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## Author Manuscript

Faculty of Biology and Medicine Publication

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Published in final edited form as:

**Title:** The role of angiography in the congruence of cardiovascular measurements between autopsy and postmortem imaging.

**Authors:** Troxler R, Minoiu C, Vaucher P, Michaud K, Doenz F, Ducrot K, Grabherr S

**Journal:** International journal of legal medicine

**Year:** 2018 Jan

**Issue:** 132

**Volume:** 1

**Pages:** 249-262

**DOI:** 10.1007/s00414-017-1652-0

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# International Journal of Legal Medicine

## The role of angiography in the congruence of cardiovascular measurements between autopsy and postmortem imaging --Manuscript Draft--

<b>Manuscript Number:</b>	
<b>Full Title:</b>	The role of angiography in the congruence of cardio-vascular measurements between autopsy and post-mortem imaging
<b>Article Type:</b>	Original Article
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<b>Funding Information:</b>	
<b>Abstract:</b>	<p><b>Abstract</b></p> <p><b>Introduction:</b> Post-mortem CT angiography is the method of choice for the post-mortem imaging investigations of the cardio-vascular (CV) system. However, autopsy still remains the gold standard for CV measurement. Nevertheless, there aren't any studies on CV measurements on the multi-phase post-mortem angiography (MPMCTA) which includes comparisons with autopsy. Therefore, the aim of this study is to compare CV measurements between the native CT-scan and the three phases of the MPMCTA to find out which of these modalities correlate the best with autopsy measurements.</p> <p><b>Methods:</b> For this study we selected retrospectively 50 post-mortem cases that underwent both MPMCTA and autopsy. A comparison was carried out between the CV measurements obtain with imaging (aorta; heart cavities and cardiac wall thicknesses; maximum cardiac diameter and cardiothoracic ratio) and at the autopsy (aorta; cardiac valves, ventricular thicknesses and weight).</p> <p><b>Results:</b> Our results show that the dynamic phase displays an advantage for the measurement of the aortas. However, the MPMCTA is not accurate to measure the cardiac wall thicknesses. The measurements of the heart cavities show no correlation with the heart valves. The cardiothoracic ratio measured by the MPMCTA show no correlation with the heart weight. Nevertheless, the maximum cardiac diameter exhibits a correlation with the latter on the venous and dynamic phase.</p> <p><b>Conclusions:</b> These results show that only few CV parameters measured with imaging correlate with measurement obtained at the autopsy. These results indicate that in order to better estimate values obtained at the autopsy, we need to define new reference values for the CV measurement on MPMCTA.</p>

<p><b>Author Comments:</b></p>	<p>Professor Th. Bajanowski  Editor-in-Chief  International Journal of Legal Medicine</p> <p>Lausanne, January 10th 2017</p> <p>RE: Manuscript for submission - original article</p> <p>Dear Prof. Bajanowski,</p> <p>Please find enclosed a manuscript concerning the field of forensic radiology entitled "The role of angiography in the congruence of cardio-vascular measurements between autopsy and post-mortem imaging", which we would like to submit in the esteemed International Journal of Legal Medicine.</p> <p>This paper describes a comparison between the cardiovascular (CV) measurement obtain with imaging (aorta; heart cavities and cardiac wall thicknesses; maximum cardiac diameter and cardiothoracic ratio) and at the autopsy (aorta; cardiac valves, ventricular thicknesses and weight). The aim of this study is to compare CV measurements between the native CT-scan and the three phases of the multi-phase post-mortem angiography to find out which of these modalities correlate the best with autopsy measurements.</p> <p>In fact post mortem angiography and imaging are more and more used in the daily work of forensic pathology. However, no references values for the measurements of cardiovascular parameters exist today in post mortem imaging, and those there are used for clinical measurements are not applicable for deceased bodies.</p> <p>This is why we believe that our paper is surly attractive to the readers of the International Journal of Legal Medicine. We are looking forward to your response and hope that the manuscript will be considered for publication.</p> <p>Yours sincerely,</p> <p>Silke Grabherr</p>
<p><b>Suggested Reviewers:</b></p>	<p>Axel Heinemann  Heinemann@uke.uni-hamburg.de</p> <p>Krzysztof Wozniak  mpwoznia@cyf-kr.edu.pl</p>

## **Title page**

# **The role of angiography in the congruence of cardiovascular measurements between autopsy and postmortem imaging**

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### **Financial Disclosures**

For this study, the authors did not have any financial support.

### **Keywords**

Forensic imaging, MPMCTA, cardio-vascular measurement, autopsy

### **Acknowledgements**

The authors want to thank Melissa Jotterand for her help in preparing the manuscript for submission.

**The role of angiography in the congruence of cardio-vascular measurements between autopsy and post-mortem imaging**

**Keywords:** forensic imaging, MPMCTA, cardio-vascular measurement, autopsy

## **Abstract**

**Introduction:** Post-mortem CT angiography is the method of choice for the post-mortem imaging investigations of the cardio-vascular (CV) system. However, autopsy still remains the gold standard for CV measurement. Nevertheless, there aren't any studies on CV measurements on the multi-phase post-mortem angiography (MPMCTA) which includes comparisons with autopsy. Therefore, the aim of this study is to compare CV measurements between the native CT-scan and the three phases of the MPMCTA to find out which of these modalities correlate the best with autopsy measurements.

**Methods:** For this study we selected retrospectively 50 post-mortem cases that underwent both MPMCTA and autopsy. A comparison was carried out between the CV measurements obtain with imaging (*aorta; heart cavities and cardiac wall thicknesses; maximum cardiac diameter and cardiothoracic ratio*) and at the autopsy (*aorta; cardiac valves, ventricular thicknesses and weight*).

**Results:** Our results show that the dynamic phase displays an advantage for the measurement of the aortas. However, the MPMCTA is not accurate to measure the cardiac wall thicknesses. The measurements of the heart cavities show no correlation with the heart valves. The cardiothoracic ratio measured by the MPMCTA show no correlation with the heart weight. Nevertheless, the maximum cardiac diameter exhibits a correlation with the latter on the venous and dynamic phase.

**Conclusions:** These results show that only few CV parameters measured with imaging correlate with measurement obtained at the autopsy. These results indicate that in order to better estimate values obtained at the autopsy, we need to define new reference values for the CV measurement on MPMCTA.

## **Introduction**

The post-mortem CT angiography (PMCTA) is the method of choice for the post-mortem (PM) imaging investigations of the cardio-vascular (CV) system [1-4]. It is actually performed in a series of forensic medical centers around the world [4-6]. The PMCTA can be performed on single organs [6, 7] or on the whole body [1, 4, 8-11]. The first one consists in injecting a targeted organ in situ or after its extraction from the body [8]. The second one is a CT angiography that visualizes the whole CV system [5]. It is more useful in detecting vascular abnormalities [4, 6, 9, 11], which cannot be seen with a conventional autopsy.

The standardized protocol developed by Grabherr and al. allows PMCTA of great qualities [12] with three angiographic phases [12]: The multi-phase post-mortem CT angiography (MPMCTA). This latter allows a good opacification and visualization of the CV system, provided that the injected volume is enough to fill completely this system [12]. Some studies compare the MPMCTA with the autopsy findings [3, 5, 12, 13] in order to implant imaging as an accurate tool to determine the cause of death. Furthermore, MPMCTA is the method of choice to visualize vascular abnormalities, such as vessel dissection, aneurism and occlusion. It's also the best way to find the bleeding source in case of fatal haemorrhage, to see gunshot and stab wounds' trajectories, to display myocardial infarction and to investigate vascular anatomy, especially after a surgical operation with suspicion of malpractice. All these indications [1-5, 9, 11-13] make the MPMCTA one of the best techniques to investigate the CV system.

