Computed Tomography: The Revolution in Postmortem Angiography

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Multidetector computed tomography (MDCT) is the most widespread tool in modern forensic radiology. Thanks to a short examination time, high spatial resolution, and the possibility of reconstructions in different axes and two and three dimensions, it is an excellent method for rapidly examining a whole body and performing a first analysis of lesions. In clinical radiology, the sensitivity of MDCT can be increased by injecting contrast agent and enhancing the obtained images, leading to better visualization of organ tissues and of the vascular system. This clinical experience inspired researchers in postmortem imaging to start investigating the possibility of performing postmortem MDCT angiography. Similar to the clinical experience, the aim is to increase the sensitivity of postmortem computed tomography (PMCT) and allow investigation of the vascular system, which is often too complex to examine in conventional autopsy, especially if small vessels are to be investigated. However, the application of contrast agent postmortem is challenging and differs from the process in clinical angiography, principally because of the absence of cardiovascular circulation and postmortem changes in the body. Although there are multiple classic methods for performing postmortem angiography, they cannot simply be transferred to modern forensic imaging because they focus primarily on single organs or on embryos and fetuses. Therefore, to overcome these problems, different approaches have been developed for performing modern, minimally invasive PMCT angiography (PMCTA). Once such a technique is established, questions arise about how to interpret the images because they differ from those of clinical angiography. Additionally, the injection of contrast medium into a body that is associated with a medico-legal or forensic investigation implies the problem of eventual alteration of the results or further analyses that are normally performed in such cases.

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This chapter explains the meaning of PMCTA and the challenges encountered in establishing methods that are applicable in legal medicine; it gives a short overview of the most frequently used techniques in modern forensic imaging.

6.1 Postmortem Angiography—the Key to Visualizing the Vascular System

The presence of multiple classic techniques of postmortem angiography (PMA) is already proof of the importance of visualizing the vascular system. As noted in Chap. 4, the older anatomists knew that visualizing the vessels helps in understanding their anatomy and in investigating their pathology and variants. This knowledge has also been shared by forensic pathologists who have applied the injection of contrast agents to facilitate pathologic findings in blood vessels, especially those that are difficult to render visible by autopsy dissection.

With the appearance of modern forensic imaging, the wish to forensically visualize the vessels has increased. Every forensic pathologist knows that the cause of death is often hidden in the vascular system. This unseen information can be represented by a vascular section leading to bleeding in cases of trauma or by a vascular occlusion and stenosis in cases of natural death resulting from, for example, cardiovascular disease. Investigation of the vascular system must be part of the postmortem evaluation to correctly assign the cause of death. Classic autopsy allows examination of vessels thanks to specific techniques such as the detailed dissection of the heart with the cross-sectional investigation of coronary arteries. However, only vessels that are specifically sought can be seen and investigated. The lumen is visualized only after opening the vessel and the resulting emptying. This act can lead to considerable artefacts, and outcomes strongly depend on the experience of the physician performing the dissection. Once a vessel is opened there is no way back, and the investigation cannot be repeated. In a standard autopsy, the vascular system is investigated only partially,

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encompassing mostly the main vessels. A detailed examination of the different branches of the vascular system requires well-honed skills and can be time-consuming.

In clinical radiology, the investigation of the vascular system is of utmost importance in modern medical investigations. To plan and focus operation techniques, the search for the exact bleeding source is, for example, important for referring the patient to the correct expert and for rapidly performing the intervention to stop the bleeding. The installation of modern multidetector computed tomography (MDCT) units in the emergency admission area has greatly facilitated the initial evaluation of injuries. In fact, modern developments in computed tomography (CT) scanning have elevated this tool to among the most important in emergency radiology. Thanks to immense advances in computing and the development of multislice scanning, the spatial resolution is impressive, and images can be obtained and reconstructed immediately (see also Chap. 1). The initial radiologic evaluation of visceral injuries by means of MDCT and CT angiography allows assessment of the extent of organ and vessel injury and especially facilitates the search for active bleeding sources. This detection serves as a baseline for the decision to use conservative treatment, minimally invasive intervention, or open surgery [1, 2]. Therefore, CT angiography is the most widely used method for detecting and localizing clinically active hemorrhages of unknown sources in living patients [3]. In forensic pathology, similar needs arise to arrive at the exact cause and mechanism of death. The determination of the exact source of bleeding can be essential in cases of gunshot wounds or sharp trauma in which the deadly trajectory has to be determined, or in cases of suspected medical malpractice in which the bleeding can occur from a manipulated or originally ligatured vessel or from another vessel near the surgery site.

