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Post-mortem imaging of sudden cardiac death

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Abstract:	<p>Post-mortem imaging is increasingly used in forensic practice in cases of natural deaths related to cardiovascular diseases, which represent the most common causes of death in developed countries. While radiological examination is generally considered to be a good complement for conventional autopsy, it was thought to have limited application in cardiovascular pathology. At present, MDCT, CT-angiography and cardiac MRI are used in post-mortem radiological investigation of cardiovascular pathologies. This review presents the actual state of post-mortem imaging for cardiovascular pathologies in cases of sudden cardiac death (SCD), taking into consideration both the advantages and limitations.</p> <p>The radiological evaluation of ischemic heart disease, the most frequent cause of SCD in the general population of industrialised countries, includes the examination of the coronary arteries and myocardium. Post-mortem CT angiography is very useful for the detection of stenoses and occlusions of coronary arteries, but less so for the identification of ischemic myocardium. MRI is the method of choice for the radiological investigation of the myocardium in clinical practice, but its accessibility and application are still limited in post-mortem practice.</p> <p>There are very few reports implicating post-mortem radiology in the investigation of other causes of SCD, such as cardiomyopathies, coronary artery abnormalities and valvular pathologies. Cardiomyopathies representing the most frequent cause of SCD in young athletes cannot be diagnosed by echocardiography, the most widely available technique in clinical practice for the functional evaluation of the heart and the detection of cardiomyopathies. Post-mortem CT-angiography and MRI have the potential to detect advanced stages of diseases when morphological substrate is present, but these methods have yet to be sufficiently validated for post-mortem cases. Genetically determined channelopathies cannot be detected radiologically. This review underlines the need to establish the role of post-mortem radiology in the diagnosis of SCD.</p> <p>Keywords: sudden cardiac death, post-mortem CT-angiography (PMCTA), post-</p>

	mortem MRI (cardiac PMMR)

Title page

Title: **Post-mortem imaging of sudden cardiac death**

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Abstract

Post-mortem imaging is increasingly used in forensic practice in cases of natural deaths related to cardiovascular diseases, which represent the most common causes of death in developed countries. While radiological examination is generally considered to be a good complement for conventional autopsy, it was thought to have limited application in cardiovascular pathology. At present, MDCT, CT-angiography and cardiac MRI are used in post-mortem radiological investigation of cardiovascular pathologies. This review presents the actual state of post-mortem imaging for cardiovascular pathologies in cases of sudden cardiac death (SCD), taking into consideration both the advantages and limitations.

The radiological evaluation of ischemic heart disease, the most frequent cause of SCD in the general population of industrialised countries, includes the examination of the coronary arteries and myocardium. Post-mortem CT angiography is very useful for the detection of stenoses and occlusions of coronary arteries, but less so for the identification of ischemic myocardium. MRI is the method of choice for the radiological investigation of the myocardium in clinical practice, but its accessibility and application are still limited in post-mortem practice.

There are very few reports implicating post-mortem radiology in the investigation of other causes of SCD, such as cardiomyopathies, coronary artery abnormalities and valvular pathologies. Cardiomyopathies representing the most frequent cause of SCD in young athletes cannot be diagnosed by echocardiography, the most widely available technique in clinical practice for the functional evaluation of the heart and the detection of cardiomyopathies. Post-mortem CT-angiography and MRI have the potential to detect advanced stages of diseases when morphological substrate is present, but these methods have yet to be sufficiently validated for post-mortem cases. Genetically determined channelopathies cannot be detected radiologically. This review underlines the need to establish the role of post-mortem radiology in the diagnosis of SCD.

Keywords: sudden cardiac death, post-mortem CT-angiography (PMCTA), cardiac post-mortem MRI (cardiac PMMR)

Introduction - Radiological post-mortem examination for cardiovascular pathologies

Radiological imaging plays a very important role in the diagnosis of cardiac pathologies in the living. In forensic post-mortem practice, radiological examination has proven to be a very useful tool for cases such as gunshot wounds, physical child abuse and victim identification. In the last fifteen years computed tomography and magnetic resonance imaging (CT and MRI) have been increasingly used in routine forensic practice and research. Undetermined causes of death and sudden cardiac deaths represent an important part of forensic practice and these cases are increasingly investigated with modern radiological techniques. Radiological post-mortem examination was initially considered to be of limited benefit and low accuracy for the investigation of cardiovascular pathologies [1]. The introduction of post-mortem CT-angiography (PMCTA), which enables the investigation of the vascular lumen, has proven to be very promising [2-7] and the first post-mortem MRI (PMMR) studies have yielded interesting results for the investigation of ischemic myocardium [8,9].

The goal of this paper is to discuss the advantages and limitations of post-mortem imaging for the diagnosis of cardiac pathologies in sudden cardiac death.

Sudden cardiac death

Although definitions of sudden death and sudden cardiac death (SCD) vary greatly, the most widely accepted definition of SCD is a sudden and unexpected death that occurs within one hour of symptom-onset. For unwitnessed deaths, victims observed alive within 24 hours before death meet the definition [10,11]. The underlying cause of sudden death is most frequently cardiovascular in origin, with ischemic heart disease being most common in the general population [11].

Any sudden, unexpected or unexplained death warrants medico-legal investigation. Sudden cardiac death autopsies should be performed according to guidelines set by the fields of forensic medicine and cardiovascular pathology. Classical investigation of SCD includes the evaluation of clinical history, autopsy and histology examination, and sometimes the analysis of cardiac biomarkers and/or genetic analyses for channelopathies. No gold standards currently exist for the post-mortem radiological evaluation of cardiovascular pathologies.

