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## Author Manuscript

Faculty of Biology and Medicine Publication

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Published in final edited form as:

**Title:** Evaluation of postmortem MDCT and MDCT-angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease.

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**Journal:** The international journal of cardiovascular imaging

**Year:** 2012 Oct

**Issue:** 28

**Volume:** 7

**Pages:** 1807-22

**DOI:** [10.1007/s10554-012-0012-x](https://doi.org/10.1007/s10554-012-0012-x)

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# International Journal of Cardiovascular Imaging

## Evaluation of postmortem MDCT and MDCT- angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease --Manuscript Draft--

<b>Manuscript Number:</b>	CAIM2528R1
<b>Full Title:</b>	Evaluation of postmortem MDCT and MDCT- angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease
<b>Article Type:</b>	Original Article
<b>Keywords:</b>	postmortem radiology; CT angiography; ischemic heart disease; coronary thrombosis
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<b>Abstract:</b>	<p><b>Purpose:</b> The goal of this study was to evaluate the diagnostic value of postmortem multi- computed tomography (MDCT) and MDCT-angiography for sudden cardiac deaths related to ischemic heart disease.</p> <p><b>Methods:</b> 23 cases were selected based on clinical history and the results of native MDCT, multiphase post-mortem CT-angiography and conventional autopsy were compared.</p> <p><b>Results:</b> Radiological examination showed calcification of coronary arteries in 78 % of the cases, most of which were not detailed at autopsy. MDCT-angiography allowed better visualization of the coronary arteries than MDCT and permitted the evaluation of stenoses and occlusions. Of the 14 cases of coronary thrombosis detected at conventional autopsy, 11 were visible as stop of perfusion with CT-angiography and 3 were found to be partly perfused. 1 case had an old thrombosis with collateral circulation. 1 case had a coronary artery postmortem clot found with MDCT-angiography.</p> <p><b>Conclusions:</b> Coronary artery calcifications are more easily detected and documented with radiological examination than with conventional autopsy. MDCT is of limited diagnostic value for ischemic heart disease. MDCT-angiography, when correctly interpreted, is a reasonable tool to view the morphology of coronary arteries, rule out significant coronary artery stenoses, identify occlusions and direct sampling for histological examination.</p>

## Evaluation of postmortem MDCT and MDCT- angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease

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### Abstract

*Purpose:* The goal of this study was to evaluate the diagnostic value of postmortem multi- computed tomography (MDCT) and MDCT-angiography for sudden cardiac deaths related to ischemic heart disease.

*Methods:* 23 cases were selected based on clinical history and the results of native MDCT, multiphase post-mortem CT-angiography and conventional autopsy were compared.

*Results:* Radiological examination showed calcification of coronary arteries in 78 % of the cases, most of which were not detailed at autopsy. MDCT-angiography allowed better visualization of the coronary arteries than MDCT and permitted the evaluation of stenoses and occlusions. Of the 14 cases of coronary thrombosis detected at conventional autopsy, 11 were visible as stop of perfusion with CT-angiography and 3 were found to be partly perfused. 1 case had an old thrombosis with collateral circulation. 1 case had a coronary artery postmortem clot found with MDCT-angiography.

*Conclusions:* Coronary artery calcifications are more easily detected and documented with radiological examination than with conventional autopsy. MDCT is of limited diagnostic value for ischemic heart disease. MDCT-angiography, when correctly interpreted, is a reasonable tool to view the morphology of coronary arteries, rule out significant coronary artery stenoses, identify occlusions and direct sampling for histological examination.

### Introduction

Atherosclerosis leading to ischemic heart disease is the most frequent cause of death in industrialized countries [1]. Ischemic heart disease, resulting from impaired cardiac blood supply, is mostly related to atherosclerotic coronary artery stenosis and can manifest as angina pectoris, acute myocardial infarction, chronic ischemic heart disease or sudden death.

1 The diagnosis of ischemic heart disease is based on the clinical symptoms of the patient, and can be confirmed  
2 by electrocardiography, laboratory analyses, and in selected cases, by radiological examinations such as  
3 echocardiography and coronary angiography. Invasive coronary angiography is currently the “gold standard” for  
4 assessing coronary artery stenosis, although it has been associated with serious complications [2]. Cardiac multi-  
5 detector computed tomography (MDCT), including contrast-enhanced MDCT coronary angiography, is  
6 considered a powerful diagnostic tool for the assessment of coronary disease in acute and in chronic cases [3]. It  
7 can also be used as a rule-out test in patients with a low to intermediate likelihood of disease, as shown by  
8 Schlattmann *et al.* in a recent meta-regression analysis [4].  
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13 In post-mortem practice, the diagnosis of ischemic heart disease is made after performing macroscopic  
14 examination and standard histology. The latter can be completed with immunostaining and the measurement of  
15 cardiac biomarkers, which are both limited by the post-mortem interval. [5]. The clinical history can be of  
16 relevance in determining the cause of death, but in most cases (especially in forensic practice) very little to no  
17 medical history is provided before the autopsy.  
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22 In recent years, as a result of the increased availability of computed tomography and magnetic resonance  
23 imaging in forensic practice, postmortem radiology is more frequently used [6,7]. Authors are currently debating  
24 if postmortem radiology should be a complementary examination or if it can be considered as a good  
25 replacement for conventional autopsy [8-10]. Postmortem MDCT appears to be very useful in demonstrating  
26 traumatic lesions. Recent studies, however, have highlighted its limited application and low accuracy in cases of  
27 natural deaths, especially in the field of cardiovascular pathology [10]. At the same time, some pioneer studies  
28 involving postmortem MDCT-angiography and cardiac pathologies have recently been published [11-13]  
29 describing the potential to overcome these weaknesses. Several authors suggest that the major limitations  
30 concerning cardio-vascular pathology could be minimized by the introduction of postmortem angiography  
31 [12,14,15]. In our practice, native MDCT has become part of the routine investigation. Cases with a suspicion of  
32 ischemic heart disease, regularly undergo a pre-autopsy MDCT-angiography using the technique of multiphase  
33 post-mortem CT-angiography (MPMCTA) [16]. Previous studies performed on whole body MDCT-angiography  
34 focused on vascular injuries in traumatic deaths. To our knowledge, imaging of cardiovascular disease has yet to  
35 be evaluated in detail.  
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45 The goal of this pilot study was to evaluate the diagnostic potential of MDCT and MPMCTA for the  
46 investigation of cases suspected of having ischemic heart disease by comparing the findings of native post-  
47 mortem MDCT, MPMCTA and conventional autopsy (including the histological examination of coronary  
48 arteries and myocardium).  
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## 52 **Material and method**

### 53 *Subjects*

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56 23 cases were retrospectively selected based on their clinical histories that were suggestive of death due to  
57 ischemic heart disease (Tab. 1) The autopsies were performed between 2009 and 2010 in accordance with  
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1 international guidelines [17,18] by two forensic pathologists, one in training and one certified by the national  
2 board. The age of the subjects ranged from 37 and 89 years with a mean of 52.3+/-12.2. There were 21 males  
3 and 2 females. The post-mortem interval ranged from a few hours to approximately 3 days.  
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#### 7 *Radiological examination and interpretation*