Another regular application of CT angiography in clinical practice is cardiac MDCT, including contrast-enhanced CT coronary angiography. In addition to allowing the assessment of clinical symptoms, electrocardiography and cardiac biomarker investigations are essential to diagnose cardiac infarction. To assess the presence or absence of treatable coronary stenosis, invasive coronary angiography is currently the gold standard in clinical practice [4]. However, because it is an invasive method, intensive research has been done to improve the technique of cardiac MDCT, including contrast-enhanced MDCT coronary angiography. In fact, today this method is considered a powerful diagnostic tool for the assessment of coronary disease in acute and chronic cases. It can be used as a rule-out test in patients with a low to intermediate likelihood of disease, as shown by Schlattmann and coworkers in a recent meta-regression analysis [5]. CT angiography is the method of choice for the assessment of both the arterial lumina and wall disease. It has also proved useful for assessment of the degree of myocardial perfusion and the detection of any previous infarctions, which can be done by measuring the myocardial attenuation using Hounsfield units [6]. In this sense, clinical and postmortem investigations again have the same aims because a detailed analysis of the coronary arteries is also important for the diagnosis of death as is the assessment of any fresh or preexisting myocardial lesions. By filling the coronary arteries with contrast agent in the context of postmortem CT angiography (PMCTA), the same and even better results should be expected than those from clinical coronary angiography. In fact, the possibility of using high radiation doses and the absence of any motion artefacts arising from cardiac movements should lead to better images with higher resolution.

Observation of the application of MDCT angiography in clinical practice makes evident why researchers working in the field of modern postmortem imaging have urged the development of PMCTA. The spatial resolution and rapidity of MDCT as well as the possibility of performing imaging in different axes render this radiologic tool ideal for use in postmortem investigations. Also, more and more centers of forensic and legal medicine have access to MDCT units, either in a clinical radiology department or even in their own centers (see Chap. 2). This may be the reason why modern techniques of PMA were all developed in combination with PMCT as the imaging tool. In fact, with important research progress in postmortem radiology, especially in PMCT, several research groups started investigating the possibility of injecting contrast media in combination with PMCT, rendering the vascular system visible to obtain a diagnosis, similar to how it is done in today's clinical radiologic practice.

6.2 The Challenge of Postmortem Contrast Media Application

The application of contrast media in postmortem radiology clearly differs from that in clinical radiology [7]. Several problems can arise that are not known in clinical CT angiography. These problems primarily concern injection of contrast agent, interpretation of the obtained images, and the effects that the contrast agent injection has on other medicolegal exams (see Table 6.1).

6.2.1 The Challenge of Performing PMCTA

The difficulty of performing PMCTA is especially attributable to the simple fact that the investigated body lacks cardiovascular circulation. This absence leads to stasis of any contrast medium that is injected because no intravascular flow exists. An external mechanism is necessary to transport the medium through the body. In addition, the fact that the vascular system is mostly empty, collapsed, or filled with gas

Table 6.1 Challenges for the application of contrast media postmortem and the solution to overcome them

	Problem	Consequence	Possible solution
Problems for performance of angiography	Absence of cardiovascular circulation	No transport of contrast agent	Mechanical extracorporeal transport (installation of pump/perfusion device/ cardiopulmonary resuscitation)
	Emptiness of the vascular system	No mixture with blood, collapsed vessels	Injection of high volume of perfusate/ contrast agent mixture
	Porosity of the vascular system	Extravasation of contrast agent throughout the vascular wall	Injection of hygroscopic or oily solutions
	Postmortem changes due to autolysis	Extravasation of contrast agent in regions of high enzymatic activity	Injection of hygroscopic or oily solutions (eventual increase in viscosity of the oil)
Problems interpreting the obtained images	Postmortem blood clots	Image of vascular occlusion/ stenosis	Standardizing methods and establishing guidelines for radiologic interpretation
	Remaining blood	Depending on the contrast agent: – Mixture with blood (no quantification of blood possible) – Mo mixture with blood (image of layering)	Use of oily contrast agent Standardizing methods and establishing guidelines for radiologic interpretation
	Extravasations of contrast agent due to postmortem changes	False-positive images of "bleeding"	Performance of a native CT phase before the contrast agent injection
Problems performing additional analysis	Dilution/mixture of blood with contrast agent	No quantification of blood loss during autopsy possible Alteration of analysis (toxicology, clinical chemistry, genetics)	Evaluation of influences of the contrast agent and guidelines for sampling/ interpretation Oily contrast agent (no mixture with blood)
	Contamination of the body with unsterile contrast agent	Alteration of microbiologic exams	Guidelines for sampling before contrast agent injection
	Influence on body tissue	Possible alteration/artefacts in histology, immunohistology, and genetic analysis	Evaluation of influences of the contrast agent and guidelines for sampling/ interpretation