According to the textbooks and recommendations set in the field of the cardiovascular pathology, the standard gross examination of the heart includes the following measurements of the opened heart, emptied of post-mortem clot and vessels trimmed to within 1 cm of the heart: total heart weight, free wall thickness of the left ventricle, right ventricle and of the septum (excluding trabeculae) as well the circumference of valve rings [14-16]. The post-mortem assessment of the aorta comprises the measurements of the wall circumference at various levels.

These measurements have to be compared with references values and are ones of the key pieces of information used to help determine if cardiovascular pathology exists. It is therefore essential to find radiological measurements thanks to MPMCTA that correlate to the ones obtained at autopsy. Furthermore, the clinical radiologic parameters could not simply be applied because in post mortem imaging, there are others reference values [17-21].

However, to our knowledge, there aren't any studies on the CV measurements on MPMCTA which includes comparisons with autopsy finding. Although, CV measurements on native post-mortem CT-scan already exist in some studies [17-24].

Therefore, the aim of this present study is to compare some CV measurements between the native CT-scan and the three phases of the MPMCTA to find which of these four methods correlate the best with the autopsy measurements.

## **Methods and materials**

The following study was approved by the Cantonal Ethics Committees on research involving humans (CER-VD; N°130/15)

### **Subjects**

50 post-mortem cases investigated between October 2013 and June 2014 in the University Center of Legal Medicine in Lausanne were retrospectively included in this study. The inclusion criteria were all cases that

underwent a native CT-scan followed by MPMCTA and a medico-legal autopsy. The exclusion criteria were the following: cases with prosthetic valve or pacemaker, polytrauma cases and cases with a dissection of the thoracic aorta associated with a cardiac tamponade. The latter did not permit accurate CV measurements.

### **Radiological investigations**

A native CT-scan of the corpse in supine position with the arms crossing with each other on the abdomen, from the skull vertex to the pelvis (genitals included), was performed before any manipulation. The scans were done using a General Electric (GE) Lightspeed 8-slices CT-scanner, using the parameters exposed in table 1.

Then, an external examination was performed before the MPMCTA. The latter was carried out according to the protocol developed by Grabherr and al [12]. MPMCTA is performed with by injecting a mixture of 3.5 litres of paraffin oil and contrast agent 6% (210 ml of Angiofil®) [12, 25] through a modified heart-lung machine, Virtangio® perfusion device, to reproduce a flow within the body's vascular system. Firstly, the "arterial phase" consists in filling, via the femoral artery, the arterial vascular system with 1200ml of a mixture made of paraffin oil with contrast agent. This allows the visualization of the arterial bed with the CT-scan. Then, the "venous phase" consists in filling, via the femoral vein, the venous vascular system with 1800ml of the mixture. Finally, the "dynamic phase" is an acquisition of CT scan imaging while injecting additional 500ml of the mixture in the arterial vascular system and an autonomously backflow from the femoral vein. Thanks to this synchronization of contrast agent perfusion with imaging acquisition, the CV system can be visualized as in vivo on "the dynamic phase". MPMCTA included three CT-scan (arterial, venous and dynamic) phases of the body in the same position as the native CT-scan, from the skull vertex to the knees, with the same device used for the native CT-scan but with different parameters [table 1]

### **Radiological measurements**

A team of two board-certified radiologists decided upon common agreement on the location where each of the CV measurements should be performed. The CT measurements were carried out using a market available software (Advantage Window – GE, AW Server 2.0). Then, all the measurements were made by a medical student, who was trained by the two radiologists, using the mediastinal or bone window, using always the same level for the same anatomical structure, in the four phases of the MPMCTA (native, arterial, venous and dynamic), for each of the cases in order to permit an accurate comparison. Each of the measurements were reviewed and confirmed during a second view by a board-certified radiologist.

The diameter of the descending aorta was measured in an axial view at the level of the emergence of the right pulmonary artery [Figure 1]. The abdominal aorta was measured in an axial view, also on its minor axis, at the level of the departure of the renal arteries [Figure 2]. The method used to measure the descending and abdominal aorta were the same for the native CT-scan and the three phases of the MPMCTA. Whenever situation was imposing, the diameter of the vessels was measured on their minor axis to avoid an overestimation. So to illustrate that principle, comparisons are made between aorta and cylinders on a sectional view. If the latter is not exactly perpendicular, the cross sectional area will be elliptical and will not allow an accurate measurement of the real diameter.

All cardiac measurements were carried out using a reformatted four-chamber view derived from the algorithm proposed by Michael T Lu and al [26]. The method consists in creating a plane axe through the cardiac apex and the midpoint of the mitral valve using a sagittal view. On the reformatted four-chamber a scrolling was



performed to find the two slices that permit the best visualization of the right and the left heart cavities respectively.

On the slice depicting the left cardiac cavities, the left atrium and ventricle were measured, as well as the inter-ventricular septum and left ventricular wall thicknesses [Figure 3]. The left atrium was measured on the minor axis from the left to the right inner walls. The left ventricle was measured midway between the mitral valve and the cardiac apex on the minor axis from the outer left ventricular wall and the inner right ventricular cavity. The measurements of the right cardiac cavities were carried out similarly. On the slice that depicted the latter, the right atrium and ventricle were measured, as well as the right ventricular wall thickness [Figure 4]. The right atrium was measured on the minor axis from the left to the right inner walls. The right ventricle was measured midway between the tricuspid valve and the cardiac apex on the minor axis from the outer right ventricular wall and the inner right ventricular cavity. The methods to measure the heart cavities were identical for the three phases of the MPMCTA.

The cardiothoracic ratio (CTR) was measured according to the method proposed in the literature [21, 23] consisting in finding and measuring on an axial plane the maximum cardiac diameter from the right to the left. Then, the maximum thoracic diameter was measured on the same slice in a similar manner [Figure 5]. Thus, the CTR was calculated by dividing the maximum cardiac diameter with the maximum thoracic diameter.

### **Autopsy**

Autopsies were performed in accordance with international guidelines [14, 27, 28] by two forensic pathologists (including at least one board-certified). During the procedure, CV measurements were collected as follows: descending and abdominal aorta circumferences were measured in the proximal part and at the level of the renal arteries respectively. The left and right ventricular wall thicknesses were measured one centimetre below the cardiac valves on an axial slice, the same goes for the inter-ventricular septum thickness. The circumferences of the four cardiac valves (tricuspid, mitral, aortic and pulmonary) were also measured. The emerging points of the great cardiac vessels were cut and the heart (with epicardial fat) was excised. The hearts was emptied of post mortem clots and weighed [29] unfixated on a precision electronic balance (DIBAL 0 – 15 kg range, 1 g intervals).

### **Statistical methods**

A convenient sample size of 50 cases was chosen. Parameters that were not measurable on CT-scans were identified and described. The prevalence and underlying patterns were described for each CT-scan phase. The adjusted coefficient of determination ( $R^2$ ) was measured to test the correlation between autopsy and radiological measurements using analysis of variance. For the aorta, the minimal diameter was calculated from the circumference measured during the autopsy for comparability with radiological measurements. To test whether other phases than the dynamic phase were better at modelling true values measured at the autopsy, we used computed the Bayesian Information Criterion (BIC) to compare non-nested models (native CT-scan, arterial phases, venous phase and dynamic phase). We then used Raftery's rule [30] to define to what extent another phase was an improvement over the dynamic phase (0-2: weak; 2.1-6: positive; 6.1-10: strong; >10: very strong). All analysis were performed with STATA 12.0 (StataCorp LP, College Station, TX, USA).