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10 MDCT-angiography was carried out using the standardized protocol for MPMCTA [12] which was approved by  
11 the local ethics committee. Following the protocol, a native CT-scan was performed prior to any manipulation of  
12 the body with a 8-row CT-unit (CT LightSpeed 8, GE Healthcare, Milwaukee, WI, USA) using the following  
13 scan parameters: field of view (FOV) 50 cm, slice thickness 2.5 mm, interval of reconstruction 2 mm, 120 kVp,  
14 280 mA and 150 second scan time. After the collection of post-mortem liquid samples for toxicological  
15 screening and analyses of cardiac biomarkers under CT-guidance [12], cannulation of the femoral vessel on one  
16 side was performed using cannulas (MAQUET GmbH & Co. KG, Rastatt, Germany) with a diameter of 16-  
17 French for arteries and 18-French for veins. A recently developed pressure-controlled perfusion device  
18 (Virtangio®, Fumedica AG, Maquet®, Muri, Switzerland) was used to inject a mixture of contrast agent  
19 (Angiofil®, Fumedica AG, Muri, Switzerland) and paraffin oil (liquid paraffin obtained from the local  
20 pharmacy) according to the protocol proposed by Grabherr *et al* [16]. This oily contrast has an appropriated  
21 viscosity for the perfusion of human bodies [19], allowing for optimal perfusion conditions for high-resolution  
22 postmortem angiography and simultaneously avoiding histological artifacts. The arterial phase of MPMCTA  
23 was carried out using the following scan parameters: field of view 50 cm, slice reconstructed thickness 1.25 mm,  
24 interval of reconstruction 0.6 mm, 120 kVp, 280 mA and a scan time of 140 seconds. Scan parameters of the  
25 venous and dynamic phase were: field of view 50 cm; slice reconstructed thickness 2.5 mm; interval of  
26 reconstruction 1.2 mm, 120 kVp, 280 mA and a scan time of 140 seconds.  
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37 The radiological interpretations of all images were performed by both a board certified radiologist specialized in  
38 vascular radiology and a board certified forensic pathologist trained in forensic imaging. They were both blinded  
39 to the autopsy results. Segments of coronary arteries that were deemed to be unperfused or stenosed greater than  
40 75% with CT- angiography were subsequently evaluated histologically as the stenoses greater than 75% or  
41 occluded lumen are associated with hemodynamically significant disturbances which lead to myocardial  
42 infarction and explain the sudden cardiac death. Above the 75% cut-off, the stenosis is considered as the highly  
43 probable cause of death after exclusion of other causes [17].  
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50 After CT-angiography, stenoses and occlusions of coronary arteries were further evaluated upon autopsy and  
51 histological examination.  
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#### 57 *Conventional autopsy*

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1 During the autopsy procedure a transverse slide of myocardium was systematically taken for histological  
2 examination, along with at least 5 labeled blocks of myocardium: the anterior, lateral and posterior wall of the  
3 left ventricle, the interventricular septum and the lateral wall of the right ventricle, in order to correlate the  
4 coronary artery pathology with the myocardial findings in the area which it supplies. For most cases the  
5 proximal and medial parts of coronary arteries were retained for decalcification prior to dissection. In several  
6 cases only the most stenosed fragments were histologically analyzed.  
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## 10 11 **Results**

12 All results are reported in Table 1  
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### 19 *Coronary calcifications*

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21 In 78% of the analyzed cases (18/23), calcification of coronary arteries was found on radiological examination.  
22 Calcifications were easily detected with both native CT- scan and CT- angiography. The calcifications were  
23 associated with coronary thromboses in 12 cases. There were no calcifications found in 2 cases (cases n° 4 and  
24 n°5, aged 37 and 42, respectively), but angio-CT revealed a stenosis of 50 to 75% of one coronary artery,  
25 suspected to be related to a vulnerable plaque/thrombosis. Pathological investigation revealed the presence of an  
26 acute thrombosis related to an eroded plaque. In another case of a 45 year old jogger (case n°17), only a small  
27 calcification of the left anterior descending artery (LAD) was found, and a 75% narrowing in the middle part of  
28 the LAD was confirmed by autopsy and histological examination (Fig 1). A calcium score was not evaluated in  
29 this pilot study and the extent of coronary calcification found on radiological examination was not systematically  
30 described in the autopsy reports, therefore the correlation between the two was not evaluated in this retrospective  
31 study. MDCT or MPMCTA appears to be a more sensitive means of detecting calcifications than conventional  
32 autopsy. Radiological examination also provides a simpler means of documenting the calcification status of all  
33 coronary arteries.  
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### 45 *Coronary stenosis/ atherosclerotic vulnerable plaque/ thrombosis*

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47 13 cases were selected, and a thrombosis was found in 11 of them. In one suspected case (n°15), a postmortem  
48 clot was responsible for the stop of perfusion. In another case (n°17), CT-angiography revealed a ~75% stenosis  
49 of the LAD that was not initially observed by the forensic pathologist in training upon a longitudinal opening of  
50 the vessel. A retrospective morphological exam of the same case permitted detection of a gross intramural plaque  
51 with significant stenosis of the lumen. The histological examination of the myocardium demonstrated signs of an  
52 early subendocardial infarct (Fig. 1).  
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57 In each of two previously mentioned cases (n°4 and n°5), CT- angiography revealed the presence of a 50-75%  
58 stenosis of the coronary artery and autopsy demonstrated a thrombosis related to eroded plaques.  
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1 In one case (n°2), the common trunk of the left coronary artery could not be perfused during CT-angiography,  
2 likely due to a technical problem (i.e. remaining blood or post-mortem clot inside the vessel). The artery was  
3 described to be normal at autopsy. Unfortunately, the common trunk was not collected for histological  
4 examination.  
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7 A coronary thrombosis was found during autopsy in 14 cases: acute or subacute in 11 cases, of various ages in 2  
8 cases and old in 1 case. A ruptured plaque was found in 7 cases (Fig. 2) and an eroded plaque in 6 cases (Fig. 3).  
9 The mean age of all 14 cases was 56.7+/-13.7, however, upon stratification the mean age of the victims with  
10 ruptured and eroded plaques was 60.5+/-8.2 and 46+/-9.7, respectively. The details are shown in Table 1. An old  
11 recanalised thrombus with collateral circulation was detected in 3 cases (Fig. 4), which was better visualized  
12 during the radiological exam than during conventional autopsy. 3D-reconstructions from MPMCTA proved to be  
13 a very simple technique to investigate collateral circulation.  
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18 In summary, of the 14 cases of coronary thrombosis detected at autopsy, 11 were not perfused during CT-  
19 angiography, two acute thromboses related to eroded plaques were visualized as stenosis of ~50-75% and one  
20 case with an old thrombosis was described as a partial occlusion with collateral circulation.  
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24 Positive arterial wall remodeling, which is a well known reaction to plaque formation [20], was seen with CT-  
25 angiography in two cases. An increase of the cross sectional area with normal lumen dimension was observed.  
26 The remodeling was associated with an acute thrombosis in one case of a 47 year old woman (n°3). There was  
27 no description of remodeling in the autopsy report.  
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### 31 *Cardiac tamponade*

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33 Hemopericardium was described in one case and was observed in the native and angio-CT scans. CT-  
34 angiography, however, permitted better visualization of the ruptured wall situated in the apical part of the left  
35 ventricle, as the contrast agent leaked through the rupture (Fig. 5). These findings were confirmed during the  
36 conventional autopsy.  
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### 41 *Signs of infarction*

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45 Histological patterns of infarction vary with infarct dating, ranging from the absence of histological lesion to old  
46 myocardial scar. These histological findings cannot be detected with certitude during CT examination. In 5  
47 cases, however, a “pathological enhancement” (mean Hounsfield Units  $\geq$  than 100) of the myocardium was  
48 observed in regions which correlated with the localization of the infarction. While the arterial phase mostly  
49 showed a diffuse enhancement of the concerned myocardium, enhancement increased in the subendocardiac  
50 layer during the venous and dynamic phase.  
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### 55 *Post-mortem clot and other artifacts*

