these non-culprit lesions is subject of extensive research, because their  
90 presence confers a greater risk of future major adverse cardiac events (MACE) [2, 3]. Recent studies  
91 showed that complete revascularization results in improved outcomes compared to treatment of the  
92 culprit lesion only. [4-6] However, non-selective revascularization of all non-culprit lesions may lead  
93 to overtreatment.

94 The selection of non-culprit lesions qualifying for revascularization is often based on whether a  
95 lesions causes ischemia, as determined by invasive measurements such as the fractional flow reserve  
96 (FFR). [7] In patients with stable coronary artery disease (CAD), FFR-guided complete  
97 revascularization results in better outcomes compared to angiography guided complete  
98 revascularization. [8] Nevertheless, the MACE rates at longer term follow-up remains significant in  
99 the presence of non-significant CAD. [9] In patients presenting with MI this recurrence rate of  
100 ischemic events is even higher. [10] A recent study demonstrated a MACE rate of 23% in acute  
101 coronary syndrome (ACS) patients vs. 11% in patients with stable CAD at 3.4-years follow-up, after  
102 FFR based deferral of revascularization. Among these ACS patients, especially those presenting with  
103 NSTEMI had a high event rate (42%). [11]

104 Apart from coronary physiology, the structural components of non-culprit lesions might provide  
105 other markers for future adverse events. Autopsy studies have granted insight into the lesion  
106 characteristics that are associated with plaque rupture, and subsequent MI or sudden death. These  
107 lesions tend to contain a large lipid pool with a thin overlying fibrous cap, and display a large degree  
108 of outward remodeling. [12, 13] These 'thin-cap fibroatheromas' (TCFA) are more frequently  
109 observed in both culprit- and non-culprit lesions of patients presenting with MI than in patients

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3 110 presenting with stable CAD. [14-16] Therefore, screening for vulnerable plaques on top of  
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5 111 physiological measurements, should be evaluated for non-culprit lesions.  
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8 112 Analysis of lesion composition can be performed in vivo with the use of intravascular imaging  
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10 113 techniques such as intravascular ultrasound (IVUS), near infrared spectroscopy (NIRS) and optical  
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12 114 coherence tomography (OCT). [17] Prospective studies using IVUS and NIRS showed that  
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14 115 identification of lesions at higher risk for future events is feasible. [18, 19] However, OCT might prove  
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16 116 more suitable for this purpose, due to its specific characteristics. OCT has a 10-20 times higher spatial  
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18 117 resolution than IVUS, allowing for better detection of TCFA. Moreover, a complete acquisition of a  
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20 118 coronary segment can be provided within a couple of seconds, with a single pullback. Last,  
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22 119 (semi)automated analysis of images is more feasible due to the high resolution of the acquired  
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24 120 images. [20] Nevertheless, OCT has yet to be prospectively validated for its ability to identify lesions  
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26 121 at risk for future MACE in MI patients.  
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31 122 For future studies on potential preventive revascularization or more aggressive pharmacological  
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33 123 therapy in patients with high risk lesions, prospective studies with clinical outcomes are imperative.  
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35 124 In the PECTUS-obs study, we aim to relate OCT-derived plaque characteristics of not significantly flow  
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37 125 limiting, non-culprit lesions to clinical outcome in patients presenting with MI.  
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## 127 **Methods and analysis**

### 128 *Overview*

129 The PECTUS-obs study is designed as an international multicenter prospective observational study.  
 130 Eligible patients have to undergo an index CAG during hospitalization for an acute myocardial  
 131 infarction, which reveals one or more non-culprit lesions accessible for imaging with OCT. FFR-  
 132 measurements of these non-culprit lesions are made during the same index procedure, or during a  
 133 staged procedure. Any FFR-nonsignificant lesions are subsequently imaged with OCT. Additional  
 134 criteria are listed in table 1. A total of 438 patients will be included. A flow-chart of the study design  
 135 is depicted in figure 1.

**Table 1. Inclusion- and exclusion criteria**

Inclusion criteria	Exclusion criteria
<p style="text-align: center;"><b>Clinical</b></p> <ul style="list-style-type: none"> <li>- Age <math>\geq</math> 18 years</li> <li>- Hospitalization with a STEMI or NSTEMI for which patient is subjected to invasive coronary angiography (within the last 6 weeks).</li> </ul> <p style="text-align: center;"><b>Angiographical</b></p> <ul style="list-style-type: none"> <li>- Patient has <math>\geq</math> 1 non-culprit, target lesion(s) with following additional characteristics:               <ul style="list-style-type: none"> <li>o Lesion has visual stenosis of 30-90%.</li> <li>o Lesion is non-obstructive (FFR <math>&gt;</math> 0.80).</li> <li>o Lesion is not in-stent restenosis.</li> </ul> </li> </ul>	<p style="text-align: center;"><b>Clinical</b></p> <ul style="list-style-type: none"> <li>- Pregnancy.</li> <li>- Hemodynamic instability, respiratory failure, or Killip class <math>\geq</math> 3 at time of inclusion.</li> <li>- Previous CABG.</li> <li>- Indication for revascularization by CABG.</li> <li>- Estimated life expectancy <math>&lt;</math> 3 year.</li> </ul> <p style="text-align: center;"><b>Angiographical</b></p> <ul style="list-style-type: none"> <li>- Anatomy of target lesion(s) is unsuitable for OCT catheter crossing or imaging (aorta-ostial lesions, too small diameter segment, severe calcifications, chronic total occlusion, distal lesions prohibiting OCT imaging).</li> </ul>
<p><b>Table 1. Inclusion- and exclusion criteria</b>            CABG, coronary artery bypass grafting, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction, OCT, optical coherence tomography, STEMI, ST-elevation myocardial infarction</p>	

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3 137 *Patients and enrolment*  
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6 138 Patients presenting with MI (ST-elevation and non ST-elevation) are screened for potential inclusion  
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8 139 in the study. Patients are treated according to the current guidelines for the management of ACS,  
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10 140 including referral for CAG and (potential) PCI of the culprit artery. In case of one or more non-culprit  
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12 141 lesions of intermediate stenosis (30-90%), clinically indicated FFR measurements are performed in  
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14 142 order to determine if these non-culprit stenoses are hemodynamically significant (figure 2). If a  
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16 143 stenosis is non-significant (FFR > 0.8) and the patient is eligible for inclusion based on the criteria  
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18 144 listed in table 1, informed consent is obtained for participation in the study. If the FFR is  $\leq 0.80$   
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20 145 (hemodynamically significant), the patient is revascularized according to the current therapeutic  
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22 146 guidelines.  
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27 147 *Timing of FFR measurements and informed consent*  
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30 148 FFR measurements of non-culprit lesions are performed either during the index CAG, or during a  
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32 149 staged procedure within 6 weeks. If non-culprit lesions are assessed during the index procedure,  
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34 150 patients are approached for participation after revascularization of the culprit artery and any FFR  
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36 151 measurements. After oral consent, the OCT pullbacks are performed of all FFR-negative stenosis.  
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38 152 Written informed consent is acquired after the procedure. If non-culprit lesion will be evaluated  
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40 153 during a staged procedure, written informed consent is acquired prior to the staged procedure.  
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44 154 *OCT-imaging*  
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47 155 After administration of intracoronary nitrates an OCT pullback of the target lesion is acquired using  
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49 156 the FD-OCT ILUMIEN system (Abbott, USA) over a normal 0.14" guidewire or pressure wire. The OCT  
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51 157 system is CE marked and deployed as intended by the manufacturer. For effective clearing of blood  
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53 158 from the imaging field angiographic contrast media is injected. For the average coronary vessel 14 ml  
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55 159 of contrast media is injected using an automated injector at a rate of 4 mL/s at 300 PSI. The contrast  
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57 160 amount and/or infusion rate can be adjusted proportionally to coronary artery diameter to ensure  
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3 161 good image quality. The segment of interest is scanned with a pull-back speed of 18 mm/sec (54mm  
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5 162 segment). The entire OCT-pullback is recorded simultaneously with fluoroscopy to ensure that the  
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7 163 anatomy of the OCT pullback can be linked to the angiogram. Multiple runs are allowed in case of  
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10 164 poor image quality. In case of multiple target lesions eligible for OCT imaging, OCT imaging of each  
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12 165 target lesion is performed. OCT images are not used for procedural guidance.  
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#### 15 166 *Blood sampling*