creates differences that must be considered. In clinical radiology, the contrast agent mixes with the blood of the patient, but in postmortem radiology it is mostly the only liquid present in the vascular lumina. For this reason, the quantity of the injected liquid must be increased to fill the vessels.

Although thanatologic changes in the vascular system are rarely investigated and understood (see Chap. 5), the experiences of early anatomists, thanatologists, and modern researchers have all led to the same conclusion: The vascular system becomes more and more "porous" with increasing postmortem delay, leading to the rapid leakage of injected liquid from the vascular lumina and massive edema in the surrounding tissue [8–10]. This very important factor was the reason that many approaches for developing specific perfusion liquids have been tested by pioneers of the classic methods of PMA (see Chap. 4).

6.2.1.1 The Challenge of Reading PMCTA

In addition to the difficulties that have to be overcome in performing PMCTA, there are also challenges to reading the radiologic images once the angiography is done. It is evident that any radiologic interpretation of postmortem images requires specific training and that the best way to increase understanding of the data is to conduct interdisciplinary lectures with radiologists and forensic pathologists together (see Chap. 3). This interaction allows an increase in the sensitivity of the reading and a way to avoid misinterpretation arising from simple postmortem changes such as postmortem rigidity or putrefaction. Of course, all of these pitfalls can be encountered when reading PMCT images. However, the performance of PMA brings even more difficulties because specific postmortem changes that create specific artefacts can be observed within the vascular system. The reading of PMCTA images thus requires special care and training. The artefacts encountered depend not only on the condition of the investigated body (e.g., putrefaction, alteration caused by trauma) but also on the contrast material used, the cannulation site, and the perfusion volumes applied. Most artefacts are therefore specific to each technique and are mentioned in the relevant chapters. However, some of them are consistent for all methods. For example, residual blood in the vessels can lead to images of "layering" [11], meaning the formation of two liquid layers in the vessels (Fig. 6.1). The presence of postmortem blood clots leads to an image with filling defects that can mimic vascular occlusion or stenosis. Although the layering images can, with training, be recognized as artefacts, the filling defects arising