1 In one case, a postmortem clot of a coronary artery was suspected upon radiological imaging (Fig. 6 a). The  
2 autopsy investigation excluded the presence of a thrombosis and complimentary investigations showed that death  
3 was related to acute alcohol and methadone intoxication.  
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5 A pulmonary artery embolism was suspected after performing CT angiography in 3 cases (Fig. 6 b), but none of  
6 them were confirmed by autopsy investigations.  
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## 8 **Discussion**

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11 Imaging of ischemic heart disease includes the evaluation of the coronary arteries and myocardium, both in a  
12 clinical and postmortem setting [21-25].  
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15 In a clinical setting, the myocardium and coronary arteries can be radiologically evaluated with  
16 echocardiography, nuclear cardiology, cardiac CT and magnetic resonance techniques. Cardiac CT allows for the  
17 non-invasive imaging of coronary arteries and, in selected patients, plays an important role for the diagnosis of  
18 coronary artery disease. The visualization of coronary arteries in clinical practice, however, can be difficult as  
19 they are small and constantly in motion. The last limitation is not an obstacle in the postmortem setting.  
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24 In our study the native CT-scan was not very helpful for the diagnosis of ischemic heart disease, as observed in  
25 previous studies [10]. Only calcifications of coronary arteries and evident cardiac pathological findings, such as  
26 cardiac tamponade, were observed. The most relevant yet subtle lesions such as coronary occlusions, stenoses  
27 and myocardial ischemia were not detected with the native CT-scan, despite the fact that post mortem imaging  
28 lacks the clinical limitation of coronary artery motion.  
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32 Calcifications were observed in 78% of the cases. Focal calcifications in atherosclerotic plaques are very  
33 common, particularly in older patients. Calcifications do not have a direct causal link to thrombosis, with the  
34 exception of older individuals when the presence of diffuse intimal calcification is coupled with diffuse  
35 dilatation of coronary arteries and intimal tears at the margin of calcium plates. It is accepted that the extent of  
36 calcification roughly relates to the amount of atherosclerosis, but not to the degree of coronary artery stenosis  
37 [26,27]. Moreover, clinical observations suggest that lesions responsible for acute thrombotic episodes are  
38 generally less calcified than plaques involved with stable angina [28]. This could be one reason why the  
39 pathologist did not systematically describe this finding in the autopsy reports. Radiologically, the presence of  
40 calcium is invariably associated with coronary atherosclerosis, especially in its advanced stage. Using cardiac  
41 CT, calcium deposits in the coronary arteries can be detected and quantified with low-radiation and non-  
42 enhanced image acquisition protocols. A high coronary calcium score, when adjusted for age and gender, is  
43 considered to be predictive of coronary adverse events [29]. However, in younger patients, a population which is  
44 mostly investigated in the forensic setting, non-calcified plaques have also been linked to episodes of acute chest  
45 pain. Kwon *et al* (2011) showed that CT cannot assess the coronary stenosis of non-calcified plaques in low risk  
46 patients suspected of having coronary artery disease because coronary CT angiography coupled with coronary  
47 artery calcium has no incremental prognostic value when compared to coronary CT angiography alone [30]. It  
48 has been demonstrated that the amount of calcified plaque may not be associated with an increased risk of future  
49 coronary events [31]. In our series, no calcifications were observed in 2 cases of relatively young patients (aged  
50 37 and 42) and pathological investigations revealed the presence of acute thromboses related to eroded plaques.  
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1 In others cases, CT-angiography revealed the presence of occlusions thought to be related to acute thromboses or  
2 significant atherosclerotic plaques, while only isolated calcifications of coronary arteries were found.

3 Postmortem CT- angiography enabled better visualization of coronary arteries than native CT and allowed for  
4 the evaluation of stenoses and occlusions. Only a few recent studies have addressed this topic [12-14]. Saunders  
5 *et al.* presented the developmental stages for manual targeted in situ postmortem angiography using injections of  
6 air/Urografin® and demonstrated that large volumes of air and contrast can be injected without displacing the  
7 thrombi [13]. In a more recent study, Roberts et al. presented a series of 10 cases in which a novel method of  
8 postmortem coronary artery CT angiography was used by injecting contrast medium into the left common  
9 carotid artery. Their results showed relatively good correlation with autopsy findings. The disadvantage of this  
10 technique is related to the repositioning of the catheter after a CT control, often resulting in unsatisfactory filling  
11 of coronary arteries which necessitates turning of the patient with further injections and CT scanning [12]. We  
12 did not encounter any problems related to the positioning of the catheter or filling of coronary arteries, as the  
13 technique of PMPCTA is standardized and coronary arteries are visualized in all cases except those of massive  
14 aortic rupture. We performed histological examinations of coronary arteries permitting better evaluation of  
15 image-autopsy correlations.

16 Acute thrombosis is the result of two different pathological processes: plaque disruption and endothelial erosion.  
17 In this study, an acute coronary thrombosis was found in 13 cases: 7 were related to plaque rupture and 6 to  
18 plaque erosion. CT angiography detected “suspect” segments of coronary arteries in all 13 cases: 11 cases did  
19 not have perfused segments and in 2 cases of young victims partial occlusions were found in non-calcified  
20 coronary arteries. The victims were younger in the group of plaque erosion than that of plaque rupture, in  
21 accordance with previous pathological studies [32,33]. The results of this study indicate that MPMCTA is a  
22 reasonable tool to rule out coronary artery stenosis and to indicate suspected occlusions in order to direct  
23 sampling for histological examination. Clear patterns of vulnerable plaques (rupture versus erosion) were,  
24 however, not identified in postmortem CT nor in CT angiography in this series. This is also true in clinical  
25 practice as traditional CT-angiography is insensitive for the detection of plaques as the resolution is insufficient  
26 to visualize this lipid-rich core and fragile rupture-prone fibrous cap which is responsible for plaque rupture,  
27 inflammation, and neovascularisation [2]. The identification of patients with vulnerable plaques is difficult and  
28 the combination of several sophisticated imaging methods (i.e. OCT/Backscattered IVUS; IVUS/ Raman  
29 spectroscopy OCT-optical coherence tomography; IVUS- intravascular ultrasound) may provide the most  
30 information on the presence or absence of disease [8]. Many of these methods cannot be used in the post-mortem  
31 setting. Also eroded plaques contain no specific features that enable their detection upon radiological  
32 examination, with the exception of stenosis. It has recently been suggested that lipid and fibrous coronary plaque  
33 attenuation values are significantly modified by differences in lumen contrast densities both in and ex vivo [34].  
34 This hypothesis should be verified by large autopsy series performed after radiological postmortem examination.  
35 A prospective study would enable the evaluation of the degree of stenosis/perfusion and calcifications, as well as  
36 the remodeling in the proximal, middle and distal segments of all coronary arteries in both radiological and  
37 autopsy examinations. The labeled segments of coronary arteries should be collected and examined  
38 histologically. Labeled samples of myocardium should be collected in order to correlate coronary artery  
39 pathology with myocardial ischemia.