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18 167 During CAG, after OCT imaging is performed, 10ml of blood is drawn from the arterial sheath. This  
19  
20 168 blood is used for determination of biomarkers for plaque- or patient vulnerability.  
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#### 23 169 *OCT-imaging analysis*

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26 170 OCT-images and corresponding angiograms are analyzed off-line by trained personnel in an OCT  
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28 171 core-laboratory. Evaluation of the images is based on tissue characteristics as previously described in  
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30 172 OCT expert consensus papers. [21, 22] A plaque is deemed 'vulnerable' if it contains two of the  
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32 173 following characteristics: a lipid arc of  $\geq 90^\circ$ , a cap thickness of  $< 65 \mu\text{m}$  and either cap rupture or  
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34 174 thrombus formation. An example of a vulnerable plaque with a lipid arc of  $>90^\circ$  and a cap thickness  $<$   
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36 175  $65 \mu\text{m}$  is shown in figure 2.  
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#### 40 176 *Study end points*

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44 177 The primary study endpoint consists of a composite of major adverse cardiovascular events (all-cause  
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46 178 mortality, non-fatal MI (STEMI or NSTEMI), or unplanned revascularization) at 2-year follow-up in  
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48 179 patients with a vulnerable plaque as compared to patients without a vulnerable plaque. Secondary  
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50 180 endpoints are: MACE at 1- and 5-year follow-up, target vessel failure, target vessel revascularization,  
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52 181 target lesion failure and target lesion revascularization.  
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#### 55 182 *Exploratory analyses*

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3 183 Additional exploratory analyses will be performed by comparing non-culprit plaque characteristics in  
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5 184 patients presenting with STEMI vs. NSTEMI, in diabetic vs non-diabetic patients, and in male vs.  
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7 185 female patients. Plaque morphology will also be related to angiographic lesion features. Moreover, in  
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10 186 order to accelerate the process of OCT-imaging interpretation, automated detection of  
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12 187 morphological features associated with MACE, will be developed with the use of machine learning.  
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#### 15 188 *Follow-up and endpoint adjudication*

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18 189 At 1-, 2- and 5-years patients are followed-up by telephone contact. Medical records (including  
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20 190 coronary angiograms) from participating centers, general practitioners, and other medical centers  
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22 191 are used for the verification of endpoints. Additionally, mortality data is obtained from national  
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24 192 registries. A clinical event adjudication committee blinded to OCT-data will assess endpoints and  
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26 193 allocate any new MI or revascularization to a specific coronary vessel and lesion by comparison of the  
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28 194 baseline and follow-up angiograms.  
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#### 31 195 *Sample size calculation and statistical analysis*

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35 196 Total sample size is calculated at 438 patients. Sample size is calculated to provide at least 80%  
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37 197 power with a one sided alpha of 0.025 to identify OCT variables associated with non-culprit lesion  
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39 198 related major adverse cardiovascular events. It is based on the assumption that high risk OCT defined  
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41 199 vulnerable plaques are identified in 60% of targeted lesions, on a total event rate of 25% after two  
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43 200 years in FFR deferred lesions in patients with MI [11], and an expected hazard ratio of at least 3.5 for  
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45 201 OCT defined vulnerable plaques. [18] The power of 80% is maintained when the hazard ratio is lower  
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47 202 than expected but at least 2.0, or when the event rate is lower than expected but at least 10%.  
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49 203 Estimated loss to follow up is 5%, and inadequate OCT scans prohibiting assessment of vulnerable  
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51 204 plaque characteristics are expected in 5% of cases.  
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56 205 At 2-year follow-up, MACE in patients with vulnerable plaque characteristics will be compared to  
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58 206 patients without vulnerable plaque characteristics in terms of the hazard ratio. Descriptives will be  
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3 207 expressed as mean  $\pm$  SD (continuous data) or as frequencies and proportions (categorical data).  
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5 208 Continuous variables are presented as mean SD if normally distributed, or median [interquartile  
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7 209 range] if not normally distributed. Categorical variables are presented as counts and percentages.  
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10 210 Continuous variables are compared between groups using the Student t test or its nonparametric  
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12 211 equivalent Mann-Whitney U test. The chi-square test (for comparison of proportions) will be  
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14 212 performed where appropriate. Multivariate Cox proportional hazard regression will be used to  
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16 213 correct for differences in baseline characteristics like age, sex, diabetes mellitus, hypertension,  
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18 214 dyslipidemia, indication for CAG (STEMI vs NSTEMI), history of MI and history of PCI if necessary. All  
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21 215 calculations will be generated by statistical package for social sciences software (SPSS Statistics  
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23 216 version 24; IBM Corp., Armonk, NY, USA).

#### 26 217 *Patient and public involvement*

29 218 Patients were not involved in the design of this study.

#### 32 219 **Current status**

36 220 Recruitment commenced in December 2018 and was completed in September 2020. With 2 year  
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38 221 follow-up for the primary endpoint, reporting on the study is expected in the beginning of 2023.

42 222

## 223 Discussion

224 The PECTUS-obs study was designed to investigate the association between OCT-determined  
225 characteristics of plaque vulnerability and future major adverse cardiac events in non-flow limiting,  
226 non-culprit lesions of patients presenting with MI.

227 In current practice, the decision whether or not to preventively treat a non-culprit lesion is primarily  
228 based on its physiological significance. Although this strategy is clearly superior in stable CAD, it has  
229 yet to be proven in patients presenting with MI. [8] In STEMI, several large randomized trials have  
230 shown that FFR-guided complete revascularization results in fewer MACE compared to culprit-only  
231 revascularization. [23, 24] However, randomized controlled trials directly comparing FFR-guided  
232 complete revascularization with angiography-guided complete revascularization in STEMI have not  
233 yet been conducted, and the only two studies showing a reduction in major clinical endpoints (death  
234 and MI) after non-culprit revascularization were actually guided by angiography rather than  
235 physiology. [4, 25] For patients with NSTEMI, the evidence is even more scarce. In the only available  
236 randomized trial, the FAMOUS-NSTEMI trial, MACE rates at 1-year follow-up did not differ between  
237 patients with FFR-guided and angiography guided treatment (8.0% vs 8.6%). [26] However, this study  
238 was primarily designed to evaluate the effect of FFR-measurements on management decisions, and  
239 was not powered to assess between-group differences in clinical outcomes. The ongoing SLIM trial  
240 (NCT03562572) aims to address this gap in knowledge. Nevertheless, even if FFR-guided complete  
241 revascularization proves superior in patients with MI, the long term MACE rate remains significant.  
242 [11] It therefore remains unclear if non-culprit lesion selection based solely on FFR is sufficient, or if  
243 other features like plaque morphology need to be taken into account.