### **Results**

#### **Population description**

The population of the study was made of 50 medico-legal cases [table 2]. 39 male (78%) and 11 women (22%) with a mean age of 58.2 (SD: 18.3) and a mean body mass index (BMI) of 27.2 (SD: 4.8) causes and

circumstances of death were the following: natural cardiac (n = 10); natural other (n = 10) including haemorrhage, pulmonary embolism and cerebral infarct; traumatic (n = 15); intoxication (n = 3); other (n = 12) including asphyxia, multiple organ failure, medical errors and unknown. The mean delays between death and MPMCTA and between MPMCTA and autopsy were 1.4 days (SD: 0.7) and 0.6 day (SD: 0.2) respectively.

#### **Feasibility of assessment on CT-scan**

As the vascular system needs to be filled completely for the measurements, and the vessels are filled in different phases, it was important to investigate which measurement could be obtained in which phase. Additionally, we had to verify if all measurements were feasible to be taken in all cases.

On the dynamic phases, the right ventricular wall thickness was always measurable. However, the measurements of the left ventricular wall and the inter-ventricular thicknesses were impossible for 7 and 3 cases respectively. In cases where the measurements of the left ventricular wall thickness were not possible on the dynamic phase (n = 7), 2 cases were measurable on the venous phase. In the 3 cases where the inter-ventricular septum thicknesses were not visible on the dynamic phase, 1 case was measurable on the venous phase. But in all cases, the unmeasurable thicknesses on the dynamic or venous phase were impossible on the arterial phase.

At least one of the thickness measurements (right or left ventricular wall and inter-ventricular septum) was unrealizable on the arterial phase for 24 cases (48%). In comparison, on the dynamic phase, the latter were impossible only for 7 cases (14%; Fisher's exact test  $p < 0.001$ ).

With respect to the venous phase, the left ventricular wall thickness measurement was impossible for 7 cases, but 2 cases were measurable on the dynamic phase. Regarding the inter-ventricular septum thickness, 3 cases were unmeasurable on the venous phase; one of them became measurable on the dynamic phase. To summarize, the measurement should be carried out on priority on dynamic phase and if not feasible, on the venous phase.

#### **Correlation of the descending and abdominal aorta between autopsy and imaging:**

The autopsies performed after the radiological examinations allow a direct comparison between diameters measured on the CT-scan and the circumferences of the aortas at the dissection. Concerning the descending aorta, the different measurements are exposed in the table 3. A good correlation was obtained between the dynamic phase and the autopsy ( $R^2 = 0.382$ ;  $p < 0.001$ ). The BIC performed proved that the dynamic phase is the best to estimate the value measured at the autopsy [table 4]. The other phases of the MPMCTA and the native CT-scan were less accurate to measure the real diameter of the aorta (native = 8.6; arterial = 13.2; venous = 3.9). The measurement of the abdominal aorta, exposed in table 3, showed similar results. The correlation between autopsy and dynamic phase was equally good ( $R^2 = 0.486$ ;  $p < 0.001$ ) and the BIC analyses displayed the great advantages to perform the measurements on the dynamic phase (native = 19.2; arterial = 14.7; venous = 6.2) [table 4].

#### **Correlation of the cardiac thicknesses between autopsy and imaging**

The measurements of the cardiac thicknesses (right and left ventricular wall and inter-ventricular septum) were carried out at the autopsies, as well as the aortas diameters [table 3]. However, unlike the aorta, the measurements of the thicknesses displayed no correlation [table 4]. The  $R^2$  calculated for the right, the left ventricular wall thicknesses and the inter-ventricular septum were 0.004, 0.07 and 0.087 respectively. Furthermore, the BIC performed didn't display an advantage to measure the thickness on the dynamic phase for the three thicknesses [table 4].

#### **Correlation between the cardiac valves and heart cavities**

We did not find any significant correlation between the right atrium and the tricuspid valve on the dynamic phase ( $R^2 = <0.001$ ); the right ventricle and the pulmonary valve on the dynamic phase ( $R^2 = 0.027$ ); the left atrium and the mitral valve on the dynamic phase ( $R^2 = <0.001$ ); the left ventricle and the aortic valve on the dynamic phase ( $R^2 = <0.001$ ) [table 5]. Moreover, the BIC analyses didn't display an advantage to make the measurement on any phases.

Finally, the absence of association between the cardiac valves and heart cavities was not in connection with the PM delays or the causes of death.

#### **Correlation between the heart weight and the CTR or the maximum cardiac diameter**

There was no correlation between the CTR and the heart weight on the dynamic phase [table 6] ( $R^2 = 0.075$ ;  $p < 0.05$ ). Furthermore, the BIC analyses didn't point out any advantage to measure the CTR on one phase over another to get a good correlation with the heart weight.

Nevertheless, we found a significant correlation between the maximum cardiac diameter and the heart weight on the dynamic phase [table 6] ( $R^2 = 0.418$ ;  $p < 0.001$ ). Moreover, the BIC analyses displayed the great advantage to make the measurement on the dynamic or the venous phase (BIC = -0.2), compared to the native CT-scan (BIC = 11.9) and the arterial phase (BIC = 9.9).

Finally, the BIC analyse of the best two modalities (the venous phases for the CTR and the maximum cardiac diameter) to get the best correlation with the heart weight displayed the huge advantage to use the maximum cardiac diameter, instead of the CTR, on the venous phase (BIC = 22.5).

#### **Discussion**

CT- angiography is the gold standard in clinical practice for imaging evaluating of the CV system [31-34].

Thanks to the development of the MPMCTA, the investigation of the CV system has become a routine tool also in forensic medicine. However, autopsy still remains the method of choice for CV measurements.

As mentioned above, these measurements determine if CV pathology exists. Indeed, they are important because an increased heart weight can be suggestive of hypertrophic cardiomyopathy, some valvular diseases, advanced stage of ischemic heart disease, pulmonary hypertension and other chronic diseases. All of which should be carefully considered during autopsy and histological examination [29, 35, 36]. It is considered that measurements of the circumferences of valves is not useful in valve stenosis, but can be useful for incompetence [16, 37]. An increase of aortic diameter suggests the most frequently an aortic disease dominated by aneurysms of various types related to inflammatory or no inflammatory media degeneration [38, 39].

Moreover, in post-mortem it is impossible to assess the heart function because the echocardiography, the reference examination used for living, cannot be performed. Therefore, the CV measurements at autopsy are the only objective parameters of a pathological heart function.

However, as demonstrated by the literature [17-21], the great importance of the PM changes does not allow an application of the clinical radiologic parameters and reference values. For that reason, the necessity to find thanks to MPMCTA new radiological CV measurements that correlate with autopsy finding became an essential field of research in PM imaging.

For that reason, we decided to answer the following questions with this study: Do radiological CV measurements performed on post-mortem PMCT and MPMCTA correlate with autopsy CV measurements and in which phase of the MPMCTA the best correlation can be obtained?

Our results show that the dynamic phase displays a promising advantage for the measurement of the aorta. However, the MPMCTA is not accurate to measure the heart wall thicknesses. Moreover, the measurements of the heart cavities show no correlation with the heart valves circumferences. Finally the CTR measured by the MPMCTA show no correlation with the heart weight. However, the maximum cardiac diameter exhibits a good correlation with the latter thanks to MPMCTA, especially on the venous and dynamic phase.