1 In our series, no thromboses were found in 8 cases: 4 cases had a stenosis of one coronary artery and 2 cases had  
2 left ventricular hypertrophy. One must questions if the pre-existing thrombosis could have been be eventually  
3 dislodged in some of these cases. Although impossible to exclude this hypothesis, it seems unlikely considering  
4 that in this first series even very discrete lesions, such as eroded plaques, were visualised with the angiographic  
5 CT-examination. The advantage of PMPCTA is that there is no direct mechanical manipulation of the coronary  
6 arteries. As the cannulation site is located in one inguinal region with a very low perfusion pressure (1200 ml in  
7 90 seconds for the arterial phase), the perfusion flow in the coronary arteries is slower than in vivo. It has been  
8 shown that coronary artery spasm or myocardial hypertrophy may provoke an ischemic event without any  
9 thrombosis, and that sudden death may result from an associated arrhythmia. It is also widely accepted that the  
10 diagnosis of death related to chronic ischemic heart disease can be made in the presence of narrowing of 75 % or  
11 more in at least one of the main coronary arteries as long as other complimentary analyses, such as toxicology or  
12 clinical chemistry, are negative.  
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19 Coronary CT-angiography, like invasive angiography, is a morphological imaging technique and cannot  
20 demonstrate the functional relevance of stenoses. This is particularly relevant in clinical practice for patients  
21 with borderline degrees of stenosis [35], where CT and CT angiography are unable to detect myocardial  
22 ischemia and necrosis. As shown in the Meijboom study, CT can help rule out coronary stenosis and myocardial  
23 ischemia, but even pronounced atherosclerotic changes and stenosis seen on CT do not reliably predict the  
24 presence of ischemia that can be visualised by perfusion imaging [36,35]. In our post-mortem series,  
25 pathological enhancement of the myocardium was observed in 5 cases and is thought to be an indirect sign of a  
26 myocardial lesion. Angiography is a promising soft tissue imaging technique, however, more studies are needed  
27 to determine its potential. Post-mortem magnetic resonance imaging does not have this limitation and can  
28 identify soft tissue lesions [11], but its accessibility is more limited than MDCT or CT-angiography and its  
29 usefulness is still being evaluated for post-mortem examinations. Postmortem CT- angiography and cardiac MRI  
30 have their advantages and disadvantages. The biggest advantage of post-mortem CT angiography is the ability to  
31 detect stenoses or occlusions although Ruder *et al.* [37] recently presented a postmortem assessment of coronary  
32 artery disease by MRI and suggested that chemical shift artifacts along the coronary arteries may be considered a  
33 marker of vessel patency, thus improving the ability of minimal autopsy procedures to detect coronary artery  
34 disease. Jackowski presented a case report [38] with a postmortem MRI based diagnosis of sudden coronary  
35 artery occlusion and peracute septal myocardial ischemia without the application of contrast agents. More studies  
36 are needed to establish the postmortem radiological diagnostic gold standards and to determine their cost-  
37 effectiveness. Both methods have been associated with specific postmortem\_artifacts. At present we have more  
38 experience with the postmortem CT-scans than postmortem MRI which was introduced more recently. In regards  
39 to the dislodgement of a thrombus, unperfused postmortem MRI has not been shown to do so while the  
40 possibility has not been excluded for angiography techniques.  
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53 The disadvantage of both postmortem techniques is that angio-CT and cardiac MRI require dedicated technical  
54 equipment as well as radiologists experienced in the field of postmortem radiology. MRI equipment is more  
55 expensive than CT and radiological norms defining the space required for magnetic shielding are different than  
56 that for CT. CT is employed with greater and greater frequency, while postmortem MRI exists in only a few  
57 academic research centers. Radiological CT exams are faster and have a higher resolution due to a higher  
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1 radiation dose and smaller slices. The high radiation dose is of no concern in post-mortem imaging. Although  
2 MRI is the method of choice for the investigation of the myocardium, CT-angiography remains the best  
3 technique for the investigation of the coronary arteries and any related calcifications which are a weakness of  
4 MRI. CT-angiography perfusion enables the evaluation of the vascular lumen which can often be collapsed or  
5 filled with remaining blood or gas bubbles in the cadavers. Without the opacification of the lumen, the  
6 interpretation of the presence or absence of stenoses is not possible. At present, MRI can not differentiate  
7 between post-mortem clots and pathological thrombi. Postmortem clots can only be identified after reperfusing  
8 the vessels and comparing the images of the different phases of post-mortem angiography, thus avoiding any  
9 misinterpretation.

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16 At present, histology remains the reference method for the post-mortem diagnosis of ischemic heart disease.  
17 According to the current recommendations in the field of autopsy practice and cardiovascular pathology  
18 [17,18,24,39-41], histological examination of the myocardium should be performed in order to assess the time  
19 dependent histological patterns of ischemia. Some pathological findings, such as acute coronary occlusive  
20 thrombosis or myocardial rupture, are practically certain to represent the cause of death, whereas, the  
21 interpretation of chronic macroscopic findings, such as those described in ischemic heart disease, is more  
22 delicate. Considering the medical responsibility implications and potential third party involvement, an accurate  
23 diagnosis and dating are essential. Correlations between autopsy and histological findings with modern post-  
24 mortem coronary artery imaging may help us to better understand the clinical and radiological aspects of acute  
25 coronary syndromes. The histology of coronary arteries is of particular importance, especially for cases of  
26 sudden cardiac death with little to no clinical history. Instant death due to ventricular fibrillation or atrio-  
27 ventricular (AV) block is a frequent complication of coronary thrombosis before medical intervention and  
28 represents 50% of acute myocardial infarction mortality [4]. Most of these patients are young and have a  
29 proximal thrombotic occlusion of the left anterior descending artery [26]. Forensic autopsies of these patients,  
30 consisting of radiological and histological examinations, are very important.

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39 Clinically, it is well recognised that there is no relationship between the degree of coronary stenosis and the  
40 onset of symptoms, complications and acute coronary-syndrome mortality. A significant proportion of  
41 thrombotic occlusions do not develop at sites of pre-existing high-grade stenosis or plaque formation. Up to 75%  
42 of vulnerable plaques leading to acute infarction are associated with stenoses having a previous diameter of less  
43 than 50%. Only a minor percentage of occlusions develop on stenoses with a previous diameter greater than 70%  
44 [5]. These intricate relationships need to be evaluated in larger case-control studies. The information obtained  
45 from post-mortem examinations, including CT angiography and MRI, can help improve the clinical diagnosis  
46 and treatment for the most vulnerable patients.

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52 Cardiac tamponade, which is often associated with acute myocardial infarction, can be easily diagnosed with  
53 classical autopsy and both native and CT angiography. Although postmortem CT and CT angiography enable  
54 visualization of other pathologies, such as pulmonary edema and pericardial or pulmonary effusions, these  
55 findings are not specific for ischemic heart disease and may be observed with other cardiac diseases.

1 Coronary postmortem CT angiography is a reasonable tool to view the morphology of coronary arteries, rule out  
2 coronary artery stenosis and occlusion, and direct sampling for histological examination. Radiological cardiac  
3 postmortem examination also enables the revision of many cases in which it is impossible to keep the entire  
4 heart due to legal restrictions. It is too early to postulate that this technique is sufficient to diagnose that the cause  
5 of death was related to an acute or chronic ischemic event. Postmortem cardiac radiology is a new field for both  
6 forensic pathologists and radiologists, both of whom have to learn to read the postmortem modified images,  
7 including the interpretation of possible artifacts. The visualisation and differentiation of post-mortem artifacts in  
8 CT imaging has yet to be studied.