244 In previous prospective intravascular imaging studies, plaque morphology has consistently been  
245 analyzed using IVUS. In the PROSPECT study, 697 ACS patients were subjected to three-vessel  
246 radiofrequency (RF)-IVUS imaging. [18] All atherosclerotic lesions found in the recordings were  
247 subsequently analyzed for plaque composition. After a median follow-up of 3.4 years, researchers



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3 248 found that non-culprit lesions with a minimal lumen area (MLA) of 4.0 mm<sup>2</sup> or less, a plaque burden  
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5 249 of 70% or greater, and those classified as TCFA were associated with a higher rate of MACE.  
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7 250 Following PROSPECT, several other studies confirmed the association between RF-IVUS-derived  
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9 251 vulnerable plaques and MACE. [27, 28] The main limitation of RF-IVUS when it comes to identifying  
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11 252 TCFA is its poor resolution. In the landmark study by Burke et al., 95% of ruptured plaques had a  
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13 253 fibrous cap thickness of less than 65µm. [29] More recent reports found that cap thickness of lesions  
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15 254 classified as TCFA ranges from 54-84µm. [30] RF-IVUS has a spatial resolution of approximately 150  
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17 255 µm, leaving it below the detection range for cap thickness in these lesions. Moreover, of all plaque  
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19 256 features that are related with adverse outcomes, cap thickness seems to be the most important. [30]  
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21 257 As mentioned earlier, with a spatial resolution of approximately 10µm, we expect that OCT is more  
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23 258 suitable for identifying TCFA. However, prospective data on the association between OCT-derived  
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25 259 vulnerable plaques and future events are limited. Recently, the arsenal of invasive imaging modalities  
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27 260 was broadened by NIRS. The ATHEROREMO-NIRS study proved that NIRS-derived lipid core burden  
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29 261 index (LCBI) was associated with MACE at a patient level, whereas the LRP study later expanded on  
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31 262 this observation by showing that NIRS can also identify plaques vulnerable to future MACE. [19, 31]  
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33 263 The CLIMA study investigated the association between a predefined combination of four high risk  
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35 264 plaque features (MLA <3.5 mm<sup>2</sup>, fibrous cap thickness <75µm, a lipid arc >180°, and the presence of  
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37 265 macrophage clusters) and clinical events in patients that underwent OCT imaging of the proximal  
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39 266 LAD. [32] This combination of features proved to be an independent predictor of events with a  
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41 267 hazard ratio of 7.54. However, this study differed from the current design in several aspects. Even  
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43 268 though CLIMA involved prospective follow-up, patients were only included after undergoing OCT-  
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45 269 imaging for a clinical indication. Moreover, imaging had to be performed on a predefined segment  
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47 270 (proximal-mid LAD) that could not include, or be adjacent to, a stenosis of ≥ 50%. Therefore OCT-  
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49 271 imaging in this study was used to screen a fixed vessel segment that was relatively free of stenosis,  
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51 272 whereas the PECTUS-obs evaluates targeted OCT-imaging of angiographically determined stenoses of  
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53 273 intermediate severity that are FFR-negative.  
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3 274 The COMBINE study shares more similarities with the current study design. [33] In this prospective  
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5 275 registry of patients with diabetes requiring invasive angiography, OCT imaging of FFR non-flow  
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7 276 limiting lesions revealed that patients with TCFAs had increased target lesion related MACE  
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10 277 compared to patients without TCFAs (13.3% vs. 9.7%) at 18 month follow-up. [34] In this study  
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12 278 however, only 25% of included patients had presented with an ACS at baseline.  
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## 280 **Conclusion**

281 The PECTUS-obs is the first prospective study to assess the incremental value of OCT imaging of FFR-  
282 deferred non-culprit lesions in patients presenting with MI. If intracoronary imaging with OCT is able  
283 to identify lesions associated with worse outcome, this might warrant studies on focal or  
284 pharmacological intervention of OCT-determined vulnerable plaques.

## 285 **Ethics and dissemination**

286 This study has been approved by the Medical Ethics Committee of the region Arnhem-Nijmegen (file  
287 number 2018-4763). All participants gave informed consent prior to inclusion in the study. The  
288 results of this study will be disseminated in a main paper and additional papers with subgroup  
289 analyses.

## 290 **Author contributions**

291 NvR conceived the idea. NvR and JHQM designed the study protocol. ST designed the statistical  
292 analyses. JHQM and NvR drafted the manuscript. AB, RHJAV, MM, AVP, PL, OVK, RD, RMO, JpVK, EKA,  
293 DJvdH, SR, EL, CC, PD, MAHVl and RJvG provided critical revisions and substantial intellectual input.  
294 All authors agreed with the final version of the manuscript.

## 295 **Competing interests**

296 None declared.

## 297 **Funding**

298 This study was financially supported by Abbott Vascular, and Health Holland.

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3 393 **Figures**  
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5 394 **Figure 1.** PECTUS-obs flowchart  
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7 **Figure 1.** PECTUS-obs flowchart

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9 CAG, coronary angiography, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction, OCT,  
10 optical coherence tomography, STEMI, ST-elevation myocardial infarction  
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15 396 **Figure 2.** Lesion assessment in the PECTUS-obs study  
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17 **Figure 2.** Lesion assessment in the PECTUS-obs study

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19 **Upper left:** CAG shows a non-culprit lesion (red box) in the proximal RCA. The radiopaque marker  
20 inside the vessel at the location of the lesion represents the OCT lens.  
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23 **Lower left:** FFR- measurement of the lesion reveals that it is non flow-limiting (FFR = 0.94).  
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26 **Right:** OCT-imaging shows an atherosclerotic plaque with a lipid arc of 200° and a minimal fibrous  
27 cap thickness of 4 µm. This lesion therefore meets the criteria for a vulnerable plaque.  
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29 CAG, coronary angiography, FFR, fractional flow reserve, OCT, optical coherence tomography, RCA, right coronary  
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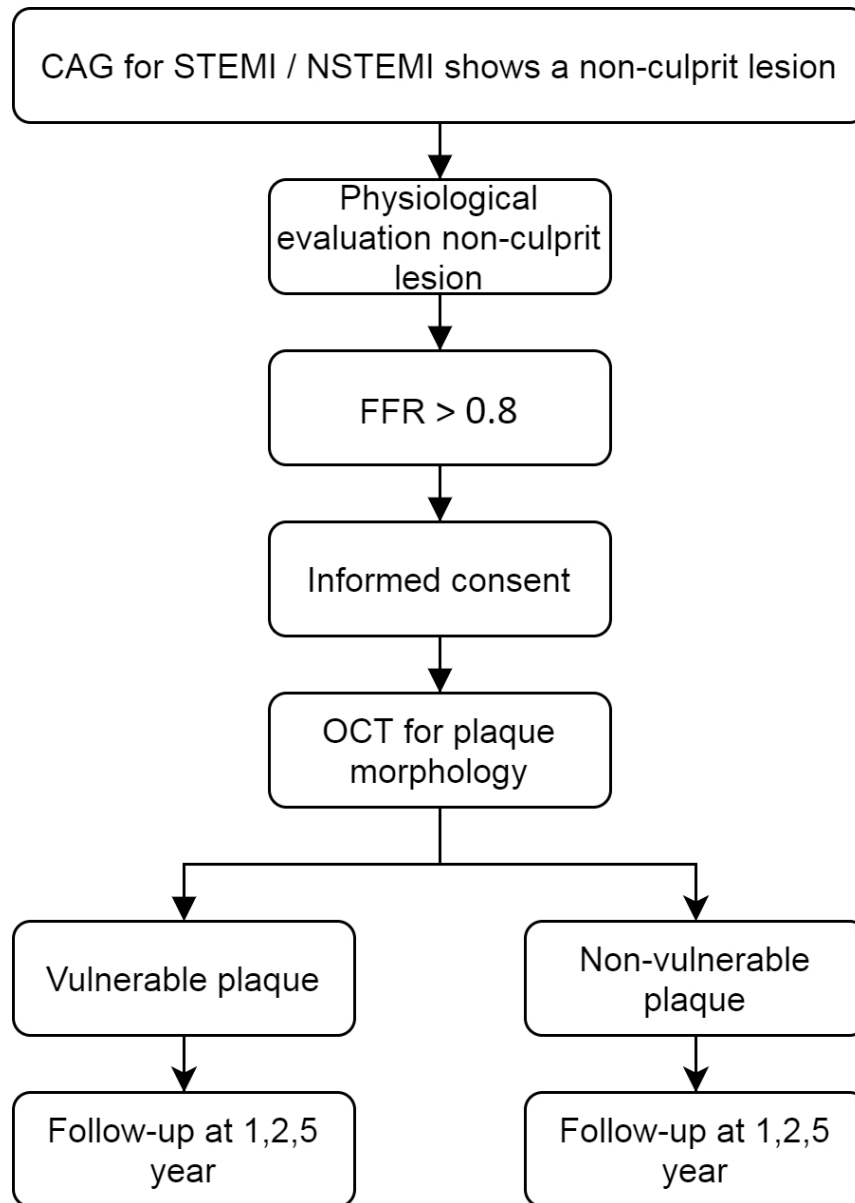