More explicitly, the measurement of the descending and abdominal aortas in the dynamic phase exhibit the stronger correlation with the autopsy compared to the two others phases of the MPMCTA and the native CT-scan. Moreover, the BIC analyses display the importance to measure these vessels on the dynamic phase. This first result is not surprising. Indeed, as proposed by the literature [3, 12, 25], unenhanced CT-scan doesn't allow a good visualization of the CV system. Therefore, it's important to use contrast media to measure accurately the diameter of the aorta. A further important point is the usefulness of the dynamic phase. This latter allows a more effective filling of the vascular system to obtain images of greater quality, thus allowing to measure the diameter of the vessels [12]. In addition, the filling volume offsets the flattening by the surrounding tissue as mentioned by the literature [12, 19]. Furthermore, although it is a well-known fact that the diameter of the aorta decrease after death [18, 19, 24]; this effect is attenuated by the increasing diameter of the vessel caused by the injection of a lipophilic contrast media [8, 40].

Concerning the weak correlation between the heart walls' thicknesses on MPMCTA and at the autopsy, our results are quite surprising. Moreover, the BIC analysis didn't show an advantage to perform the measurements of the heart walls and the inter-ventricular septum on the dynamic phase.

In effect, as demonstrated by the literature [4, 5, 22], CT-scan is a poor technique to clearly visualise the cardiac soft-tissue. Therefore, it's difficult to measure the three thicknesses accurately. Also, an important pitfall of MPMCTA compared to clinical practice, is that both ECG gated cardiac CT and cardiac MRI, allow the measuring of the left ventricular wall thickness to be performed during the tele-diastolic phase of the cardiac cycle, while the myocardium is relaxed, thus avoiding an overestimation, due to the contracted cardiac muscles [32]. However, as proposed by Grabherr and al [25], the high radio-opacity of the contrast media allows a better delineation of the inner walls in the heart cavities. Finally, as proposed by Okuma and al [17], the CT-scan didn't allow a good distinction between the heart walls, the papillary muscles and the epicardial fat. This latter cause an over-estimation of the heart walls and the inter-ventricular septum at the MPMCT compared to the autopsy, where only the myocardium is measured, but not the trabecular muscles that cover the inner layer of the ventricle.

In order to explain the weak correlation between the measurements obtain at the MPMCTA and at the autopsy, we formulate some hypothesis. Firstly, although the long-axis views of the heart is the routine way to assess the heart wall thicknesses in our center, the latter, could not be the method of choice to measure them. Secondly, the shorter range of the thickness measurements, compared to the aortas, could be more conclusive to cause a weak correlation with a slight variation in measurements. Finally, some individual differences related to the forensic pathologists in charge of the autopsy could explain this result too.

Therefore, while MPMCTA is the best method to allow the measurements the heart wall and the inter-ventricular septum thicknesses; this study display the fact that the long-axis of the heart didn't allow an accurate measurement of the thicknesses compared to the autopsy. To overcome this point, we can propose two possibilities. The first one consists in finding another measurement that better correlate with the ones obtained at

the autopsy. The second one consists in measuring the heart wall on the magnetic resonance imaging. This latter should allow a better visualization and demarcation of the soft tissues, as proposed by Aghayev and al [22, 41]. With regard to the correlation between the cardiac valves measurements obtain at the autopsy and the heart cavities measured on CT-scan, our results are slightly surprising. In effect, the statistical analysis showed no correlation. Furthermore, the BIC analysis didn't display an advantage to carry out the heart cavities measurements on any phase of the MPMCTA.

At the autopsy, the four valves (aortic, tricuspid, pulmonary and mitral) circumferences were measured [**table 3**] but the diameter of the heart cavities (left and right atriums, left and right ventricles) were not recorded in autopsy and is therefore not included in standard autopsy protocols. However, with imaging this measure is easy to obtain [**table 3**]. Through this method, the correlations were calculated between the different structures seen, if the radiological measurements were correlated to the ones provided by the autopsy.

In spite of the anatomical proximities and the pathological functioning [42-51], that urged our study to analyse the correlation between the right atrium and the tricuspid valve, the right ventricle and the pulmonary valve, the left atrium and the mitral valve, the left ventricle and the aortic valve; our results didn't display any correlation. This outcome could be explained by two hypotheses. Firstly, although the autopsy still remains the gold standard to measure the valve circumference; the heart cavities measurement on the CT-scan undertook in accordance with our methodology could not be the best way to estimate these latter. Another measurement, such as the volume of the heart cavities, could be better correlated to the autopsy measurements. Secondly, the cases with a severe valvular incompetence and a dilatation of the valve annulus were treated with a prosthetic valve.

Unfortunately, the latter had to be excluded from our study, in accordance with our methodology.

However, MPMCTA is still the better way to evaluate the heart cavities in contrast to the native CT-scan.

Indeed, as explained above for the aorta, enhanced CT-scan provides a better visualization and delimitation of the cavities [3, 12, 25]. Moreover, as mentioned by Shiotani and al. [20] in PMCT, the left atrium seems to be collapsed compared to the right atrium because of its anatomical position and the weight of the heart. In addition, Aghayev and al [22]. displayed the difficulty to evaluate the right atrium in case of hypovolemia resulting from a fatal haemorrhage. These two examples highlight the limitation of the unenhanced CT-scan to assess the heart cavities. However, it is important to mention that in PM examination, the atrium size is evaluated in order to determine if a dilatation is present.

With respect to the correlation between the heart weight at the autopsy and the CTR just as the maximal cardiac diameter on the CT-scan, our results were quite surprising. In fact, as demonstrated by the literature, CTR can be measured reliably on the CT-scan compared to the routine gold standard chest film [52, 53]. However, our results display only a weak significant correlation on the venous and the dynamic phase of the CTR with the heart weight. In addition, the BIC analyse didn't show any advantage to perform the measurements on any phase. This result is in agreement with Jotterand and al. [21] who didn't display a significant correlation between the heart weight and the CTR on the native CT-scan.

This lack of correlation could be explained by two hypotheses. Firstly, in agreement with our methodology, the CTR was measured on only one axial slice of the CT-scan. The latter was the one with the maximal cardiac diameter, and therefore not necessarily the maximal thoracic diameter. For that reason, this method tends to overestimate the CTR. But our study tests an easy-way to measure the CTR in the routine practice. This fact was also pointed out by Winklofer and al. [23] Secondly, although it was mentioned by Jotterand and al. [21], our

study didn't take into account the dilatation of the heart to measure the CTR. The latter overestimates the maximal cardiac diameter.

However, a good and significant correlation was found between the heart weight and the maximal cardiac diameter on the venous and the dynamic phase. Moreover, the BIC analyse display the great advantage to measure the latter on these two phases. This discovery is especially important due to the fact that the heart weight is a potentially key factor of cardiomyopathies [29]. This is why it is important to find a radiological measurement that accurately correlates with the heart weight obtained at the autopsy. Until today, the latter still remains the gold standard.

Nevertheless, our study highlights the usefulness of the MPMCTA, thanks to the venous and dynamic phase, to evaluate the heart weight. It proves the need to fill the heart cavities to perform a measurement that correlate significantly with the heart weight.

In summary, the results of our study show that only the measurement of the descending and abdominal aorta, that are regularly measured in autopsy, can be obtained by MPMCTA, especially on the dynamic phase in a comparable way to autopsy measurements. Furthermore, the heart weight measured at the autopsy correlate significantly with the maximal cardiac diameter obtained on the venous and the dynamic phase.