Epidemiology and causes of sudden cardiac death

Cardiovascular pathologies are the most common causes of death in developed countries. In recent prospective studies using multiple sources in the United States, Netherlands, Ireland, and China, SCD rates range from 50 to 100 per 100,000 in the general population [12,13]. The true incidence of SCD remains unknown and is likely under-reported since sudden arrhythmic events are often misclassified as drownings, traffic traumas or epileptic seizures [14,15]. The most common clinical finding associated with SCD in the general population is ischemic heart disease. According to epidemiological studies, approximately 80% of SCD cases can be attributed to this disease. 10-15% of SCDs result from cardiomyopathies with a morphological substrate, such as hypertrophic cardiomyopathy (HCM), arrhythmogenic right

ventricular cardiomyopathy/dysplasia (ARVC/D) and myocardial infiltrative diseases (i.e. sarcoidosis). In the remaining 5-10%, the cause of SCD is related to either a structurally abnormal congenital cardiac condition (i.e. coronary artery abnormalities) or to cardiac channelopathies [11].

The causes and incidences of SCD in younger individuals vary according to the study and population. The major limitation of SCD evaluation is the lack of adequate or available autopsies. In the Irish study comprising 116 victims between 14-35 years of age, the most frequent causes of death were sudden unexplained death syndrome (26.7%), coronary artery disease (20.7%), HCM (14.7%) and idiopathic left ventricular hypertrophy not fulfilling criteria for HCM (10.3%) [16]. In a recent retrospective study, Eckart *et al.* reviewed 902 non-traumatic sudden deaths in individuals with a mean age of 38 ± 11 years. They showed that in those <35 years of age the leading cause of death was sudden unexplained death (41.3%); whereas in those ≥ 35 years of age the leading cause of death was atherosclerotic coronary artery disease (73.2%) [17].

Sports-related SCD or SCD in athletes fall into a separate group. Mass media has focused a lot of attention on young athletes who die suddenly while training or during competition. Such deaths illustrate that vigorous exertion can transiently increase the risk of SCD and highlights the paradox that physical activity can have both a positive and a negative impact on an individual's health. The reported causes of SCD among athletes differ between studies, with a high proportion due to HCM in the United States [18] and due to ARVC in Italy [19]. A Danish study performed in 2010 reported the incidence rate of SCD in competitive athletes to be higher than that of the general population. The most common autopsy findings were ARVC, sudden unexplained death and coronary artery disease [20].

Ischemic heart disease

Ischemic heart disease (IHD) related to atherosclerotic disease and impaired cardiac blood supply continues to be the most frequent cause of death in the general population in industrialized countries [11]. IHD refers to a group of clinico-pathological conditions, which include angina pectoris (stable or unstable), acute myocardial infarction, chronic ischemic heart disease with or without heart failure and SCD. Plaque rupture is the primary underlying cause of luminal thrombosis, responsible for provoking acute coronary syndromes such as myocardial infarction and sudden cardiac death. The secondary mechanism, more frequent in younger individuals, is related to plaque erosion [21]. Instant death due to ventricular fibrillation or atrio-ventricular block is a frequent complication of coronary thrombosis and is responsible for 50% of acute myocardial infarction mortality [22]. Chronic ischemic heart disease can be deemed the cause of death if at least one of the main coronary arteries has a narrowing of 75% or more, and complimentary analyses (i.e. toxicology and clinical chemistry) are negative. Also non-atherosclerotic coronary artery diseases can provoke ischemic events. These diseases include late stage of obliterative intimal thickening, coronary artery dissection, ostial stenosis, coronary arteritis and aneurysm, coronary emboli, coronary artery spasm and myocardial bridging.

In clinical practice, the diagnosis of IHD is largely based on the presence or absence of specific symptoms. The diagnostic gold standards are electrocardiography and cardiac biomarkers. Stress testing and/or angiography are often used to identify and treat coronary artery disease. Invasive coronary angiography is currently the “gold standard” for assessing coronary artery stenosis [5]. It can be used as a rule-out test in patients with low to intermediate likelihood of disease, as shown by Schlattmann *et al.* in a recent meta-regression analysis [23]. Cardiac multi-detector computed tomography (MDCT), including contrast-enhanced MDCT coronary angiography, is considered to be a powerful diagnostic tool for the assessment of coronary disease in acute and chronic cases [3]. CT angiography is the method of choice for the assessment of both the arterial lumen and wall disease. CT angiography has also proven to be useful for the assessment of the degree of myocardial perfusion and the detection of any previous infarctions with the measurement of myocardial attenuation using Hounsfield units. Decreased perfusion is associated with reduced myocardial enhancement. In addition, old infarctions show lower CT attenuation than recent ones [24]. Cardiac MRI is a reference standard for the assessment of ventricular function and may help identify and classify scars for risk stratification [25].

The biggest clinical challenge is the detection of patients with vulnerable plaques that are subject to either plaque rupture or erosion. Even the combination of imaging techniques fails to accurately pinpoint vulnerable plaques. It is recognised that coronary CT-angiography can detect two important features of coronary plaque vulnerability: a large, soft plaque and focal vascular remodelling [26]. Other morphological characteristics of a vulnerable plaque, such as thin cap fibroatheroma and a lipid core, can be identified with angioscopy, high frequency intravascular ultrasound, intravascular MRI and optical coherence tomography. Active inflammation in high-risk plaques can be detected using intravascular thermography [27]. Coronary artery calcifications, detectable by CT but not MRI imaging, are considered to be predictors of a cardiovascular event and plaque burden. There are, however, controversial opinions concerning the role of calcium, especially since some studies have suggested that it may be protective against the development of acute coronary syndrome [28].