Figure 1. PECTUS-obs flowchart

46 CAG, coronary angiography, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction,  
47 OCT, optical coherence tomography, STEMI, ST-elevation myocardial infarction

50 318x445mm (72 x 72 DPI)

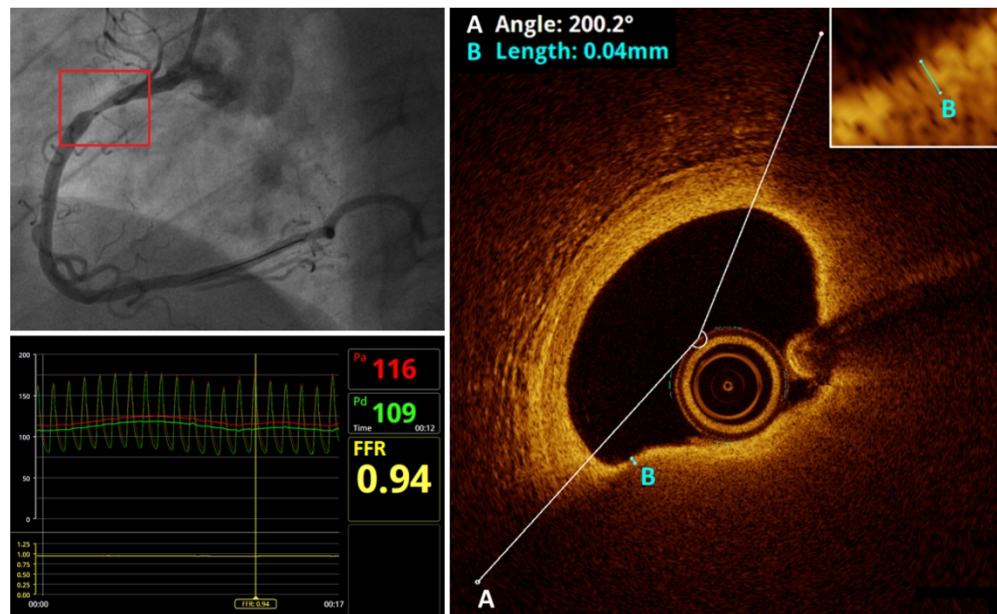


Figure 2. Lesion assessment in the PECTUS-obs study

Upper left: CAG shows a non-culprit lesion (red box) in the proximal RCA. The radiopaque marker inside the vessel at the location of the lesion represents the OCT lens.

Lower left: FFR- measurement of the lesion reveals that it is non flow-limiting (FFR = 0.94).

Right: OCT-imaging shows an atherosclerotic plaque with a lipid arc of 200° and a minimal fibrous cap thickness of 4  $\mu$ m. This lesion therefore meets the criteria for a vulnerable plaque.

CAG, coronary angiography, FFR, fractional flow reserve, OCT, optical coherence tomography, RCA, right coronary artery

274x167mm (120 x 120 DPI)



# BMJ Open

## Identification of anatomic risk factors for acute coronary events by Optical Coherence Tomography in patients with myocardial infarction and residual non-flow limiting lesions: Rationale and design of the PECTUS-obs study.

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2021-048994.R1
Article Type:	Protocol
Date Submitted by the Author:	29-Apr-2021
Complete List of Authors:	Mol, Jan-Quinten; Radboudumc, cardiology Belkacemi, Anouar; Isala Hospitals, Department of Cardiology Volleberg, Rick; Radboudumc, Department of Cardiology Meuwissen, Martijn; Amphia Hospital, Department of Cardiology Protopopov, Aleksey; Regional state hospital, Cardiovascular Center Laanmets, Peep; North Estonia Medical Centre, Department of Cardiology Krestyaninov, Oleg; FSBI National Medical Research Center named after E N Meshalkin, Department of Cardiology Dennert, Robert; Dr Horacio E Oduber Hospital, Department of Cardiology Oemrawsingh, Rohit; Albert Schweitzer Hospital, Department of Cardiology van Kuijk, Jan-Peter; Sint Antonius Hospital, Department of Cardiology Arkenbout, Karin; Tergooi Hospitals, Department of Cardiology van der Heijden, Dirk-Jan; Medisch Centrum Haaglanden, Cardiology Rasoul, Saman; Zuyderland Medical Centre Heerlen; Maastricht Universitair Medisch Centrum+, Cardiology Lipsic, Erik; University Medical Centre Groningen, Department of Cardiology Teerenstra, Steven; Radboud University Medical Center, Department for Health Evidence Camaro, Cyril; Radboudumc, Cardiology Damman, P.; Radboudumc, Department of Cardiology van Leeuwen, Maarten; Isala Hospitals, Department of Cardiology van Geuns, Robert-Jan; Radboudumc, Cardiology van Royen, Niels; Radboudumc, Department of Cardiology
<b>Primary Subject Heading</b>:	Cardiovascular medicine
Secondary Subject Heading:	Cardiovascular medicine
Keywords:	Coronary heart disease < CARDIOLOGY, Coronary intervention < CARDIOLOGY, Myocardial infarction < CARDIOLOGY

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4 1 **Identification of anatomic risk factors for acute coronary events by**  
5 2 **Optical Coherence Tomography in patients with myocardial**  
6 3 **infarction and residual non-flow limiting lesions: Rationale and**  
7 4 **design of the PECTUS-obs study.**  
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32 2799

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34 *Keywords*

35 Myocardial Infarction (MI), Non-culprit Lesion, Fractional Flow Reserve (FFR), Optical Coherence

36 Tomography (OCT), Vulnerable Plaque

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45

## 46 **Abstract**

### 47 **Introduction**

48 In patients with myocardial infarction, the decision to treat a non-culprit lesion is generally based on  
49 its physiological significance. However, deferral of revascularization based on non-ischemic fractional  
50 flow reserve (FFR) values in these patients results in less favorable outcomes compared to patients  
51 with stable coronary artery disease (CAD), potentially caused by vulnerable non-culprit lesions.  
52 Intravascular optical coherence tomography (OCT) imaging allows for in vivo morphological  
53 assessment of plaque 'vulnerability', and might aid in the detection of FFR-negative lesions at high  
54 risk for recurrent events.