The other measurements such as the heart wall thicknesses, the heart cavities and the CTR differ from the measurement obtained at the autopsy. This is why we need to define new reference values for the CV measurement on post-mortem CT-scan and MPMCTA that better estimate the values obtained at the autopsy; because the latter still remains the gold standard.

### **Limitations**

Firstly, the retrospective design of this study did not allow us to include cases of important cardio-vascular disease with clear signs of cardiac hypertrophy or valvular deficiencies, making correlations more difficult to detect. Secondly, this was an exploratory study; therefore we relied on a convenient sample size for which we assumed to have enough power to test our hypothesis. Even if we did not report corrected p-values for multiple testing, the observed correlation were strong enough to remain significant even after correction.

Finally, our observations do not extend to corpses in an advanced state of decomposition.

### **Conclusion**

According to our knowledge, this is the first study that compares CV measurements between the native CT scan with the three phases of the MPMCTA and the autopsy. The results of the latter are promising on the possibility of measuring CV parameters obtained at the autopsy with the imaging; such as measuring the aorta and the cardiac wall thicknesses, estimate heart weight and cardiac valves diameters though the maximal cardiac diameter and the heart cavities, respectively. However, as demonstrated by some inconclusive results, we need to carry out more studies on this field of research to allow the CV measurements on MPMCTA to become a routine tool in forensic imaging.

### **Conflicts of interest**

None of the authors has a conflict of interest.



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## **Figure Legends**

### **Fig. 1:**

Measurement of the descending aorta diameter (yellow arrows) on the minor axis in axial section: a) Native CT-scan; b) Arterial phase; c) Venous phases; d) Dynamic phase; R: right; L: left

### **Fig. 2:**

Measurement of the abdominal aorta diameter (yellow arrows) on the minor axis in axial section: a) Native CT-scan; b) Arterial phase; c) Venous phase; d) Dynamic phase; R: right; L: left

### **Fig. 3:**

Measurement of the left cardiac cavities with a reformatted four-chamber view in axial section: a) Arterial phase; b) Venous phase; c) Dynamic phase; Visualization of the left atrium (yellow arrows); the left ventricle (orange arrows); the left ventricular wall thickness (blue arrows) and the inter-ventricular septum thickness (red arrows); R: right; L: left

### **Fig. 4:**

Measurement of the right cardiac cavities with a reformatted four-chamber view in axial section: a) Arterial phase; b) Venous phase; c) Dynamic phase; Visualization of the right atrium (yellow arrows); the right ventricle (red arrows) and the right ventricular wall thickness (blue stars) ; R: right; L: left

### **Fig. 5:**

Measurement of the cardiothoracic ratio with the maximum cardiac diameter (yellow arrows) and the maximum thoracic diameter (red arrows) in axial section: a) Native CT-scan; b) Arterial phase; c) Venous phase; d) Dynamic phase; R: right; L: left

## **Tables Legends**

**Table 1:** CT-scan parameters

**Table 2:** Population description

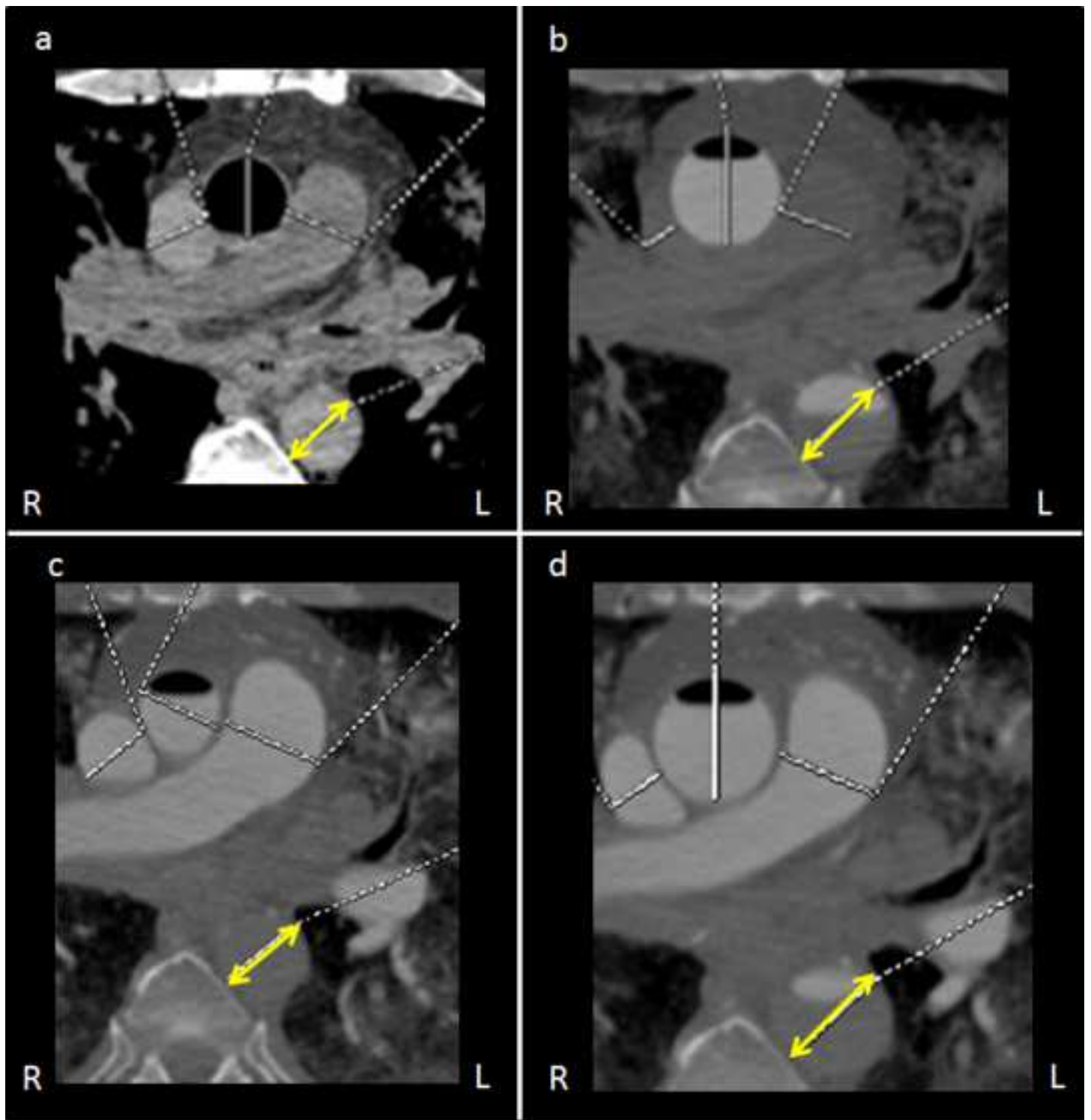
**Table 3:** Cardiovascular measurements

**Table 4:** Correlation between CV measurements at the CT-scan and the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