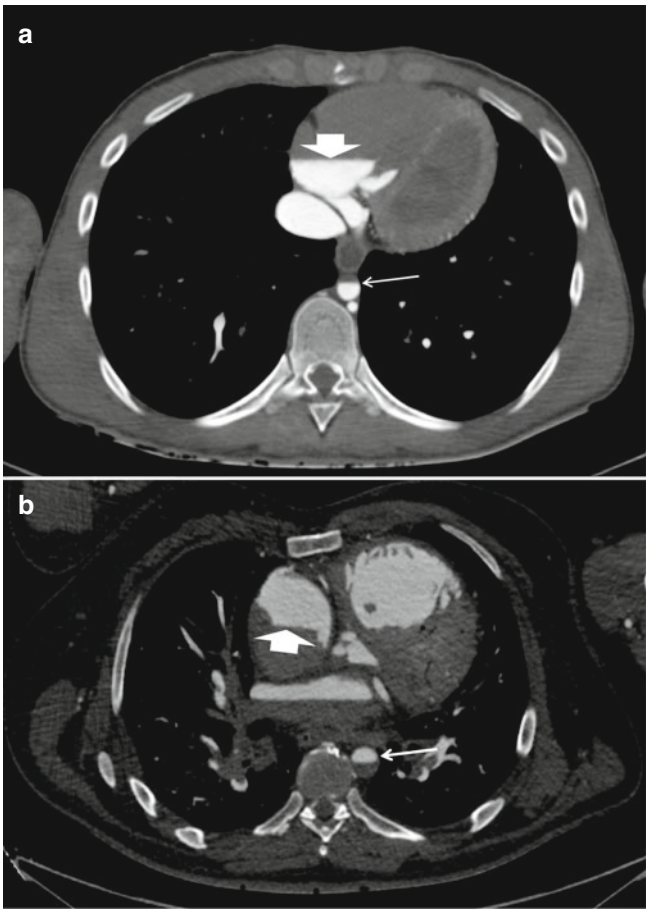

Fig. 6.1 Axial images obtained by two different whole body PMCTA methods: (**a**) PMCTA using aqueous contrast agent and PEG; (**b**) MPMCTA using the oily contrast agent mixture specifically developed for this technique. Both methods show the presence of a so-called "layering" in the vessels (*thin arrow*: layer in the thoracic aorta; *wide arrow*: layer in the cardiac cavity). However, because the aqueous contrast agent mixture is heavier than blood, it represents the inferior part of the layer (*arrows* in **a**), whereas the oily mixture takes the superior part (*arrows* in **b**) in the contrast agent/blood layering

from postmortem blood clots are tricky to recognize and can easily lead to misinterpretation. Artefacts resulting from extravasation of contrast agent can lead to the wrong diagnosis of bleeding. However, no matter which PMA technique is used, the performance of native (without contrast agent) PMCT before injection of the contrast agent can help because vital hemorrhage is associated with blood, which should be observed in the region of the extravasation on the native images. To avoid misinterpretation, it is necessary to know the consequences of the injection of the contrast agent, depending on the method that is applied. Therefore, the development and use of standardized methods are essential to permit the categorization of artefacts in order to allow their recognition and training for physicians. To date, such a specific artefact description exists only for the technique of multiphase (M) PMCTA [11].

6.2.1.2 The Challenge of Understanding the Influence of PMCTA on Other Examinations

The injection of any liquid into the body has consequences that must be understood and considered when PMCTA is performed. The consequences depend mostly on the injected liquid and the mixture that is used as well as whether or not this liquid is injected locally or through the whole body. In general, any liquid can potentially alter the composition of biological samples and interfere with specific postmortem investigations. Therefore, the forensic pathologist should know in detail any interaction between the chosen method of PMCTA and other examinations that should be performed. In addition, water-soluble contrast agents will mix with the remaining blood, rendering the separation of the two liquids impossible. This mixing precludes quantifying the blood found in body cavities during autopsy and changes the performance and outcome of quantitative toxicologic analysis. In contrast, oily liquids can be separated from blood at any point because they automatically separate from the hydrosoluble blood, enabling quantification of hemorrhage during autopsy and the performance of toxicologic analysis of most substances even after PMCTA and autopsy [7].

To date, little literature exists concerning the systematic investigation of the influences and consequences of PMCTA techniques on other postmortem examinations. However, toxicology, clinical chemistry, histology, immunohistology, microbiology, and genetics investigations are regularly performed in forensic pathology. In general, samples for such analyses are recommended to be taken before the injection of contrast agent [7, 12, 13]. However, it can happen that specific questions arise only later, and in these cases, knowledge of the interaction between the components of these examinations and the contrast agent is necessary. Therefore, such studies are of utmost importance to avoid creating conflict between exams. To date, studies exist for MPMCTA [13–19] and targeted coronary angiography (TCA) [17, 20], the most often used techniques. This information is summarized in Chaps. 29 and 30.

6.2.1.3 PMCT and Modern PMA Techniques

With the introduction of modern imaging techniques into forensic and legal medicine, research began targeting an understanding of the limitations and advantages of these techniques in postmortem investigations. Similar to clinical investigations, the idea was to increase the sensitivity of PMCT by enhancing tissue and the vascular lumina via the injection of contrast agent. Considering the challenges mentioned above, different research teams have started to develop techniques to overcome the problems of postmortem contrast agent injection. In general, these problems can be divided into whole body PMCTA techniques and local angiographies (so-called targeted techniques).

The targeted angiography of coronary arteries is especially applied in countries where investigation into cases of natural death is regularly requested. This factor was surely the reason that in the United Kingdom, two centers independently developed methods for TCA [21, 22]. The two techniques especially differ concerning the contrast agent used because the Leicester technique uses not only a clinical aqueous contrast agent but also air as a negative contrast. This method is well described in the literature, and the first studies investigating the eventual side effects on other medico-legal examinations are available and explained in detail in Chap. 8.