The post-mortem investigation of IHD is different than in classical clinical practice as it is impossible to use certain techniques, such as electrocardiography and many of the laboratory analyses, after death. The post-mortem diagnosis of IHD is based on the evaluation of the coronary arteries and myocardium. The post-mortem angiographical examination of coronary arteries was initially performed in 1899, three years after the discovery of X-rays [29]. At present, coronary arteries are investigated using PMCT/PMCTA [6,4,2,3] and/or PMMR/PMMRA [30,31].

A recent study performed on 23 forensic cases showed that PMCT is of limited diagnostic value for IHD. PMCTA, if correctly interpreted, is a reasonable tool to view the morphology of coronary arteries, rule out significant coronary artery stenosis, identify occlusions and direct sampling for histological examination. Radiological examination by PMCT or PMCTA enables the detection and documentation of coronary artery calcification better than classical autopsy. However, the visualisation and differentiation of PMCT artefacts has yet to be studied [3].

PMMR examination of ischemic myocardium was first performed on 8 autopsy cases in 2006 by Jackowski *et al.* They demonstrated that PMMR enables the detection of

myocardial infarction *in situ* and the estimation of infarct age based on signal behaviour [9]. A few authors have recently reported on the PMMR- based diagnosis of coronary artery disease related deaths [30,31,8]. Although the presence of a clot is highly indicative for a coronary event, PMMR cannot certainly differentiate between post-mortem clots and vital thromboses.

PMCTA and PMMR have both their advantages and disadvantages for the post-mortem examination of IHD. Although MRI is the method of choice for the radiological investigation of the myocardium (Fig. S1), the biggest advantage of PMCTA is its ability to investigate the vessel's lumen, enabling the detection of stenoses and occlusions (Fig. 1). Both methods are associated with a risk of thrombi dislodgement, and they do not enable the differentiation between vital and artefactual post-mortem thrombus. Radiological techniques using injected agents are very useful for the detection of coronary stenoses and occlusions, but the diagnosis must be confirmed visually and/or histologically in order to rule out post-mortem artefact. The biggest disadvantages of both post-mortem techniques are that they require dedicated and expensive technical equipment as well as physicians experienced in the fields of post-mortem radiology and cardiovascular pathology.

Cardiomyopathies

In 2006, the expert consensus defined cardiomyopathies as an important and heterogeneous group of myocardial diseases associated with mechanical and/or electrical dysfunction, usually exhibiting inappropriate ventricular hypertrophy or dilatation due to a variety of causes that frequently are genetic. Cardiomyopathies are either confined to the heart or are part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disabilities [32]. The most frequently involved cardiomyopathies in SCD, especially in young individuals, are HCM and ARVC.

In the clinical setting echocardiography is the most commonly used tool for the detection of cardiomyopathies and the functional evaluation of the heart. MRI is becoming increasingly important, as it can acquire high-resolution images of the heart in any desired plane [33]. MRI can better differentiate tissue properties, is non-invasive and has a higher resolution. Clinical MRI also has the potential to detect regional and diastolic ventricular dysfunction, which can represent early manifestations of ARVC. The current imaging tools cannot determine the aetiology of the cardiomyopathy, which is essential for both treatment and prognosis [34].

Hypertrophic cardiomyopathy/ athlete's heart

Hypertrophic cardiomyopathy (HCM) is the most common genetic cardiac disease, with a prevalence of 1:500 in the general population. HCM is an autosomal dominant disease caused by mutations in genes encoding sarcomere proteins. It is also one of the most common causes of SCD in young individuals and young athletes. In the clinical setting, HCM is defined by unexplained left ventricular hypertrophy without dilation of the ventricular chambers, in the absence of any other cardiac or systemic disease that could explain the hypertrophy. Clinically, HCM is usually characterized

by a left ventricle wall thickness ≥ 15 mm, with 13 to 14 mm considered as borderline [35].

HCM has a diverse phenotypic expression, ranging from a silent disease to very severe one. Imaging plays a key role in the diagnosis of HCM; transthoracic echocardiography remains the gold standard for the screening and initial evaluation of HCM [35]. Cardiac MRI is indicated in patients with suspected HCM when echocardiography is inconclusive or when additional information may have an impact on further management. Additional imaging techniques, including coronary angiography (invasive or CT- imaging) and positron emission tomography, may be indicated depending on the clinical picture.

HCM must be differentiated from hypertensive heart disease and physiological remodelling in athletes, as athletic hearts and secondary causes of hypertrophy (i.e. hypertension and aortic stenosis) may mimic HCM. It is well recognized that the border between physiological and pathological changes is poorly defined [10]. Cardiac MRI is very useful to show different enhancement patterns via late gadolinium enhancement in some forms of cardiac hypertrophy (cardiac amyloidosis, sarcoidosis, Fabry) [36]. The histological examination is necessary to detect constellation of hypertrophy, fibrosis and small vessel disease and myocyte disarray. These findings represent the gold standard for the pathological confirmation of the HCM diagnosis [37]. The combination of non-invasive cardiac imaging and genetic screening will further aid in the preclinical diagnosis and management of patients with HCM [36].

No post-mortem radiological observations have been reported for HCM, but PMMR alone or in conjunction with PMCTA should be considered, as previously suggested by Jackowski et al [38]. PMCT and PMCTA allow the observation of global cardiac hypertrophy (Fig. S2), which might have however many possible aetiologies. At present, the autopsy and histological examination remain the gold standard for the post-mortem diagnosis of HCM.