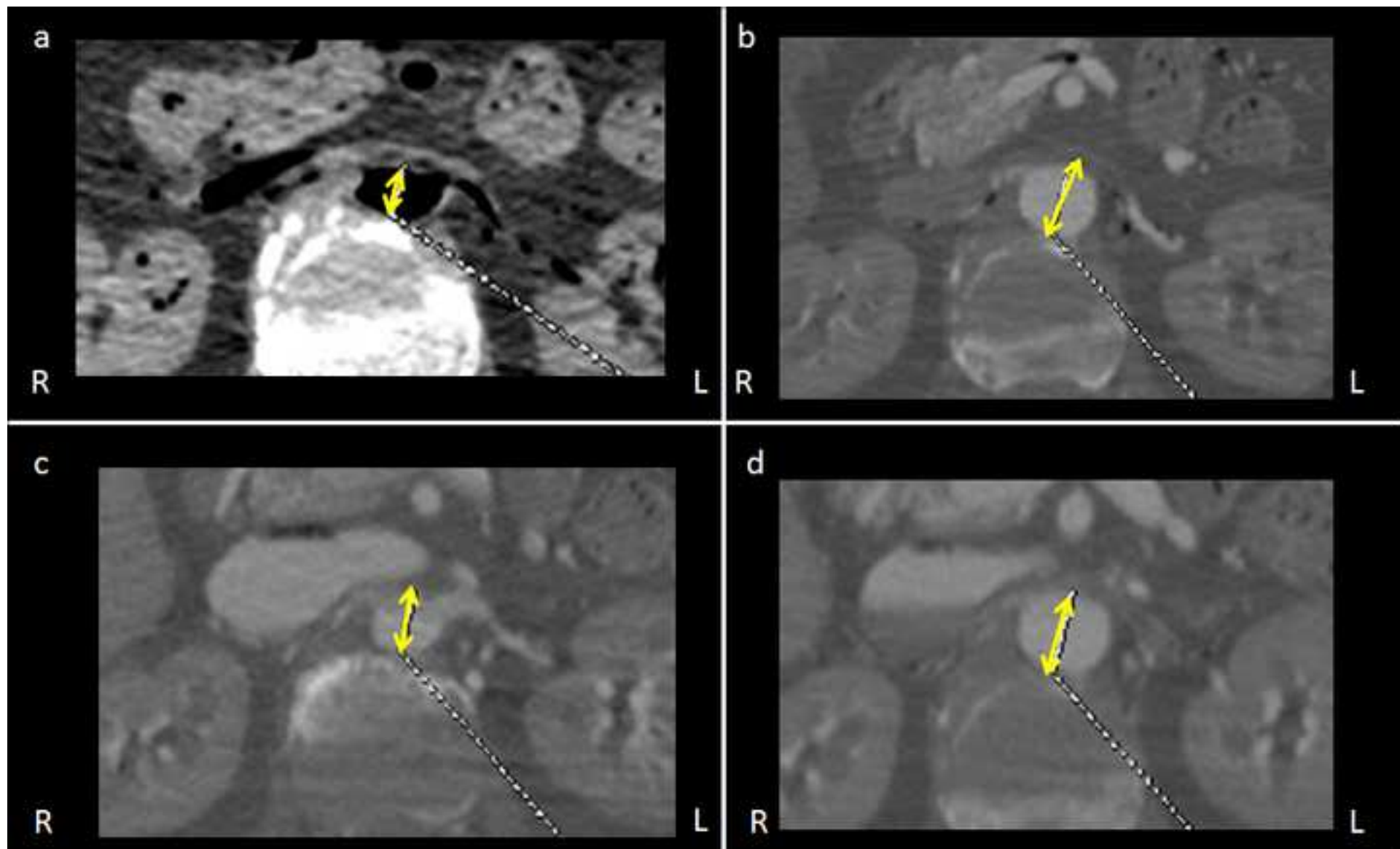
**Table 5:** Correlation between the heart cavities at the CT-scan and the cardiac valves at the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

**Table 6:** Correlation between the CTR or the cardiac diameter at the CT-scan and the heart weight at the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