### 55 **Methods and analysis**

56 The PECTUS-obs study is an international multicenter prospective observational study that aims to  
57 relate OCT-derived vulnerable plaque characteristics of non-flow limiting, non-culprit lesions to  
58 clinical outcome in patients with myocardial infarction. A total of 438 patients presenting with  
59 myocardial infarction (STEMI and NSTEMI) will undergo OCT-imaging of any FFR-negative non-culprit  
60 lesion for detection of plaque vulnerability. The primary study endpoint is a composite of Major  
61 Adverse Cardiovascular Events (all-cause mortality, non-fatal myocardial infarction, or unplanned  
62 revascularization) at 2-year follow-up. Secondary endpoints will be the same composite at 1- and 5-  
63 year follow-up, target vessel failure, target vessel revascularization, target lesion failure and target  
64 lesion revascularization.

### 65 **Ethics and dissemination**

66 This study has been approved by the Medical Ethics Committee of the region Arnhem-Nijmegen. The  
67 results of this study will be disseminated in a main paper and additional papers with subgroup  
68 analyses.

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3 69 **Registered under NCT03857971 on 28-02-2019**  
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9 **Strengths and limitations of this study**

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11 72 • The PECTUS-obs is the first prospective study to assess the incremental value of OCT imaging  
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13 73 of FFR-deferred non-culprit lesions in patients presenting with MI.  
14  
15 74 • OCT is the only imaging modality with a spatial resolution high enough to truly measure  
16  
17 75 fibrous cap thickness, the plaque feature most associated with adverse events.  
18  
19 76 • In PECTUS-obs, OCT imaging will only be performed at baseline. However, any new MI or  
20  
21 77 revascularization will be allocated to a specific coronary vessel and lesion by comparison of  
22  
23 78 the baseline and follow-up angiograms.  
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25 79 • If intracoronary imaging with OCT is able to identify lesions associated with worse outcome,  
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27 80 this might warrant studies on focal or pharmacological intervention of OCT-determined  
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29 81 vulnerable plaques.  
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## 85 Introduction

86 In patients presenting with myocardial infarction (MI), percutaneous coronary intervention (PCI) of  
87 the culprit lesion is the standard method of treatment. [1] A high percentage of these patients have  
88 additional lesions at different sites in the coronary arteries, not responsible for the acute event. The  
89 optimal treatment of these non-culprit lesions is subject of extensive research, because their  
90 presence confers a greater risk of future major adverse cardiac events (MACE) [2, 3]. Recent studies  
91 showed that complete revascularization results in improved outcomes compared to treatment of the  
92 culprit lesion only. [4-6] However, non-selective revascularization of all non-culprit lesions may lead  
93 to overtreatment.

94 The selection of non-culprit lesions qualifying for revascularization is often based on whether a  
95 lesions causes ischemia, as determined by invasive measurements such as the fractional flow reserve  
96 (FFR). [7] In patients with stable coronary artery disease (CAD), FFR-guided complete  
97 revascularization results in better outcomes compared to angiography guided complete  
98 revascularization. [8] Nevertheless, the MACE rates at longer term follow-up remains significant in  
99 the presence of non-significant CAD. [9] In patients presenting with MI this recurrence rate of  
100 ischemic events is even higher. [10] A recent study demonstrated a MACE rate of 23% in acute  
101 coronary syndrome (ACS) patients vs. 11% in patients with stable CAD at 3.4-years follow-up, after  
102 FFR based deferral of revascularization. Among these ACS patients, especially those presenting with  
103 NSTEMI had a high event rate (42%). [11]

104 Apart from coronary physiology, the structural components of non-culprit lesions might provide  
105 other markers for future adverse events. Autopsy studies have granted insight into the lesion  
106 characteristics that are associated with plaque rupture, and subsequent MI or sudden death. These  
107 lesions tend to contain a large lipid pool with a thin overlying fibrous cap, and display a large degree  
108 of outward remodeling. [12, 13] These 'thin-cap fibroatheromas' (TCFA) are more frequently  
109 observed in both culprit- and non-culprit lesions of patients presenting with MI than in patients



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3 110 presenting with stable CAD, and are a strong predictor of culprit plaque rupture in ACS. [14-17]  
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5 111 Therefore, screening for vulnerable plaques on top of physiological measurements, should be  
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7 112 evaluated for non-culprit lesions.  
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10 113 Analysis of lesion composition can be performed in vivo with the use of intravascular imaging  
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12 114 techniques such as intravascular ultrasound (IVUS), near infrared spectroscopy (NIRS) and optical  
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14 115 coherence tomography (OCT). [18] Prospective studies using IVUS and NIRS showed that  
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16 116 identification of lesions at higher risk for future events is feasible. [19, 20] However, OCT might prove  
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18 117 more suitable for this purpose, due to its specific characteristics. OCT has a 10-20 times higher spatial  
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20 118 resolution than IVUS, allowing for better detection of TCFA. Moreover, a complete acquisition of a  
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22 119 coronary segment can be provided within a couple of seconds, with a single pullback. Last,  
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24 120 (semi)automated analysis of images is more feasible due to the high resolution of the acquired  
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26 121 images. [21] Nevertheless, OCT has yet to be prospectively validated for its ability to identify lesions  
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28 122 at risk for future MACE in MI patients.  
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33 123 For future studies on potential preventive revascularization or more aggressive pharmacological  
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35 124 therapy in patients with high risk lesions, prospective studies with clinical outcomes are imperative.  
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37 125 In the PECTUS-obs study, we aim to relate OCT-derived plaque characteristics of not significantly flow  
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39 126 limiting, non-culprit lesions to clinical outcome in patients presenting with MI.  
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## 128 **Methods and analysis**

### 129 *Overview*

130 The PECTUS-obs study is designed as an international multicenter prospective observational study.  
 131 Eligible patients have to undergo an index CAG during hospitalization for an acute myocardial  
 132 infarction, which reveals one or more non-culprit lesions accessible for imaging with OCT. FFR-  
 133 measurements of these non-culprit lesions are made during the same index procedure, or during a  
 134 staged procedure. Any FFR-nonsignificant lesions are subsequently imaged with OCT. Additional  
 135 criteria are listed in table 1. A total of 438 patients will be included. A flow-chart of the study design  
 136 is depicted in figure 1.

**Table 1. Inclusion- and exclusion criteria**

Inclusion criteria	Exclusion criteria
<p style="text-align: center;"><b>Clinical</b></p> <ul style="list-style-type: none"> <li>- Age <math>\geq</math> 18 years</li> <li>- Hospitalization with a STEMI or NSTEMI for which patient is subjected to invasive coronary angiography (within the last 6 weeks).</li> </ul> <p style="text-align: center;"><b>Angiographical</b></p> <ul style="list-style-type: none"> <li>- Patient has <math>\geq</math> 1 non-culprit, target lesion(s) with following additional characteristics:               <ul style="list-style-type: none"> <li>o Lesion has visual stenosis of 30-90%.</li> <li>o Lesion is non-obstructive (FFR &gt; 0.80).</li> <li>o Lesion is not in-stent restenosis.</li> </ul> </li> </ul>	<p style="text-align: center;"><b>Clinical</b></p> <ul style="list-style-type: none"> <li>- Pregnancy.</li> <li>- Hemodynamic instability, respiratory failure, or Killip class <math>\geq</math> 3 at time of inclusion.</li> <li>- Previous CABG.</li> <li>- Indication for revascularization by CABG.</li> <li>- Estimated life expectancy &lt; 3 year.</li> </ul> <p style="text-align: center;"><b>Angiographical</b></p> <ul style="list-style-type: none"> <li>- Anatomy of target lesion(s) is unsuitable for OCT catheter crossing or imaging (aorta-ostial lesions, too small diameter segment, severe calcifications, chronic total occlusion, distal lesions prohibiting OCT imaging).</li> </ul>
<p><b>Table 1. Inclusion- and exclusion criteria</b>            CABG, coronary artery bypass grafting, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction, OCT, optical coherence tomography, STEMI, ST-elevation myocardial infarction</p>	