Arrhythmogenic right ventricular cardiomyopathy

Arrhythmogenic right ventricular cardiomyopathy/dysplasia (ARVC/D) is a genetically determined heart muscle disorder characterized by structural and functional abnormalities, mostly of the right ventricle resulting from progressive, fibro fatty replacement of the right ventricular myocardium starting from the epicardium. The left ventricle is occasionally involved as well. Fibro fatty replacement leads to wall thinning and aneurysm formation, typically located at the inferior, apical, and infundibular walls. Its estimated prevalence is between 1:1000 and 1:5000 in the general population [39,40]. The presence of fatty tissue in the right ventricular free wall is of limited diagnostic specificity as it is a common finding in normal hearts, particularly in obese and elderly individuals.

The clinical diagnosis of ARVC is currently based on the presence of different standardized Task Force Criteria as right ventricular functional and structural changes, electrocardiographical depolarisation and repolarisation abnormalities, ventricular arrhythmias, fibro fatty replacement of the myocardium and a positive

family history. The diagnosis can be established when different diagnostic criteria are present. An accurate post-mortem diagnosis of arrhythmogenic right ventricular cardiomyopathy (ARVC) is important for any surviving family members, as it is a hereditary disease and there are available treatment options for the prevention of sudden death [39,40].

In patients with structurally severe disease, all cardiac imaging methods are likely to yield abnormal findings. Echocardiography is most often the first imaging method used for the assessment of index cases and family members since it is widely available and non-invasive. CT-angiography is very helpful for the detection of akinetic or dyskinetic bulging in the triangle of dysplasia. MRI is a powerful imaging method due to its greater ability for tissue characterization. While in morphologically severe forms MRI does not add to diagnosis, MRI with gadolinium enhancement has the potential to detect regional and diastolic ventricular dysfunction, most likely related to intramyocardial fibrosis, which can be an early manifestation of ARVC. Therefore MRI is able to detect early stages and subtle cases.

The detection of fatty infiltration is not sufficient for the diagnosis of the disease, as it may present in healthy adults and patients with other myocardial diseases [41]. Considering that coronary artery disease is a common cause of left ventricular dilation and dysfunction which can mimic ARVC, this pathology should be excluded. MDCT coronary angiography has shown a negative predictive value of 100% in excluding significant CAD in patients with ARVC [24].

No comparative studies have been performed to evaluate the radiological aspects of ARVC in the post-mortem setting. Jackowski *et al* reported a case with fatty infiltration of the free right ventricular wall and thinning of the apical right ventricular wall visualised by PMMR, which was suggestive of ARVC [38]. It is possible to detect some radiological features of ARVC with PMCTA, such as fatty infiltration and right ventricular dilation (Fig. 2). However, considering the guidelines for the clinical diagnosis, and given the importance of the diagnosis for the next of kin, both the autopsy and histological examination remain the gold standards for the post-mortem diagnosis.

Channelopathies

Progress made in the fields of molecular biology and human genetics have resulted in the identification of the genetic origin of many cardiac diseases, which can lead to both structural (e.g. hypertrophic cardiomyopathy) and arrhythmogenic abnormalities (e.g. long QT syndrome, Brugada syndrome) which can result in SCD. Autopsy negative SCD are most often thought to be the result of sudden arrhythmic death syndrome. Sudden arrhythmic death syndrome cannot be detected with any of the aforementioned imaging techniques.

Cardiac sarcoidosis / myocarditis

Sarcoidosis is a multisystem granulomatous disease of an unknown aetiology, characterized by noncaseating granulomas in involved organs. The incidence of sarcoidosis varies with race. The prevalence is 10-40/100,000 persons in the United States and Europe, with an increased prevalence in African-Americans [42].

In clinical practice, the imaging methods used to evaluate sarcoidosis are echocardiography, nuclear medicine and more recently gadolinium-enhanced cardiac MRI [34]. In the post-mortem setting, PMMR and PMCT may prove to be useful for the establishment of the diagnosis and to direct sampling for histological examination, but no reports have been published to date (Fig. 3).

Myocarditis is an acute or chronic inflammatory disease of the myocardium, characterized by myocardial inflammatory infiltrates with myocyte degeneration and necrosis. In current clinical practice, myocardial biopsy is essential for the diagnosis [43,44]. Echocardiography and cardiac MRI are likely to become the non-invasive standard radiological examinations for the investigation of myocarditis and to assist in the performance of guided biopsies from the areas of marked contrast enhancement [45,46].

There are currently no reports on the post-mortem radiological imaging of myocarditis. The precise mapping of inflammatory myocardial lesions with cardiac MRI might increase the diagnostic yield of guided myocardial sampling, but the accessibility of MRI remains limited in the post-mortem setting.

Valvular abnormalities

Although rare in the general population, aortic stenosis and mitral valve prolapse are the most frequently reported valvulopathies to cause SCD in young individuals.

In clinical practice, aortic valvular disease can be satisfactorily studied with Doppler echocardiography; whereas coronary angiography can be technically difficult and may increase potential risks [24]. PMCT and PMCTA enable the visualization of calcification in aortic stenosis (Fig. S3) but mitral valve prolapse cannot be detected with post-mortem radiological imaging as it is mainly a functional disorder. It is even difficult or impossible to prove its role in causing death with an autopsy examination.

Coronary artery anomalies

Coronary anomalies occur in <1% of the general population and can range from a benign incidental finding to the cause of SCD [47,48]. Classic coronary anomalies include those in which a coronary artery originates from the contra-lateral aortic sinus or the pulmonary artery with an anomalous course [49,50].

Although invasive angiography has historically been used to diagnose coronary anomalies, MDCT imaging techniques are now an accurate non-invasive alternative [51,50]. Coronary CT-angiography provides detailed visualisation of complex coronary artery anatomy and is currently the method of choice for the detection and

classification of coronary artery anomalies [48]. MDCTA is considered to be superior to conventional angiography in delineating the ostial origin and proximal course of anomalous coronary arteries. In patients with myocardial bridging who present with chest pain or even myocardial infarction, MDCTA has the advantage of assessing the coronary artery lumen as well as the surrounding myocardium [24].