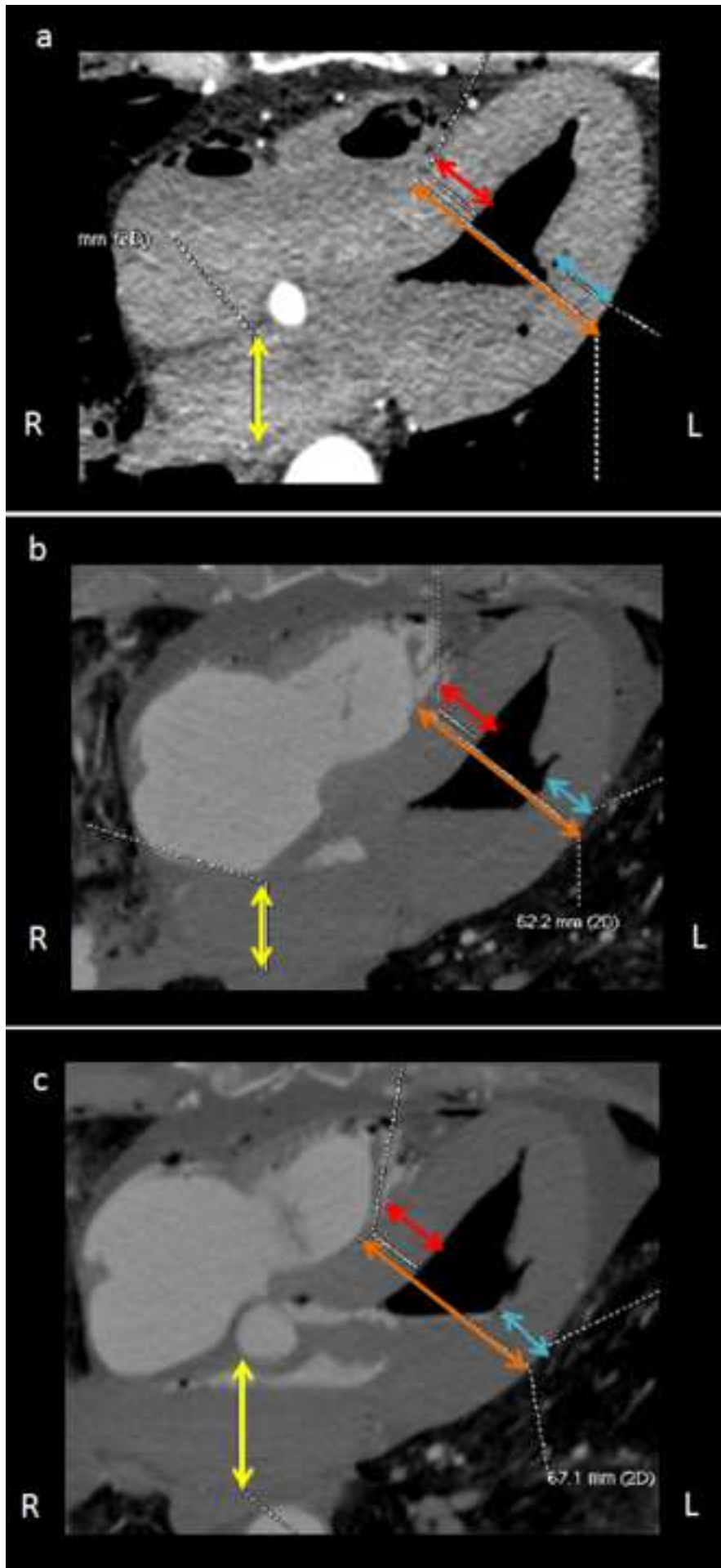
Figure



Figure

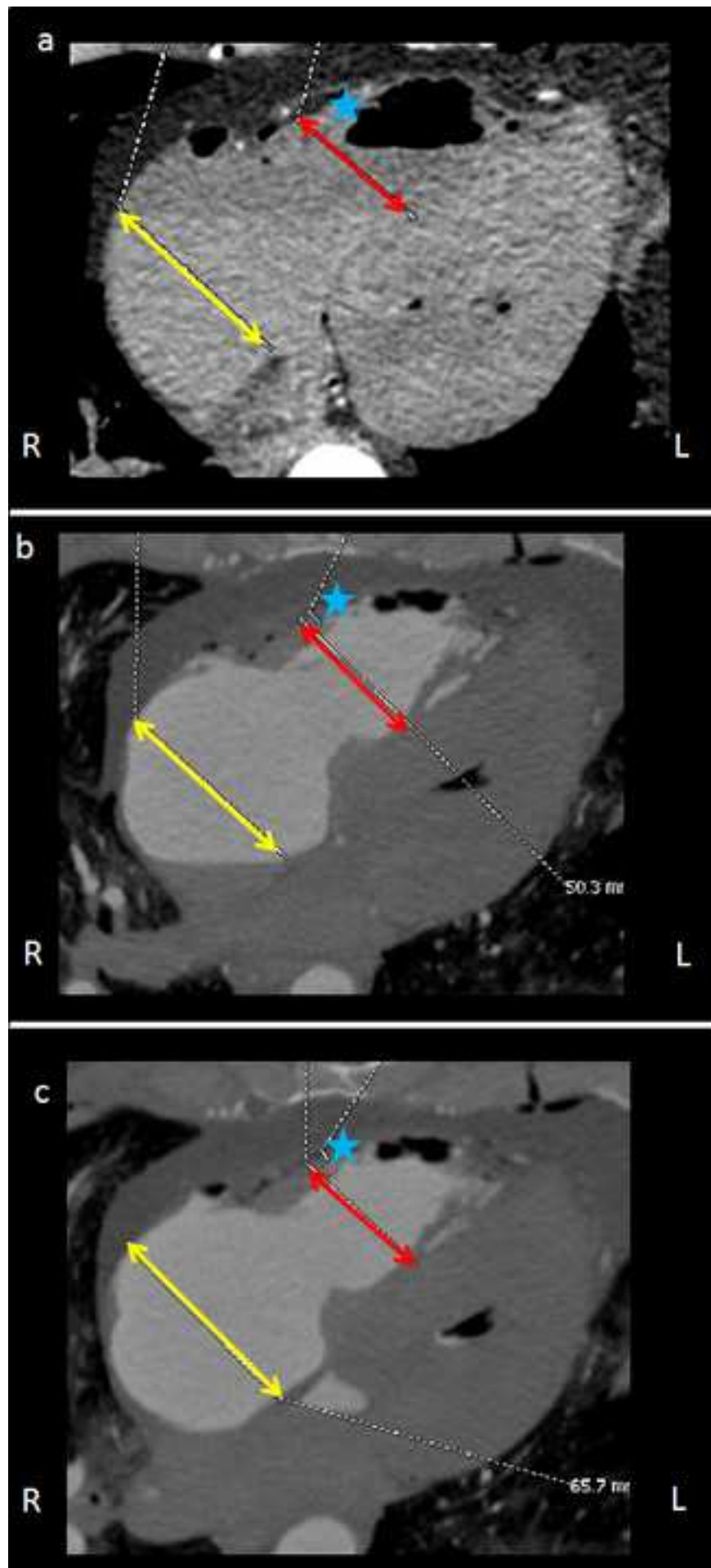


Figure

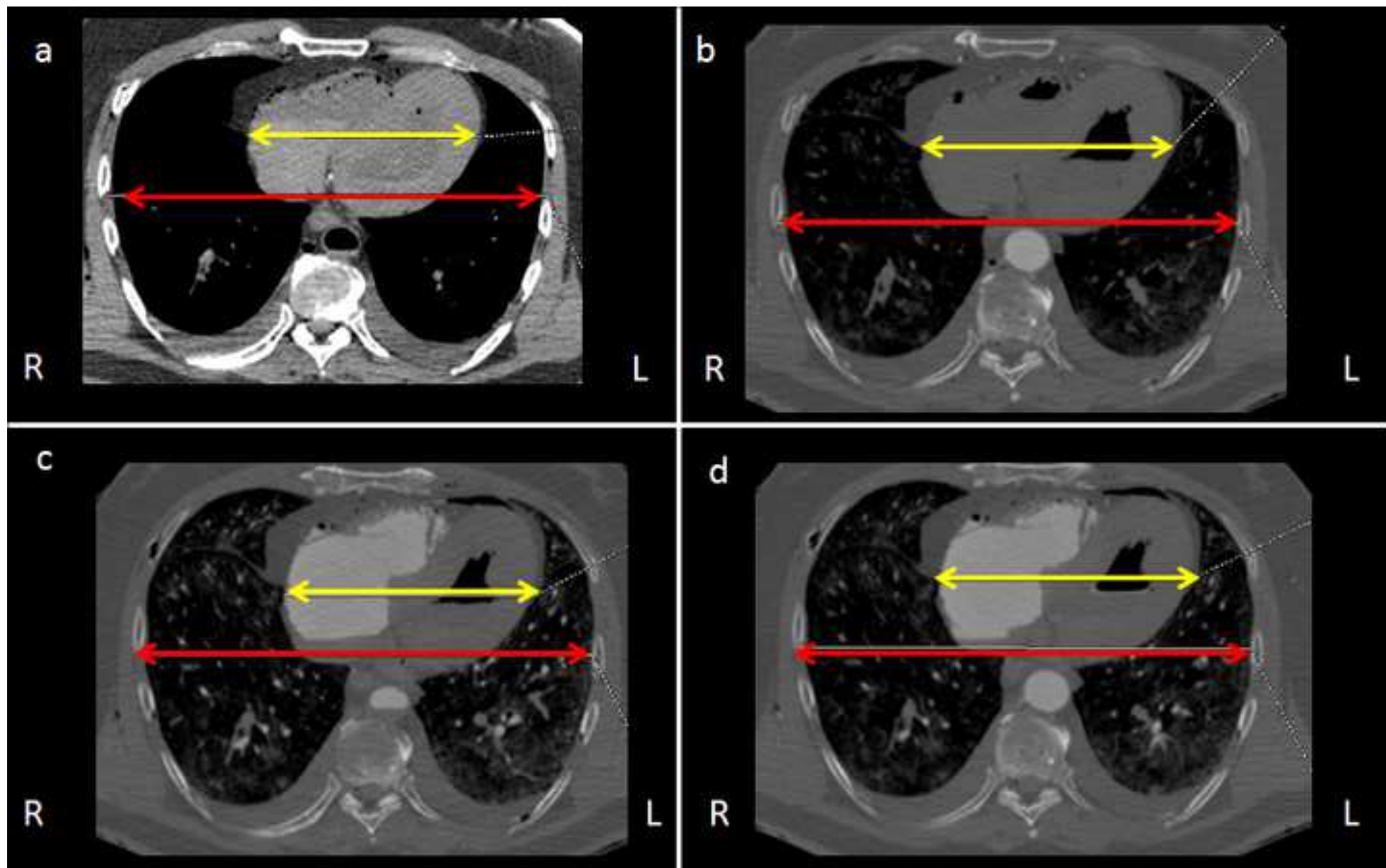




Figure



Figure



**Table1** CT-scan parameters

	Native CT-scan				MPMCTA		
	Head	Head and cervical spine	Thorax and abdomen	Lower limbs*	Arterial phase	Venous phase	Dynamic phase
Localisation	From the vertex to the base of the skull	From the vertex to D1	From the shoulders (included) to the pelvis (genitals included)	From the acetabulum (included) to the toes (included)	From the vertex to the pelvis	From the vertex to the pelvis	From the vertex to the pelvis
Scan type [s]	axial full 1.0	helical full 1.0	helical full 1.0	helical full 1.0	helical full 1.0	helical full 1.0	helical full 1.0
Field of view [cm]	25	25	50	50	50	50	50
Slices thickness [mm]	5; interval 20mm	1.25; spaced every 1mm	1.25; spaced every 1mm	1.25; spaced every 1mm	1.25; spaced every 0.6mm	1.25; spaced every 1.2mm	2.25; spaced every 2mm
Voltage [kV]	120	120	120	120	120	120	120
Dose [mA] / modulation index	300	100-350 / 15.00	100-350 / 15.00	100-350 / 15.00	300	300	300
Reconstruction algorithm	Standard	Standard bone reconstruction	Standard Bone reconstruction lung reconstruction (only on the lungs)	Standard Bone reconstruction	Standard	Standard	Standard