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3 138 *Patients and enrolment*  
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6 139 Patients presenting with MI (ST-elevation and non ST-elevation) are screened for potential inclusion  
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8 140 in the study. Patients are treated according to the current guidelines for the management of ACS,  
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10 141 including referral for CAG and (potential) PCI of the culprit artery. In case of one or more non-culprit  
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12 142 lesions of intermediate stenosis (30-90%), clinically indicated FFR measurements are performed in  
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14 143 order to determine if these non-culprit stenoses are hemodynamically significant (figure 2). If a  
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16 144 stenosis is non-significant (FFR > 0.8) and the patient is eligible for inclusion based on the criteria  
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18 145 listed in table 1, informed consent is obtained for participation in the study. If the FFR is  $\leq 0.80$   
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20 146 (hemodynamically significant), the patient is revascularized according to the current therapeutic  
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22 147 guidelines.  
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27 148 *Timing of FFR measurements and informed consent*  
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30 149 FFR measurements of non-culprit lesions are performed either during the index CAG, or during a  
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32 150 staged procedure within 6 weeks. If non-culprit lesions are assessed during the index procedure,  
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34 151 patients are approached for participation after revascularization of the culprit artery and any FFR  
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36 152 measurements. After oral consent, the OCT pullbacks are performed of all FFR-negative stenosis.  
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38 153 Written informed consent is acquired after the procedure. If non-culprit lesion will be evaluated  
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40 154 during a staged procedure, written informed consent is acquired prior to the staged procedure.  
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44 155 *OCT-imaging*  
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47 156 After administration of intracoronary nitrates an OCT pullback of the target lesion is acquired using  
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49 157 the FD-OCT ILUMIEN system (Abbott, USA) over a normal 0.14" guidewire or pressure wire. The OCT  
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51 158 system is CE marked and deployed as intended by the manufacturer. For effective clearing of blood  
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53 159 from the imaging field angiographic contrast media is injected. For the average coronary vessel 14 ml  
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55 160 of contrast media is injected using an automated injector at a rate of 4 mL/s at 300 PSI. The contrast  
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57 161 amount and/or infusion rate can be adjusted proportionally to coronary artery diameter to ensure  
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3 162 good image quality. The segment of interest is scanned with a pull-back speed of 18 mm/sec (54mm  
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5 163 segment). The entire OCT-pullback is recorded simultaneously with fluoroscopy to ensure that the  
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7 164 anatomy of the OCT pullback can be linked to the angiogram. Multiple runs are allowed in case of  
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10 165 poor image quality. In case of multiple target lesions eligible for OCT imaging, OCT imaging of each  
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12 166 target lesion is performed. OCT images are not used for procedural guidance.  
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#### 15 167 *Blood sampling*

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18 168 During CAG, after OCT imaging is performed, 10ml of blood is drawn from the arterial sheath. This  
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20 169 blood is used for determination of biomarkers for plaque- or patient vulnerability.  
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#### 23 170 *OCT-imaging analysis*

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26 171 OCT-images and corresponding angiograms are analyzed off-line by trained personnel in an OCT  
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28 172 core-laboratory. Evaluation of the images is based on tissue characteristics as previously described in  
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30 173 OCT expert consensus papers. [22, 23] A plaque is deemed 'vulnerable' if it contains two of the  
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32 174 following characteristics: a lipid arc of  $\geq 90^\circ$ , a cap thickness of  $< 65 \mu\text{m}$  and either cap rupture or  
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34 175 thrombus formation. An example of a vulnerable plaque with a lipid arc of  $>90^\circ$  and a cap thickness  $<$   
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36 176  $65 \mu\text{m}$  is shown in figure 2.  
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#### 40 177 *Study end points*

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44 178 The primary study endpoint consists of a composite of major adverse cardiovascular events (all-cause  
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46 179 mortality, non-fatal MI (STEMI or NSTEMI), or unplanned revascularization) at 2-year follow-up in  
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48 180 patients with a vulnerable plaque as compared to patients without a vulnerable plaque. Secondary  
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50 181 endpoints are: MACE at 1- and 5-year follow-up, target vessel failure, target vessel revascularization,  
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52 182 target lesion failure and target lesion revascularization.  
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#### 55 183 *Exploratory analyses*

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3 184 Additional exploratory analyses will be performed by comparing non-culprit plaque characteristics in  
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5 185 patients presenting with STEMI vs. NSTEMI, in diabetic vs non-diabetic patients, and in male vs.  
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7 186 female patients. Plaque morphology will also be related to angiographic lesion features. Moreover, in  
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9 187 order to accelerate the process of OCT-imaging interpretation, automated detection of  
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11 188 morphological features associated with MACE, will be developed with the use of machine learning.  
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15 189 *Follow-up and endpoint adjudication*

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18 190 At 1-, 2- and 5-years patients are followed-up by telephone contact. Medical records (including  
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20 191 coronary angiograms) from participating centers, general practitioners, and other medical centers  
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22 192 are used for the verification of endpoints. Additionally, mortality data is obtained from national  
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24 193 registries. A clinical event adjudication committee blinded to OCT-data will assess endpoints,  
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26 194 separate cardiovascular mortality from non-cardiovascular mortality, and allocate any new MI or  
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28 195 revascularization to a specific coronary vessel and lesion by comparison of the baseline and follow-up  
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30 196 angiograms.  
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35 197 *Sample size calculation and statistical analysis*

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38 198 The total sample size is calculated at 438 patients. The sample size is calculated to provide 90%  
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40 199 power with a one sided alpha of 0.025 to identify OCT variables associated with non-culprit lesion  
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42 200 related major adverse cardiovascular events. It is based on the assumption that high risk OCT defined  
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44 201 vulnerable plaques are identified in 60% of targeted lesions, on a total event rate of 25% after two  
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46 202 years in FFR deferred lesions in patients with MI [11, 24], and an expected hazard ratio of at least 3.5  
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48 203 for OCT defined vulnerable plaques. [19] A power of 80% is maintained when the hazard ratio is  
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50 204 lower than expected but at least 2.0, or when the event rate is lower than expected but at least 10%.  
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52 205 Estimated loss to follow up is 5%, and inadequate OCT scans prohibiting assessment of vulnerable  
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54 206 plaque characteristics are expected in 5% of cases.  
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3 207 At 2-year follow-up, MACE in patients with vulnerable plaque characteristics will be compared to  
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5 208 patients without vulnerable plaque characteristics in terms of the hazard ratio. Descriptives will be  
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7 209 expressed as mean  $\pm$  SD (continuous data) or as frequencies and proportions (categorical data).  
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10 210 Continuous variables are presented as mean SD if normally distributed, or median [interquartile  
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12 211 range] if not normally distributed. Categorical variables are presented as counts and percentages.  
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14 212 Continuous variables are compared between groups using the Student t test or its nonparametric  
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16 213 equivalent Mann-Whitney U test. The chi-square test (for comparison of proportions) will be  
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18 214 performed where appropriate. Multivariate Cox proportional hazard regression will be used to  
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20 215 correct for differences in baseline characteristics like age, sex, diabetes mellitus, hypertension,  
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22 216 dyslipidemia, indication for CAG (STEMI vs NSTEMI), history of MI and history of PCI if necessary. All  
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24 217 calculations will be generated by statistical package for social sciences software (SPSS Statistics  
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26 218 version 24; IBM Corp., Armonk, NY, USA).

### 219 *Patient and public involvement*

220 Patients were not involved in the design of this study.

### 221 **Current status**

222 Recruitment commenced in December 2018 and was completed in September 2020. With 2 year  
223 follow-up for the primary endpoint, reporting on the study is expected in the beginning of 2023.