In the post-mortem setting, PMCTA allows for excellent visualization of coronary artery anatomy (Fig. 4). Okura *et al* presented a case report of SCD with a calcified coronary artery aneurysm related to Kawasaki disease which was visualized by PMCTA imaging [52].

Sudden postoperative deaths

Sudden deaths can also occur in patients undergoing cardiovascular surgery. MDCT angiography allows for the non-invasive evaluation of coronary bypass graft patency with a high diagnostic accuracy [53,54]. MDCTA is a reliable non-invasive diagnostic method that can clearly display the stent lumen and is especially helpful for patient follow-up. This technique can be used to evaluate the full range of stent-related problems, such as stent thrombosis, jailed branches, edge stenosis, bifurcation stents, inadequate stent expansion and stent aneurysms [55].

In the post-mortem examination, PMCT allows for the detection of coronary stents and artificial heart valves, which can be difficult to visualize in the presence of severe calcifications. PMCTA can demonstrate the permeability of coronary bypass and can help guide autopsy dissection technique (Fig. 5). In occluded bypass grafts, classical dissection is necessary to rule out post-mortem artefact.

Discussion

The clinical diagnostic approach for cardiovascular pathologies is different than that involved in post-mortem forensic investigations. The clinician takes into account the anamnesis, clinical examination, electrocardiogram readings, radiological examination and measurement of cardiac biomarkers, to name a few. Many clinical diagnostic tools are useful for assessing function, and are of limited value in the post-mortem setting. On the other hand, the autopsy renders a detailed visual assessment and histological examinations of the myocardium easily accessible. The importance of establishing a diagnosis is also different. In living patients the clinical diagnosis is essential for both treatment and prognosis; in forensic practice determining the cause of death can direct the juridical investigations. An autopsy diagnosis for genetically determined cardiac pathologies is also essential for the prevention of sudden death in living family members.

The radiological cardiac examination differs in the pre and post-mortem setting. In the living, the radiological cardiac examination is aimed at the evaluation of structure and function. Cardiac physiology, filling pressures and valvular function can be assessed in detail by Doppler echocardiography [24]. The functional assessment is impossible after death, and the imaging techniques are limited to structural evaluations. Most post-mortem imaging findings are confirmed at autopsy, in order to rule out post-

mortem artefacts [56]. Advanced decomposition can destroy organ structure and gas related artifacts should be carefully analyzed [57]. That being said, post-mortem radiology has many advantages. The major advantage of postmortem radiological examination is that the artifacts related to heartbeats, for example, are not present. Radiation exposure is not a concern, and allows for the acquisition of high quality images. There are no motion related artifacts. Some specific examinations, such as CT coronary angiography, may be contraindicated in living due to the risk of an allergic response and/or the impairment of renal function, which are not an issue in the post-mortem setting.

The contribution of post-mortem radiological imaging techniques is increasing in cardiovascular pathology, but there is currently no consensus on the role of the post-mortem radiological examination in the autopsy diagnosis, especially for cardiovascular pathologies resulting in SCD. Cardiovascular pathologies present particular diagnostic challenges, both in the clinical and post-mortem setting. The guidelines for the clinical radiological examination have been established by many experts [35,40,58]. Often times, the radiological examination alone is unable to diagnose many of the hereditary cardiac diseases, such as ARVC, HCM and channelopathies. The validity of radiological post-mortem findings, without confirmation by classical autopsy, is not yet known. Most publications are based on very few observations and the results have yet to be independently verified. In this paper, we presented the state of the art for the radiological examination of cardiovascular pathologies. In post-mortem imaging, cardiovascular pathologies have been analysed by only a few groups [4,8,29,3,6,7]. While PMCTA allows for the morphological evaluation of coronary arteries and the detection of suspected stenoses and occlusions, PMMR provides superior soft tissue visualization [4,8,29,3,6,59]. Post-mortem imaging techniques, especially those associated with the intravascular injection of contrast, are able to demonstrate and document a number of cardiovascular pathologies, but some hereditary cardiac diseases, such as ARVC, HCM and channelopathies, cannot be diagnosed with these techniques.

The need to establish the diagnostic value of post-mortem radiology as well as its degree of certitude has been suggested by many authors. In 2012 Roberts *et al* published a study undertaken at two UK centres between 2006 and 2008. They investigated 182 adult deaths that underwent whole-body CT, MRI and a full autopsy. They concluded that when compared with traditional autopsy, PMCT was a more accurate imaging technique than PMMR for establishing a cause of death. The most common misdiagnosis when using post-mortem imaging was ischemic heart disease, which represents the most common cause of death in the general population. The authors underline the potential risk of systematic errors in mortality statistics that would result if imaging were to replace conventional autopsy [59]. The radiological degree of certitude is important, especially in the forensic interpretation of the case. The interpretation of the autopsy findings and the medico-legal conclusions are of great interest for the police, investigating magistrate or prosecutor, lawyers and courts. The interpretation should consider all reanimation and post-mortem artefacts [60,56]. In clinical radiology, many artefacts have been reported [61-63]. Radiological findings may also be incidental and unrelated to the cause of death. One report stated that a variety of findings suggestive of myocardial infarction were found on routine chest CT in patients who may not have had a prior diagnosis of ischemic heart disease [64]. The possible artefacts of post-mortem radiological examination should be carefully studied and considered when interpreting medico-legal cases

which might involve civil or penal responsibilities. Misinterpretations of the morphological findings and complimentary exams can contribute to a miscarriage of justice. In a study published in 2012, Murken *et al* showed that the radiologic diagnoses were often discrepant from autopsy findings, and that autopsies can help radiologists sharpen their skills and can perhaps serve as quality control mechanisms for radiology, and vice-versa [65,66].