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12 As reported in clinical practice, the diagnostic performance of coronary CT angiography can be improved when  
13 read by experienced physicians, but acquiring expertise in coronary CT angiography is slow and may take more  
14 than 1 year [10]. The information obtained from both radiology and forensic pathology in postmortem  
15 investigations can help to further the understanding of radiological evaluation in the clinical setting.  
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### 21 **Limitations**

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23 This pilot study contained a small number of cases and larger studies are needed to find statistical correlations.  
24 This study, however, highlights the importance of comparing the radiological data with the autopsy and  
25 histological findings of coronary arteries and myocardium for deaths related to ischemic heart disease. In our  
26 opinion, prospective studies should be performed to evaluate the correlations between radiological examination  
27 findings as calcium score, myocardial enhancement and autopsy and histological findings.  
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### 36 **Acknowledgements**

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39 This study was partly financially supported by the Promotion Agency for Innovation of the Swiss Confederation  
40 (KTI Nr.10221.1 PFIW-IW).  
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42 We thank the team of the unity of forensic medicine in Lausanne for their assistance and Allison Felley  
43 Jacquemont for editing the manuscript.  
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2 **Legends**  
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7 **Figures**  
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9 Fig. 1  
10

11 Case of a 45 year old man who died suddenly while jogging (case n°17): native CT image (a) shows an isolated  
12 calcification of the middle part of the LAD artery (arrow). Angio-CT (b) shows a partial occlusion (arrow) of the  
13 LAD, immediately distal to the calcification. A 3D-reconstruction performed on the data of the arterial phase of  
14 PMPCTA (c) demonstrates the localization of both lesions: the small calcification (yellow arrow) and the  
15 stenosis of LAD (red arrow). Histological examination (d) showed a significant stenosis of the LAD artery and  
16 signs of myocardial ischemia as contraction band necrosis (haematoxylin & eosin) (e)  
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22 Fig. 2  
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24 67 year old man who died suddenly while catching the train (case n°10): CT-angiography showed a calcified  
25 plaque of the RCA (yellow arrow) and a defect of perfusion (red arrow) with perihilar oedema (a). Histological  
26 examination showed a ruptured plaque of the RCA (b) and an infarct of the posterior wall of the left ventricle  
27 with diffuse infiltration of polymorphonuclear neutrophil cells (haematoxylin & eosin) (c)  
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31 Fig. 3  
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33 Sudden collapse while driving in a 54 year old man (case n°20): native CT shows multiple calcifications of LAD  
34 (a), angio-CT (b, c) calcifications and an occlusion (arrow) of LAD, histological examination of LAD reveals a  
35 thrombosis (haematoxylin & eosin) (d, e)  
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39 Fig. 4  
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41 Old recanalised thrombosis in a 53 year old man found dead at home (case n °22): native CT without  
42 significant lesions (a), PMPCTA revealed an occlusion (arrows) in the distal part of RCA (b, c). The histological  
43 examination of this region identified a recanalised thrombus in the late stages after thrombosis, in which many  
44 small capillary sized channels are seeded (Masson's trichrome) (d)  
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48 Fig. 5  
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50 Subacute infarct related to LCX thrombosis and hemopericardium in a 67 year old woman (case n°13). Rupture  
51 of the posterior wall (arrows) in CT angiography (a) and at autopsy (b). An enhancement of the infarcted  
52 myocardium is observed (\* in a) during the arterial phase of PMPCTA. 3D-reconstruction (c) performed on data  
53 of the arterial phase shows a complete occlusion (arrow) of LCX. Autopsy investigation of LCX (d) revealed an  
54 occlusive thrombosis (arrow) and histological examination of the myocardium showed a myocardial infarction  
55 (e) presented as necrosis of cardio-myocytes and diffuse infiltration of polymorphonuclear neutrophils cells  
56 (haematoxylin & eosin).  
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Fig. 6

Artifacts observed during the study: Problem of perfusion related to a post-mortem clot (a) in case n° 15 producing the image of a layer (arrow) in the ascending aorta and rendering opacification of the left coronary artery impossible (b): Stop of perfusion observed in case n°5 located in a pulmonary artery due to a post-mortem clot (arrow), suggesting a pulmonary embolism that could not be confirmed at autopsy.

### Tab 1

Overview of all findings made during autopsy, native CT and CT-angiography. Autopsy diagnosis was based on macroscopic and histologic appearance. RCA- right coronary artery, LAD- left anterior descending coronary artery; LCX left circumflex coronary artery; LMCA- left main coronary artery. Vulnerable plaque: E-eroded plaque, R-ruptured plaque, O-old thrombus. Thrombosis: 1-present. Stenosis of coronary arteries at autopsy and histological evaluation: + less than 50%, ++ 50-75 %, +++ 75% or more. Perfusion of coronary arteries in CT-angiography: NP-not perfused or stenosis more than 75%, PP-partly perfused or stenosis less than 75%. Calcifications of coronary arteries evaluated in postmortem radiological examination: + isolated calcification; ++ multiple calcifications. Histological evaluation of myocardial ischemia: AMI-acute myocardial infarct, SAMI-subacute myocardial infarct, AW- anterior wall, PW-posterior wall, S-septum, P-SW-postero-septal wall A-SW- antero-septal wall.

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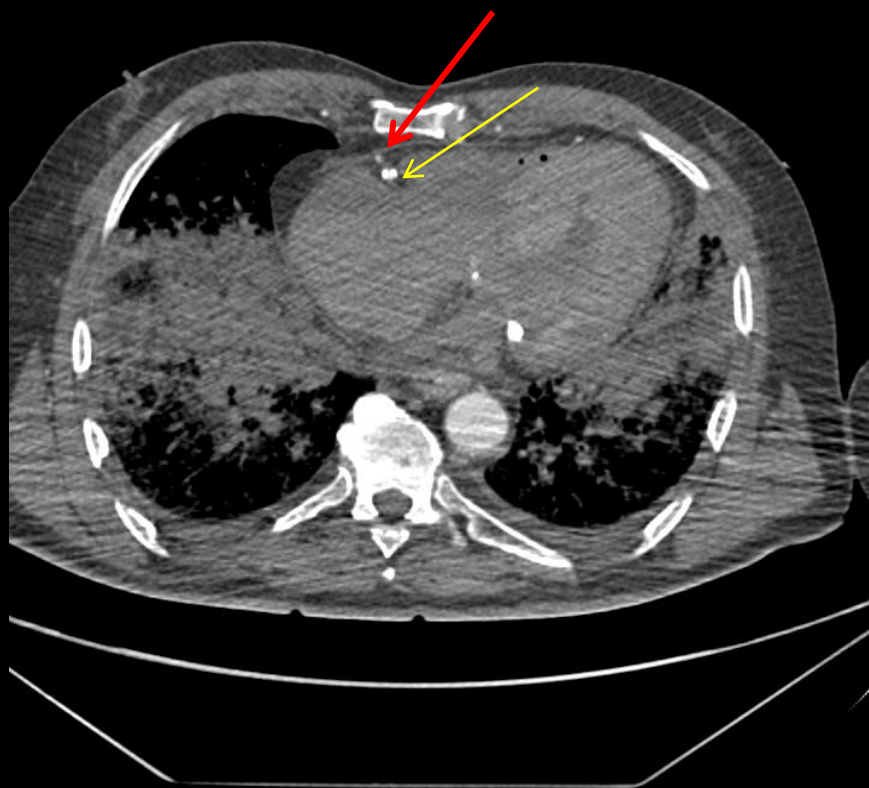


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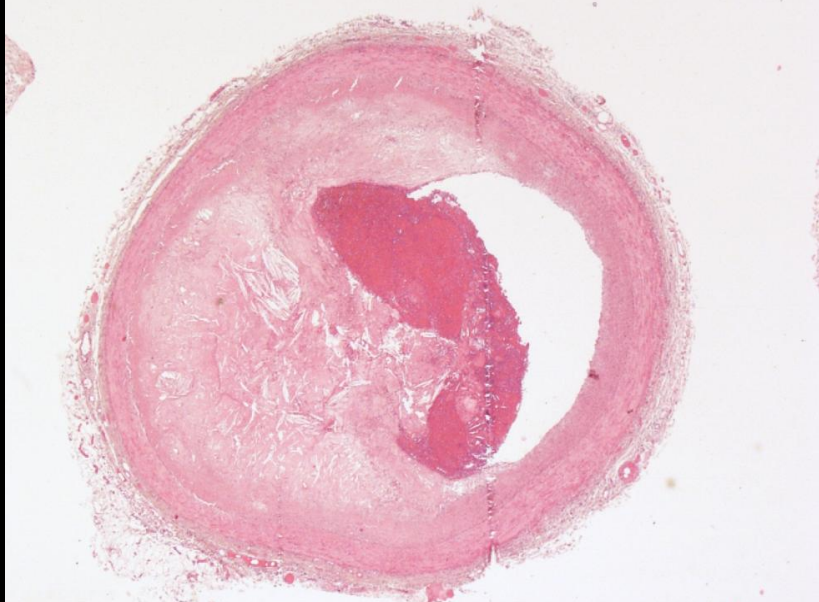