### 224 **Discussion**

225 The PECTUS-obs study was designed to investigate the association between OCT-determined  
226 characteristics of plaque vulnerability and future major adverse cardiac events in non-flow limiting,  
227 non-culprit lesions of patients presenting with MI.

228 In current practice, the decision whether or not to preventively treat a non-culprit lesion is primarily  
229 based on its physiological significance. Although this strategy is clearly superior in stable CAD, it has

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3 230 yet to be proven in patients presenting with MI. [8] In STEMI, several large randomized trials have  
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5 231 shown that FFR-guided complete revascularization results in fewer MACE compared to culprit-only  
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7 232 revascularization. [25, 26] However, randomized controlled trials directly comparing FFR-guided  
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9 233 complete revascularization with angiography-guided complete revascularization in STEMI have not  
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11 234 yet been conducted, and the only two studies showing a reduction in major clinical endpoints (death  
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13 235 and MI) after non-culprit revascularization were actually guided by angiography rather than  
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15 236 physiology. [4, 27] For patients with NSTEMI, the evidence is even more scarce. In the only available  
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17 237 randomized trial, the FAMOUS-NSTEMI trial, MACE rates at 1-year follow-up did not differ between  
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19 238 patients with FFR-guided and angiography guided treatment (8.0% vs 8.6%). [28] However, this study  
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21 239 was primarily designed to evaluate the effect of FFR-measurements on management decisions, and  
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23 240 was not powered to assess between-group differences in clinical outcomes. The ongoing SLIM trial  
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25 241 (NCT03562572) aims to address this gap in knowledge. Nevertheless, even if FFR-guided complete  
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27 242 revascularization proves superior in patients with MI, the long term MACE rate remains significant.  
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29 243 [11] It therefore remains unclear if non-culprit lesion selection based solely on FFR is sufficient, or if  
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31 244 other features like plaque morphology need to be taken into account.  
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37 245 In previous prospective intravascular imaging studies, plaque morphology has consistently been  
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39 246 analyzed using IVUS. In the PROSPECT study, 697 ACS patients were subjected to three-vessel  
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41 247 radiofrequency (RF)-IVUS imaging. [19] All atherosclerotic lesions found in the recordings were  
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43 248 subsequently analyzed for plaque composition. After a median follow-up of 3.4 years, researchers  
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45 249 found that non-culprit lesions with a minimal lumen area (MLA) of 4.0 mm<sup>2</sup> or less, a plaque burden  
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47 250 of 70% or greater, and those classified as TCFA were associated with a higher rate of MACE.  
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51 251 Following PROSPECT, several other studies confirmed the association between RF-IVUS-derived  
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53 252 vulnerable plaques and MACE. [29, 30] The main limitation of RF-IVUS when it comes to identifying  
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55 253 TCFAs is its poor resolution. In the landmark study by Burke et al., 95% of ruptured plaques had a  
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57 254 fibrous cap thickness of less than 65µm. [31] More recent reports found that cap thickness of lesions  
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59 255 classified as TCFA ranges from 54-84µm. [32] RF-IVUS has a spatial resolution of approximately 150

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3 256  $\mu\text{m}$ , leaving it below the detection range for cap thickness in these lesions. Moreover, of all plaque  
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5 257 features that are related with adverse outcomes, cap thickness seems to be the most important. [32]  
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7 258 As mentioned earlier, with a spatial resolution of approximately  $10\mu\text{m}$ , we expect that OCT is more  
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9 259 suitable for identifying TCFA. However, prospective data on the association between OCT-derived  
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11 260 vulnerable plaques and future events are limited. Recently, the arsenal of invasive imaging modalities  
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13 261 was broadened by NIRS. The ATHEROREMO-NIRS study proved that NIRS-derived lipid core burden  
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15 262 index (LCBI) was associated with MACE at a patient level, whereas the LRP study later expanded on  
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17 263 this observation by showing that NIRS can also identify plaques vulnerable to future MACE. [20, 33]  
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21 264 The CLIMA study investigated the association between a predefined combination of four high risk  
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23 265 plaque features (MLA  $<3.5\text{ mm}^2$ , fibrous cap thickness  $<75\mu\text{m}$ , a lipid arc  $>180^\circ$ , and the presence of  
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25 266 macrophage clusters) and clinical events in patients that underwent OCT imaging of the proximal  
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27 267 LAD. [34] This combination of features proved to be an independent predictor of events with a  
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29 268 hazard ratio of 7.54. However, this study differed from the current design in several aspects. Even  
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31 269 though CLIMA involved prospective follow-up, patients were only included after undergoing OCT-  
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33 270 imaging for a clinical indication. Moreover, imaging had to be performed on a predefined segment  
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35 271 (proximal-mid LAD) that could not include, or be adjacent to, a stenosis of  $\geq 50\%$ . Therefore OCT-  
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37 272 imaging in this study was used to screen a fixed vessel segment that was relatively free of stenosis,  
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39 273 whereas the PECTUS-obs evaluates targeted OCT-imaging of angiographically determined stenoses of  
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41 274 intermediate severity that are FFR-negative.  
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47 275 The COMBINE study shares more similarities with the current study design. [35] In this prospective  
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49 276 registry of patients with diabetes requiring invasive angiography, OCT imaging of FFR non-flow  
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51 277 limiting lesions revealed that patients with TCFA had increased target lesion related MACE  
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53 278 compared to patients without TCFA (13.3% vs. 9.7%) at 18 month follow-up. [36] In this study  
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55 279 however, only 25% of included patients had presented with an ACS at baseline.  
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3 280 The current prospective observational study could serve as an important step towards OCT imaging-  
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5 281 guided treatment of non-culprit lesions. However, randomized trials need to be conducted in order  
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7 282 to evaluate the efficacy of OCT-based interventions. This was attempted in a previous trial in which  
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9 283 preemptive stenting of FFR-negative OCT-identified vulnerable plaques with ABSORB bioresorbable  
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11 284 vascular scaffolds (BVS) was compared to optimal medicinal therapy alone. [37] Unfortunately this  
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13 285 trial was stopped prematurely because the ABSORB BVS was retracted from the market. The  
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15 286 currently enrolling PREVENT trial (NCT02316886) also aims to evaluate imaging-guided preemptive  
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17 287 stenting, although it utilizes IVUS and NIRS in addition to OCT. Lastly the recently published  
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19 288 PROSPECT ABSORB trial showed good safety outcomes after IVUS/NIRS-guided preemptive stenting,  
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21 289 while it was not powered for clinical endpoints.[38]  
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## 26 290 **Conclusion**

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30 291 The PECTUS-obs is the first prospective study to assess the incremental value of OCT imaging of FFR-  
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32 292 deferred non-culprit lesions in patients presenting with MI. If intracoronary imaging with OCT is able  
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34 293 to identify lesions associated with worse outcome, this might warrant studies on focal or  
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36 294 pharmacological intervention of OCT-determined vulnerable plaques.  
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## 40 295 **Ethics and dissemination**

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43 296 This study has been approved by the Medical Ethics Committee of the region Arnhem-Nijmegen (file  
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45 297 number 2018-4763). All participants gave informed consent prior to inclusion in the study. The  
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47 298 results of this study will be disseminated in a main paper and additional papers with subgroup  
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49 299 analyses.  
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## 53 300 **Author contributions**

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56  
57 301 NvR conceived the idea. NvR and JHQM designed the study protocol. ST designed the statistical  
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59 302 analyses. JHQM and NvR drafted the manuscript. AB, RHJAV, MM, AVP, PL, OVK, RD, RMO, JpV, EKA,  
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3 303 DJvdH, SR, EL, CC, PD, MAHVl and RJvG provided critical revisions and substantial intellectual input.  
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5 304 All authors agreed with the final version of the manuscript.  
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9 **305 Competing interests**