Evaluating of the cost/benefit of autopsies was suggested by some authors in order to consider post-mortem imaging as a complement and/or alternative to traditional clinical autopsies. If the goal of the autopsy is to determine the cause of death, the degree of certitude of the radiological diagnosis is very important. If an exact cause of death is not required, and if the goal of the autopsy is to exclude traumatic deaths, some autopsies may not be necessary. In selected cases, an external examination would be sufficient, while keeping in mind the limitations of this examination in the interpretation of the case.

In our opinion, post-mortem radiology should be performed in cases where additional information concerning the cause of death should be obtained or if radiological imaging may help to document pathologies before performing the destructive autopsy, which would allow for a future independent review. In the field of the cardiovascular pathology, the post-mortem radiological examination is most often not sufficient to establish the exact cause of death and autopsy remains the gold standard. More studies are needed in order to establish the validity and limitations of the post-mortem radiological assessment of cardiovascular pathologies, mainly because of the numerous post-mortem artefacts. At present, there are no non-invasive techniques that can replace the histological examination. The post-mortem radiological examination, followed by a complete autopsy, can help further the understanding and interpretation of the radiological examination in the living. The limitations of interpretation for the radiological post-mortem examination should be highlighted, especially in cases involving legal or ethical responsibilities. Over interpretation may contribute to a miscarriage of justice or to an incorrect clinical approach involving families of SCD victims.

Legends:

- Fig. 1 Coronary artery thrombosis observed in PMCTA of a 47-year-old-man who died suddenly: while the native PMCT shows only a small calcification of the left intraventricular coronary artery (arrow in a), the arterial phase of the PMCTA (b) reveals a significant stenosis (arrow in b). A 3D-volume rendering reconstruction (c) clearly demonstrates the stenosis and its exact localisation. Histological examination in H&E stained section (d) of the concerned part of the artery shows advanced fibro lipid eccentric plaque and thrombotic material in the lumen.
- Fig. 2 18-year old athletic man who died suddenly while doing sport: PMCTA (a and b) showed the dilatation of the right ventricle, a fatty aspect of the ventricular wall (arrows in a) and increased trabecularisation of the right ventricle. Conventional autopsy confirmed these findings, especially the presence of fatty infiltration in the right ventricular wall (arrows in c). Histological examination (d and e) allowed the classical diagnosis of ARVC concerning the right ventricle and the posterior wall of the left ventricle (Masson trichrome stain)
- Fig. 3 Multiorgan sarcoidosis involving the heart of a 35 year-old man who died suddenly while cycling. In PMCT (a), nodular formations in the lungs (arrow in a) were observed which aroused the suspicion of sarcoidosis as well as a massive pulmonary oedema centered on the hilum indicating cardiac failure. Histological examination of the myocardium showed typical multiple lymphatic foci, sarcoid giant cells embedded in a fibrous background without surrounding necrosis, involving both ventricles and the ventricular septum (H&E staining)
- Fig. 4 Morphologies of coronary arteries visualised by PMCTA
- a) coronary arteries in a 33 year-old man who collapsed in a night club, just after complaining about thoracic pain, electrocardiogram showed ventricular fibrillation. Reconstruction of PMCTA images allows the visualisation of a variant of coronary arteries with the circumflex artery originating from the right sinus
- b) another variant of coronary arteries: trifurcation of the left coronary artery in a 58- year-old man found dead at his home. The cause of death was attributed to an acute bronchopneumonia
- Fig. 5 Coronary artery stent (arrows) in native PMCT (a) and PMCTA (b). While the native CT-scan can only confirm the presence and localisation of the stent in the left interventricular artery, PMCTA proves the intact perfusion of the stent.
- c) Coronary bypass between the left internal mammary artery and the left interventricular artery (yellow arrow) visualized by PMCTA, with an occlusion of the left interventricular artery in its middle part (black arrow). The red arrow indicates the right internal mammary artery.