**a**



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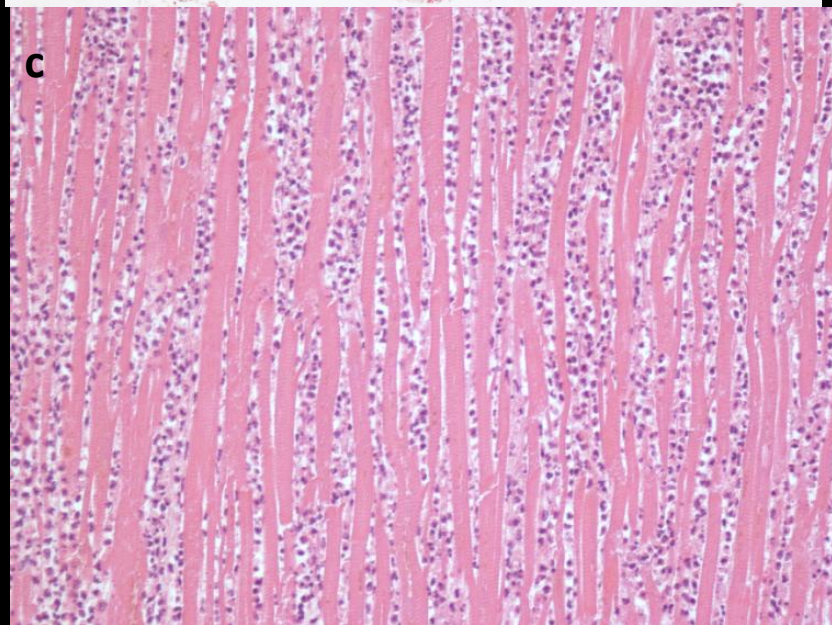


Fig. 2

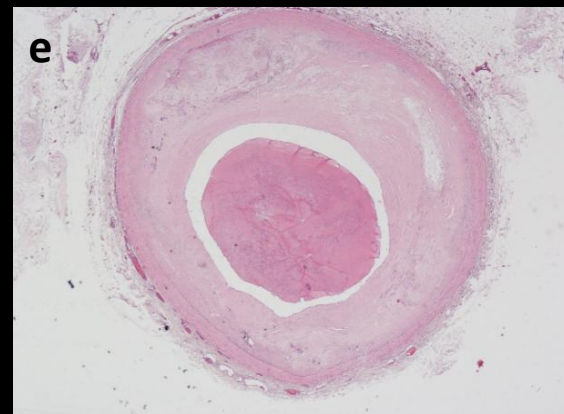
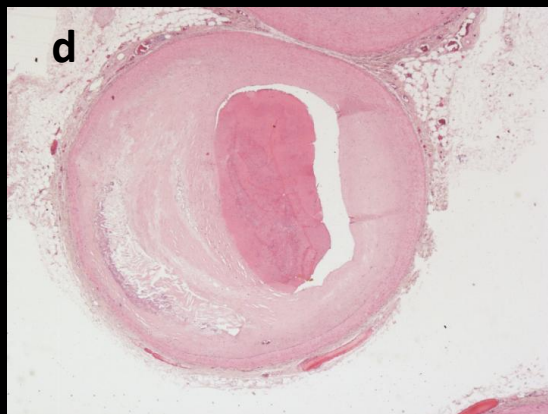
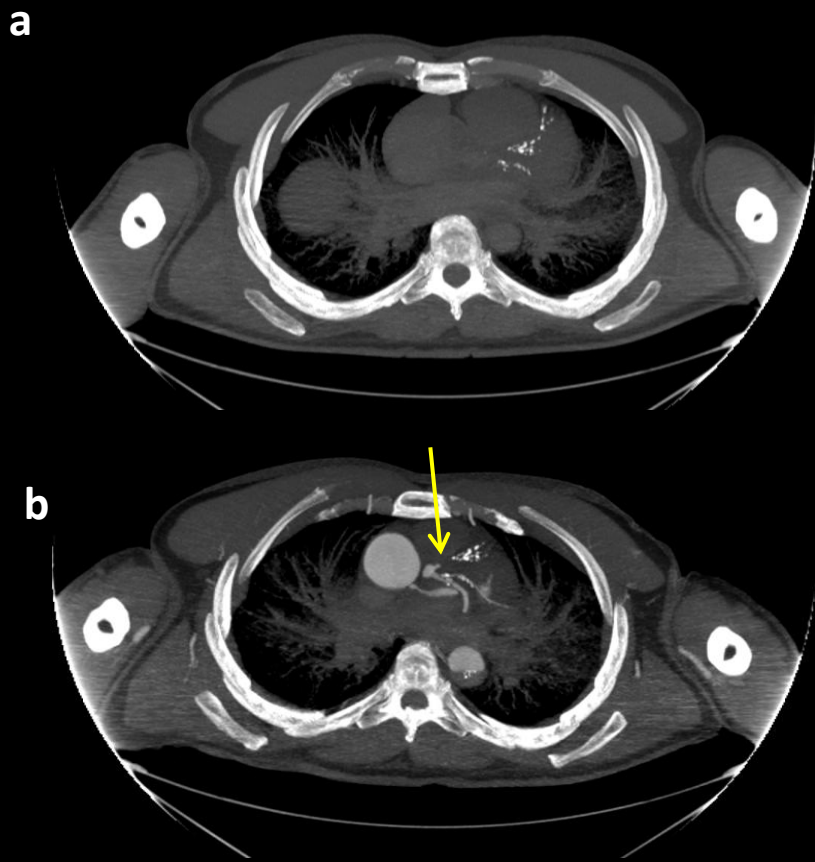
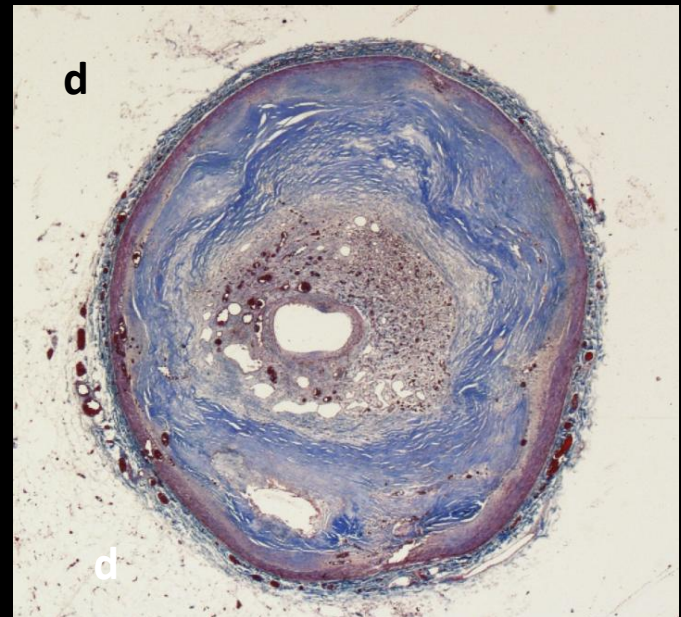
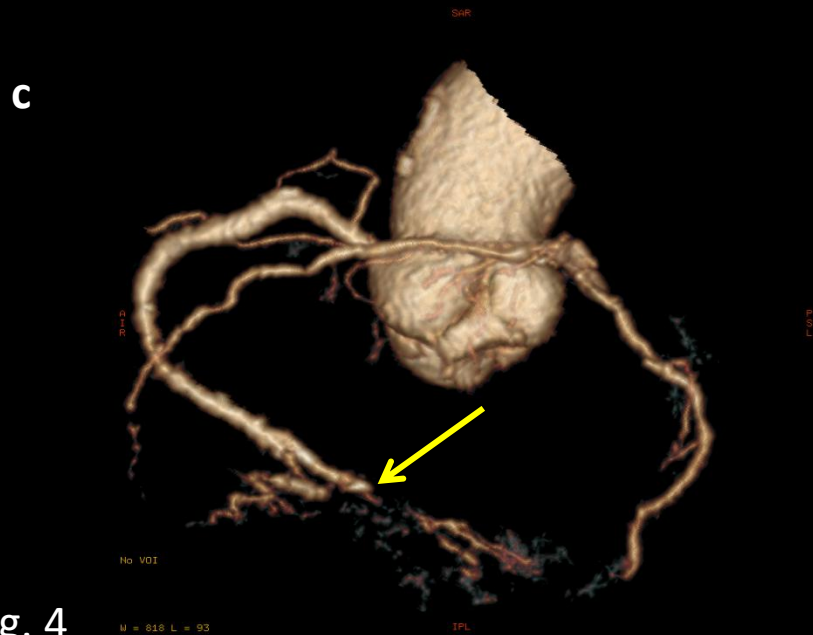
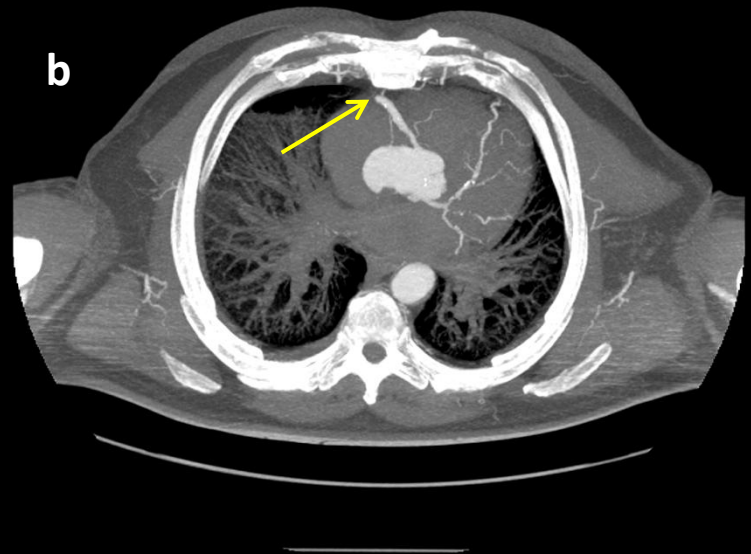