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11  
12 306 None declared.  
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15 **307 Funding**

16  
17 308 This study was financially supported by Abbott Vascular, and Health Holland. Grant numbers are not  
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20 309 applicable.  
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3 414 **Figure 1.** PECTUS-obs flowchart  
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8 416 CAG, coronary angiography, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction,  
9 417 OCT, optical coherence tomography, STEMI, ST-elevation myocardial infarction

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14 419 **Figure 2.** Lesion assessment in the PECTUS-obs study  
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17 **Figure 2.** Lesion assessment in the PECTUS-obs study  
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19 **Upper left:** CAG shows a non-culprit lesion (red box) in the proximal RCA. The radiopaque marker  
20 inside the vessel at the location of the lesion represents the OCT lens.  
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22 **Lower left:** FFR- measurement of the lesion reveals that it is non flow-limiting (FFR = 0.94).  
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24 **Right:** OCT-imaging shows an atherosclerotic plaque with a lipid arc of 200° and a minimal fibrous  
25 cap thickness of 4 µm. This lesion therefore meets the criteria for a vulnerable plaque.  
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28 CAG, coronary angiography, FFR, fractional flow reserve, OCT, optical coherence tomography, RCA, right coronary  
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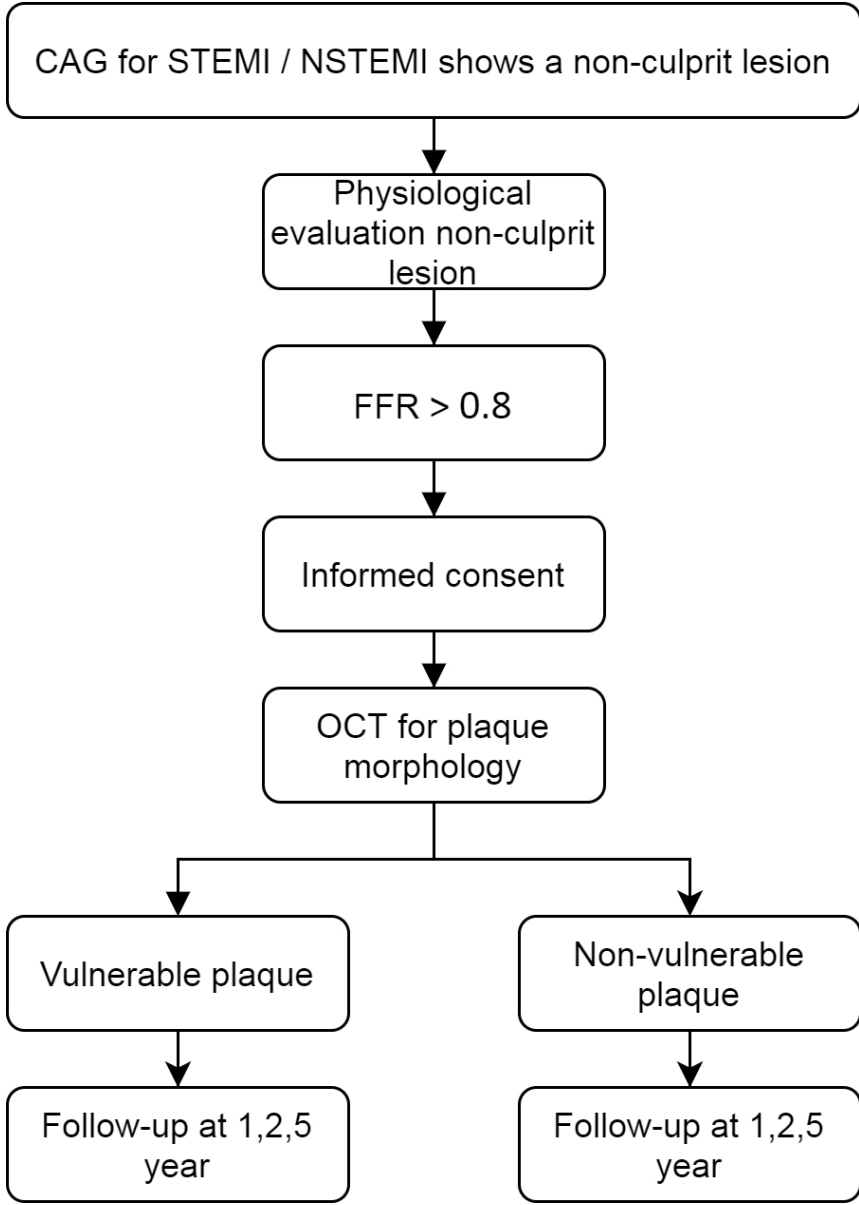


Figure 1. PECTUS-obs flowchart  
CAG, coronary angiography, FFR, fractional flow reserve, NSTEMI, Non- ST-elevation myocardial infarction, OCT, optical coherence tomography, STEMI, ST-elevation myocardial infarction

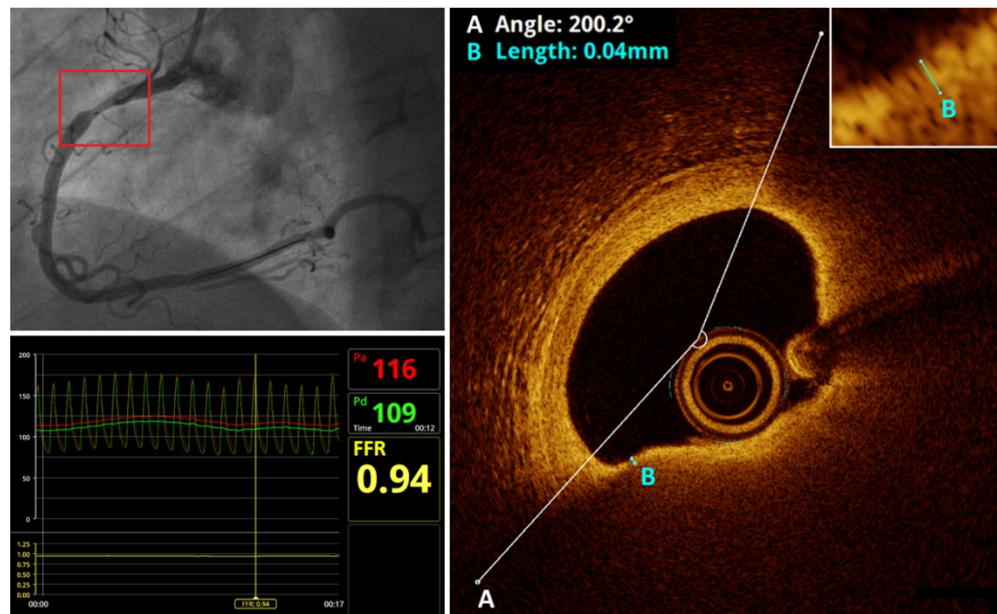


Figure 2. Lesion assessment in the PECTUS-obs study. Upper left: CAG shows a non-culprit lesion (red box) in the proximal RCA. The radiopaque marker inside the vessel at the location of the lesion represents the OCT lens. Lower left: FFR- measurement of the lesion reveals that it is non flow-limiting (FFR = 0.94). Right: OCT-imaging shows an atherosclerotic plaque with a lipid arc of 200° and a minimal fibrous cap thickness of 4  $\mu$ m. This lesion therefore meets the criteria for a vulnerable plaque. CAG, coronary angiography, FFR, fractional flow reserve, OCT, optical coherence tomography, RCA, right coronary artery

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