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Figure 1

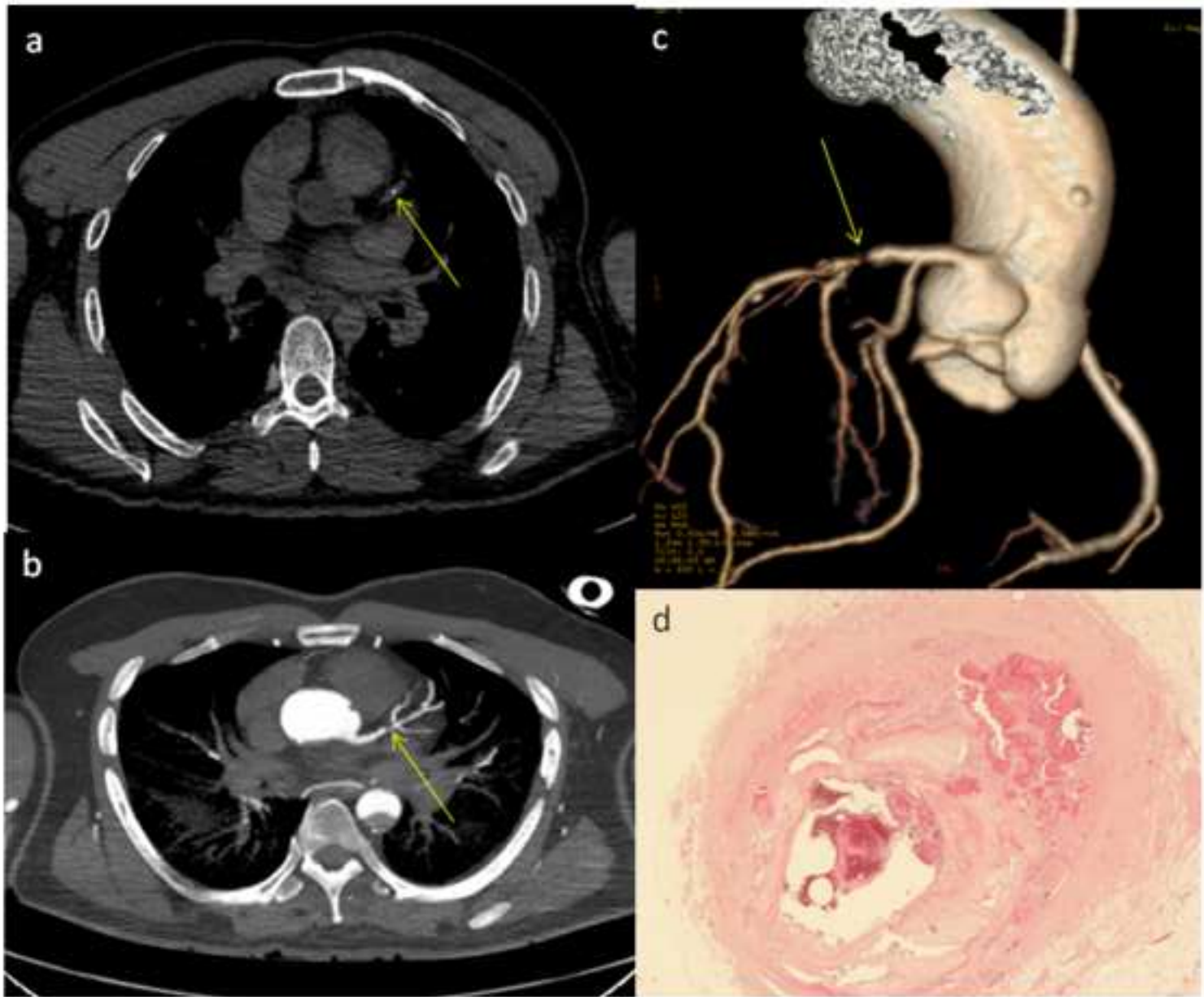


Figure 2

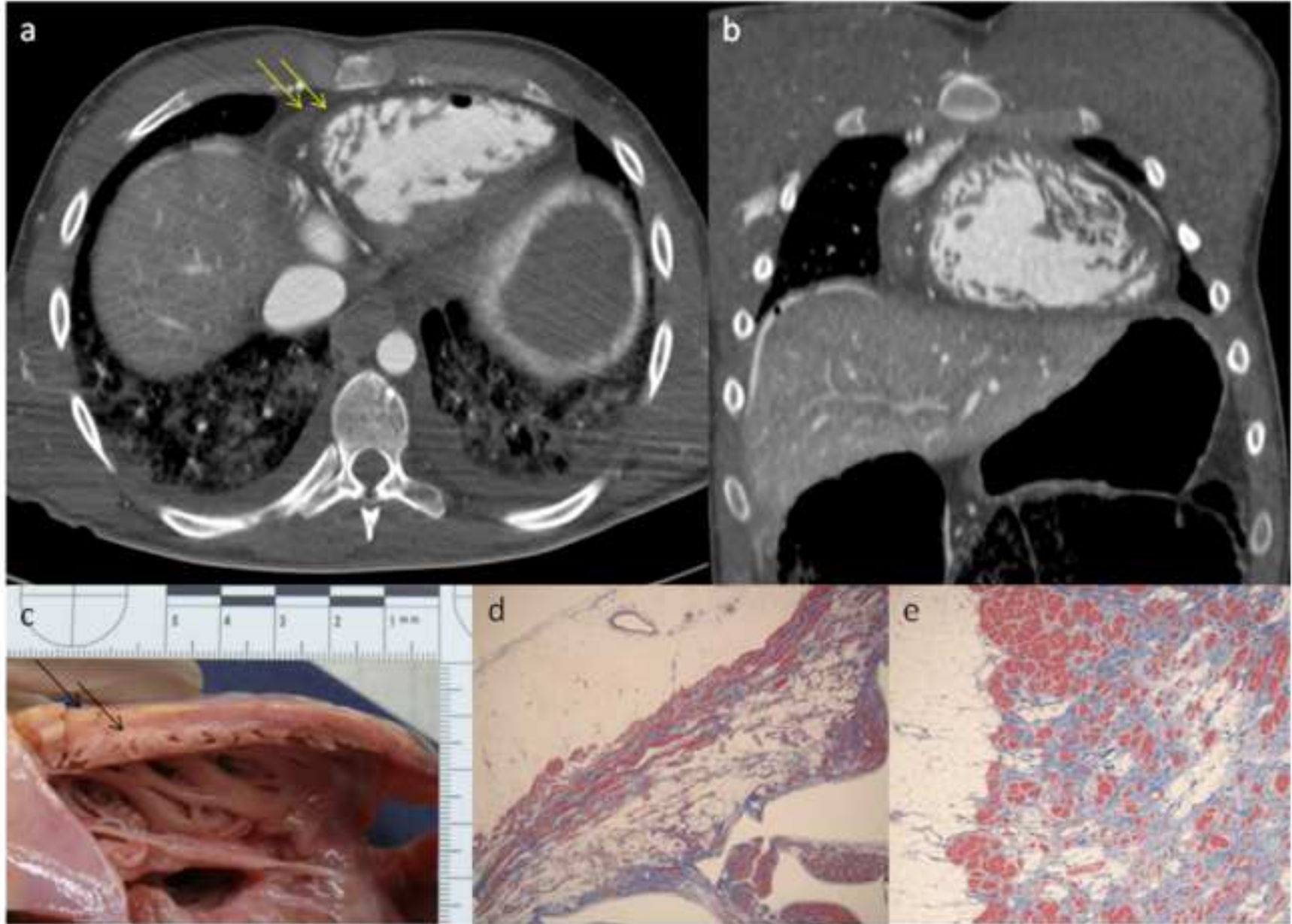