Fig. 3





**Fig. 4**

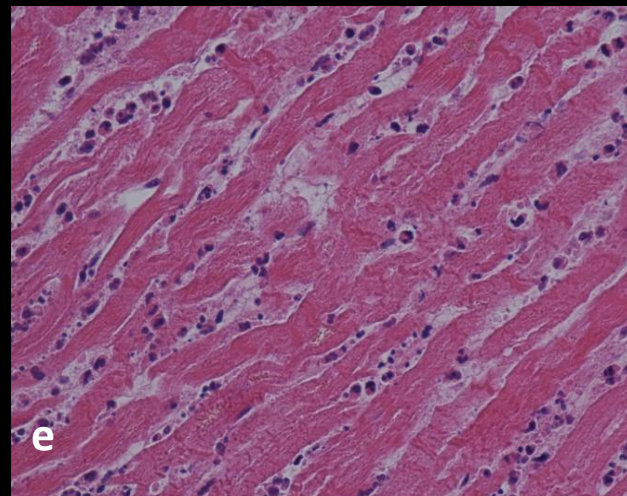
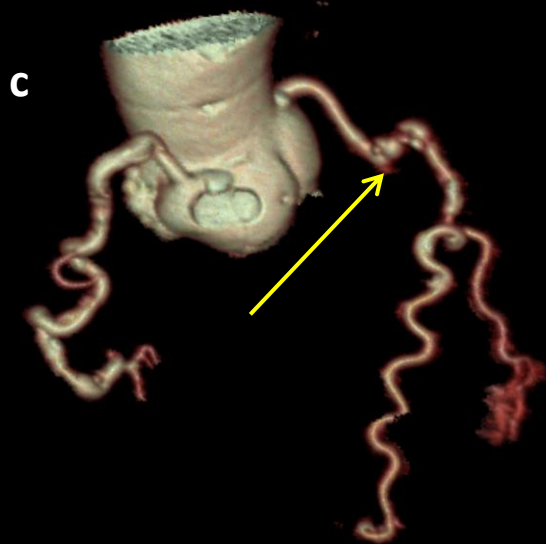
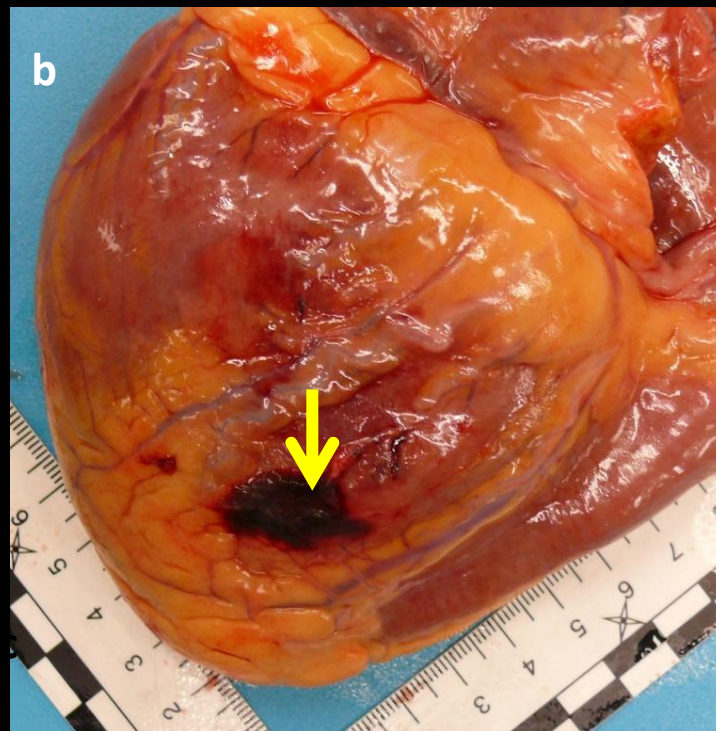
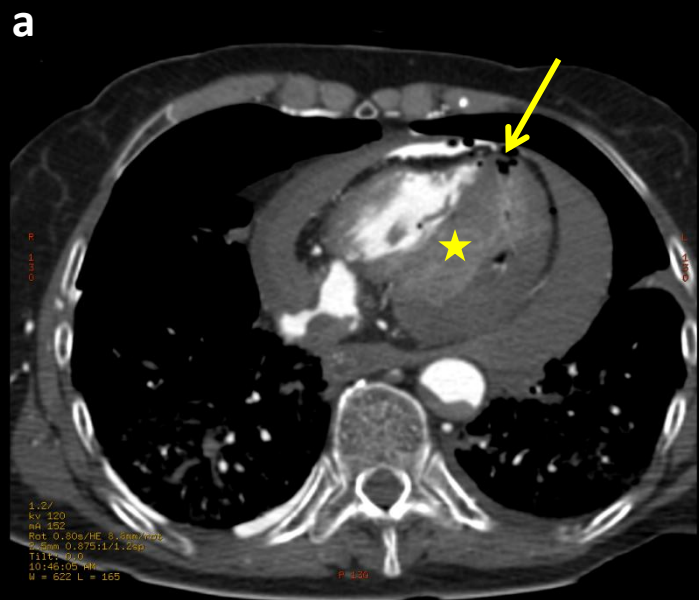