In other countries, a whole body approach has been preferred, probably with the rationale of covering the different kinds of cases investigated in these centers. The aim of those approaches is to visualize as much of the vascular system as possible, including the coronary arteries. In this way, cases of natural death and traumatic death can be examined in a manner similar to practices in the clinical emergency unit, where the radiologic examiation can provide an overview of the lesions of organs and vessels. Today, the most used whole body techniques are MPMCTA, PMCTA using cardiopulmonary resuscitation (CPR), and PMCTA using aqueous contrast agent, mostly mixed with polyethylene glycol (PEG).

MPMCTA [12] is actually the most widespread and most investigated method, which is the reason that this atlas primarily focuses on it. It is a standardized technique using specifically developed injection material (perfusion device, tubing set, and cannulas) as well as a clearly defined mixture of an oily contrast agent (Angiofil®; Fumedica, Muri, Switzerland) and paraffin oil with specific viscosity. In addition to the well-defined parameters for performing the PMCTA, guidelines exist on how to interpret the radiologic images, and the influence of the contrast agent mixture on the different medico-legal analyses has been investigated and is described in Chaps. 29 and 30.

The techniques of PMCTA using aqueous contrast agent eventually mixed with PEG are described in Chap. 7. For these techniques, no specifically defined protocol exists to date, and information concerning the injection method, injection parameters, and mixture of contrast agent varies in the literature. However, the first trials have been completed, and literature is available [10, 23–25]. The influences of these approaches on further medico-legal exams are only sporadically described, and structured studies investigating them in detail are currently lacking.

The technique of PMCTA using CPR was developed in Japan [26, 27] and is especially adapted to the local conditions where the body can be directly investigated after death in a clinical hospital. No detailed study that has investigated the influence of the contrast agent on other medico-legal analyses has as yet been reported; however, because the technique uses a low quantity of clinical contrast agent and is applied in the early postmortem phase, no interaction should be expected except for artefacts created from the external CPR. This method is described in detail in Chap. 9.

An overview of the most used PMCTA techniques and the investigations that have been done to date concerning their eventual side effects on other medico-legal examinations can be found in Table 6.2.

Table 6.2 Overview of modern methods

	Technique	Contrast media	Published investigations concerning additional examinations	Remarks
Targeted PMCTA	Oxford method of TCA	Clinical aqueous contrast agent	No	Contrast media applied only locally in the coronary arteries; therefore, no influence on extracardiac exams
	Leicester method of TCA	Clinical aqueous contrast agent mixed with air (negative contrast)	Yes (toxicology, biochemistry, immunology, genetics)	
Whole body PMCTA	MPMCTA	Mixture of medium-viscosity paraffin oil (paraffinum liquidum and oily contrast agent Angiofil®, 6 %)	Yes (toxicology, biochemistry, immunology, genetics microbiology, histology, and fatty embolism)	Most publish technique using a standardized protocol
	PMCTA using aqueous contrast agent ± PEG	Aqueous solutions eventually mixed with PEG	No	Techniques show similarities but vary in perfusion parameters and applied liquids
	PMCTA using CPR	Clinical aqueous contrast agent	No	Applied directly after in-hospital death on the clinical CT table

Key: *PMCTA* postmortem CT angiography, *TCA* targeted coronary angiography, *MPMCTA* multiphase postmortem CT angiography, *PEG* polyethylene glycol

Conclusion

The performance of PMA remains a challenge. Today's modern forensic imaging uses PMCT as a technique to visualize injected vessels because this method is increasingly implemented in medico-legal institutes and allows a rapid examination of the body with high spatial resolution and the possibility of performing reconstructions in two and three dimensions. To overcome the different challenges of performing PMCTA, various approaches are used today that differ from classic methods, which were mostly performed on single organs. Today's PMCTA methods are oriented to clinical radiology and aim to allow a minimally invasive approach for investigating the vascular system. In addition to the challenge of developing techniques for performing PMCTA, the radiologic interpretation is challenging because it presents many pitfalls and possible artefacts that have to be considered. Therefore, standardized techniques including guidelines for interpretation are needed for use in medico-legal cases. Because any application of contrast agent in a body may have side effects on other medico-legal examinations, the necessity of these studies must be taken into account, and guidelines should be established concerning sampling before the contrast agent application and performance of the examinations after PMCTA.

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