Figure 3

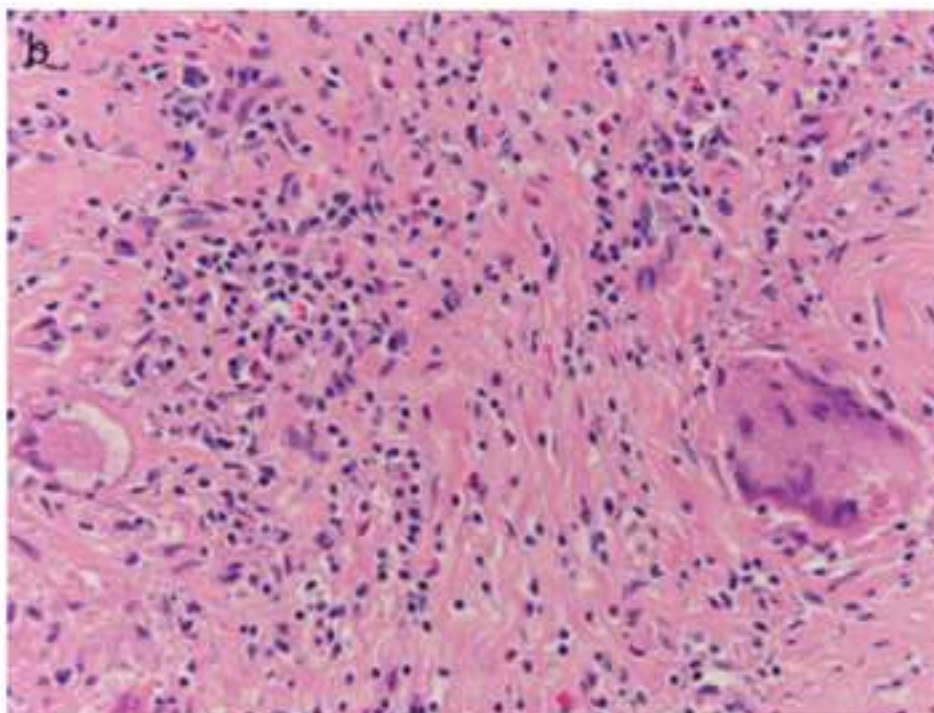


Figure 4

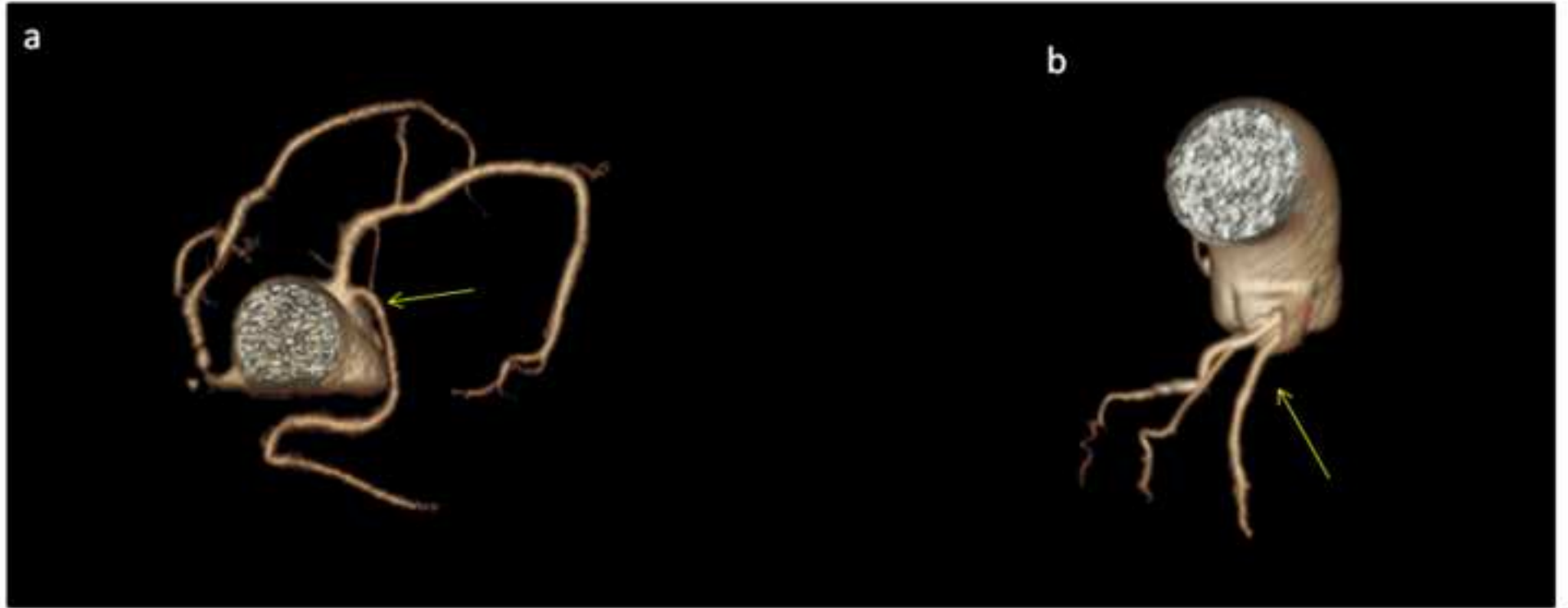


Figure 5