Fig. 5



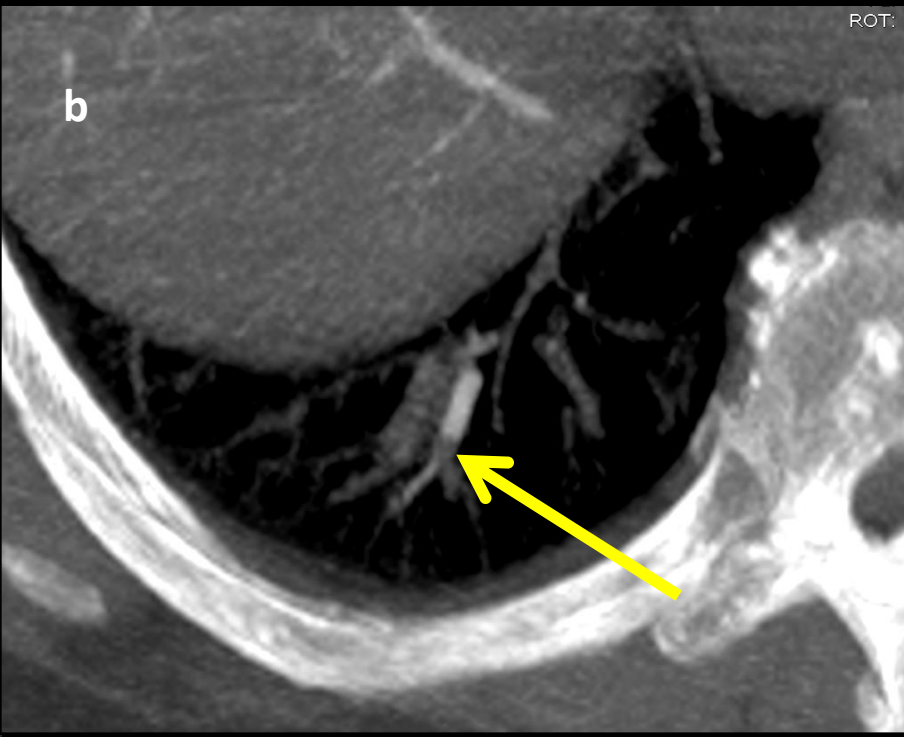


Fig. 6

N°	sex	age	Clinical history	Body weight [kg]	Heart weight [g]	Coronary arteries	Coronary arteries			Angio CT scan			Native CT scan		Myocardium (autopsy and histology findings) Other findings
							Autopsy and histological examination			cardiac/coronary findings			Calcifications of coronary arteries	others	
							Vulnerable plaque	Acute thrombosis	Stenosis	Perfusion of coronary arteries	Calcifications of coronary arteries	Other			
1	m	48	Drowning	83	500	RCA	E	1	++	NP	++	++		PW: AMI	
						LAD			+++	PP					
						LCX									
2	m	46	Found dead at home	79	500	RCA					++	++	Technical problems to visualize the common trunk	PW :AMI	
						LAD			++	PP					
						LCX			++	PP					
3	f	47	Sudden death a few hours after a chest pain	60	360	RCA							LAD positive remodelling	AW : AMI	
						LAD	R	1	+++	NP	+				
						LCX									
4	m	37	Sudden death shortly after abdominal pain	120	420	RCA							Image of pulmonary emboli		
						LAD									
						LCX	E	1		PP					
5	m	42	Sudden death shortly after chest pain	120	480	RCA							Image of pulmonary emboli	PW: AMI	
						LAD									
						LCX	E	1	++	PP					
6	m	52	Sudden death after physical effort	76	490	RCA			+	PP	++	++		AW: AMI	
						LAD			+++	PP					
						LCX									
7	m	56	Dyspnea since a few days	77	490	RCA	O		+++	NP	++	++	AW: myocardial enhancement	AW: SAMI PW: old subendocardial infarct hibernating myocardium	
						LAD	R	1	++	PP					
						LCX									
8	m	50	Found dead at home  Chest pain the day before	57	450	RCA			+	PP	++	++	AW: myocardial enhancement/ image of pulmonary emboli	AW: AMI	
						LAD			++	PP					
						LCX			+						



9	m	65	Found dead at home, suspicion of poisoning	63	490	RCA	R	1	+	NP		LAD positive remodelling	++		P-SW : SAMI
						LAD			++						
						LCX									
10	m	67	Sudden death at the train station	67	520	RCA	R	1	++	NP	++	Myocardial enhancement problem of perfusion LAD (plaques or technical problems)	++		PW: SAMI
						LAD				?					
						LCX				PP					
11	m	52	Found dead at home	65	350	RCA			+++	PP	+		+		PW: fibrosis Alteration postmortem
						LAD			+	PP					
						LCX									
12	m	52	Found dead at home by his wife	73	500	RCA				PP					PW: AMI and fibrous scar
			Any medical history			LAD									
						LCX	O+R	1		NP					
13	f	67	Found dead at home thoracic oppression since 1 week	56	300	RCA			+	PP	++	Hemopericardium	++	Hemopericardium	Hemopericardium
						LAD			+	PP		A-SW :enhancement of the myocardium and rupture			PW: SAMI and rupture of the myocardium
						LCX	E	1	++	NP					
14	m	42	Found dead at his workplace	90	470	RCA			+++	PP	++	S: enhancement of the myocardium	++		PSW : fibrosis transmural mostly subendocardiac (old infarct scar)
			Any medical history			LAD			+++	PP					
						LCX			+						
15	m	35	Found dead at home by the police, methadone and alcohol intoxication	80	490	RCA									Post-mortem fragmentation of fibres
						LAD	p-m clot			NP	++		++		
						LCX									
16	m	44	Found dead by his wife in the bed	75	390	RCA	E	1	++	NP	++		++		PW: AMI
						LAD			+	PP					
						LCX				PP					
17	m	45	Sudden death while jogging	75	460	RCA									
						LAD			+++	NP	+		+		
						LCX									
18	m	49	Sudden death after chest pain	83	480	RCA									LV hypertrophy P-SW: AMI P-SW: small foci of fibrosis
						LAD									
						LCX			+						

19	m	69	Sudden collapse while driving	71	470	RCA					++		++		LW: contraction bands
						LAD									
						LCX	R	1	++	NP					
20	m	54	Sudden collapse while driving	80	470	RCA			++		++		++		AW: a few contraction bands
						LAD	E	1	++	NP					
						LCX			++						
21	m	43	Found dead at home, History of palpitations	80	550	RCA			+						LV hypertrophy Mitral floppy valve
						LAD			+		+		+		P-SW: contractions bands
						LCX			+						
22	m	53	Found dead at home	94	440	RCA	O		++	PP	++		++		P-SW: AMI and old subendocardial infarct scar
						LAD			++						
						LCX			+						
23	m	89	Collapse followed by a fall	46	285	RCA	O+R	1	++	NP	++	LAD proximal- stent	++	Calcification of mitral valve	PW: old transmural infarct scar and SAMI
						LAD			++	PP					
						LCX									

**Title page**

**Title:** Evaluation of postmortem MDCT and MDCT- angiography for the investigation of sudden cardiac death related to atherosclerotic coronary artery disease

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