\*If needed, in case of brunt body, multiple traumatic injuries, decomposed body

**Table 2** Population description

Sample characteristics	% / Mean	n / SD
Men	78%	(39)
Cause of death		
Natural cardiac	20%	(10)
Natural other	20%	(10)
Traumatic	30%	(15)
Intoxication	6%	(3)
Other	24%	(12)
Age	58.2	(18.3)
BMI	27.2	(4.8)
PM delay [day]		
Death to MPMCTA	1.4	(0.7)
MPMCTA to autopsy	0.6	(0.2)
Death to Autopsy	2	(0.7)

**Table 3** Cardiovascular measurements

	Native Mean; SD; n	Arterial Mean; SD; n	Venous Mean; SD; n	Dynamic Mean; SD; n	Autopsy Mean; SD; n
<b>Aortas [mm]</b>					
Descending	18.8; (4.4); 50	25.1; (3.2); 50	20.8; (4.2); 50	24.3; (3.6); 50	18.8; (3.7); 50
Abdominal	9.2; (4.5); 50	17.6; (3.2); 50	14.3; (4.2); 50	18.1; (3.2); 50	14.7; (3.1); 50
<b>Thicknesses [mm]</b>					
Right ventricular wall	-	5.2; (1.8); 31	4.9; (1.9); 49	4.4; (1.7); 50	4; (1.8); 50
Left ventricular wall	-	14.5; (4); 34	15.3; (4.1); 43	15.2; (4.3); 43	13.8; (2.8); 50
Inter-ventricular septum	-	14.6; (3.8); 38	12.6; (3.4); 47	13.5; (3.5); 47	13; (3.1); 50
<b>Heart cavities [mm]</b>					
Right ventricle	-	36.8; (9.2); 50	48.5; (10.7); 50	45.8; (10.4); 50	-
Left ventricle	-	56.6; (9.2); 50	51.6; (6.6); 50	54.6; (8.2); 50	-
Right atrium	-	51; (11.5); 50	60.6; (9.2); 50	59.4; (9.2); 50	-
Left atrium	-	28.3; (8.8); 50	30; (8.1); 49	32.1; (7.8); 49	-
<b>Valves [mm]</b>					
Mitral	-	-	-	-	10.8; (1); 50
Tricuspid	-	-	-	-	12.5; (1.3); 50
Aortic	-	-	-	-	7.8; (0.8); 50
Pulmonary	-	-	-	-	8.2; (0.8); 50
Heart diameter [mm]	133.6; (13.4); 50	136.7; (13.6); 50	141.9; (12.2); 50	142.6; (12.1); 50	-
Thoracic diameter [mm]	257; (22); 50	256.6; (21.6); 50	258.6; (21.1); 50	258.8; (21.3); 50	-
Cardiothoracic ratio	0.522; (0.057); 50	0.535; (0.058); 50	0.55; (0.049); 50	0.553; (0.049); 50	-
Heart weight [g]	-	-	-	-	472.7; (112.3); 50

**Table 4** Correlation between CV measurements at the CT-scan and the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

	Dynamic phase R <sup>2+</sup> ; n	Alternative phases		
		Native CT-scan R <sup>2+</sup> ; n; BIC‡	Arterial phase R <sup>2+</sup> ; n; BIC‡	Venous phase R <sup>2+</sup> ; n; BIC‡
<b>Aortas</b>				
Descending	0.382***; 50	0.265***; 50; 8.6	0.194**; 50; 13.2	0.332***; 50; 3.9
Abdominal	0.486***; 50	0.246***; 50; 19.2	0.311***; 50; 14.7	0.418***; 50; 6.2
<b>Heart thicknesses</b>				
Right ventricle	0.004; 50	-	<0.001; 31; 0.8	0.018; 49; -1.1
Left ventricle	0.070*; 43	-	0.126*; 34; 0.9	0.056; 41; 1.6
Inter-ventricular septum	0.087*; 47	-	0.121*; 38; 3.3	0.100*; 46; -0.2

Linear regression test of significance \* P<0.05; \*\*P<0.01; \*\*\*p<0.001

+Adjusted R<sup>2</sup> using Mc Fadden's method

‡Bayesian information criterion (BIC) corresponds to the difference of prediction ability of findings during conventional autopsy for alternative CT-scan compared to the dynamic phase

**Table 5** Correlation between the heart cavities at the CT-scan and the cardiac valves at the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

	Dynamic phase R <sup>2+</sup> ; n	Alternative phases	
		Arterial phase R <sup>2+</sup> ; n; BIC‡	Venous phase R <sup>2+</sup> ; n; BIC‡
Mitral valve	<0.001; 49	<0.001; 49; 0.2	<0.001; 49; 0.4
Tricuspid valve	<0.001; 50	0.008; 50; -1.1	<0.001; 50; -0.1
Aortic valve	<0.001; 50	<0.001; 50; -0.01	<0.001; 50; 0.2
Pulmonary valve	0.027; 50	0.017; 50; 0.5	0.051; 50; -1.2

Linear regression test of significance\* P<0.05; \*\*P<0.01; \*\*\*p<0.001

+ Adjusted R<sup>2</sup> using Mc Fadden's method

‡ Bayesian information criterion (BIC) corresponds to the difference of prediction ability of findings during conventional autopsy for alternative CT-scan compared to the dynamic phase

**Table 6** Correlation between the CTR or the cardiac diameter at the CT-scan and the heart weight at the autopsy including a detailed comparison of measurements between the dynamic phase and the other phases of MPMCTA (native CT-scan, arterial phase and venous phase)

	Dynamic phase R <sup>2+</sup> ; n	Alternative phases		
		Native CT-scan R <sup>2+</sup> ; n; BIC‡	Arterial phase R <sup>2+</sup> ; n; BIC‡	Venous phase R <sup>2+</sup> ; n; BIC‡
CTR	0.075*; 50	0.044; 50; 1.6	0.044; 50; 1.6	0.09*; 50; -0.8
Cardiac diameter	0.418***; 50	0.262***; 50; 11.9	0.290***; 50; 9.9	0.421***; 50; -0.2

Linear regression test of significance\* P<0.05; \*\*P<0.01; \*\*\*p<0.001

+ Adjusted R<sup>2</sup> using Mc Fadden's method

‡ Bayesian information criterion (BIC) corresponds to the difference of prediction ability of findings during conventional autopsy for alternative CT-scan compared to the dynamic phase