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Postmortem CT Angiography in Fetuses and Children: Development, Systematic Review, and Forensic Insights from Pediatric Cases

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Département de santé et médecine
communautaires

CURML Centre universitaire romand
de médecine légale

Thèse préparée sous la direction du Prof. Dr Silke Grabherr et du Prof. Dr Emmanuel Coche

Postmortem CT Angiography in Fetuses and Children: Development, Systematic Review, and Forensic Insights from Pediatric Cases

Thèse
présentée à la Faculté de Médecine
de l'Université de Genève
pour obtenir le de grade de « Docteur en Sciences Biomédicales – Mention
médecine légale »

par
Jessica VANHAEBOST

de
Bruxelles, Belgique

Thèse n° 8

Genève

2025



**UNIVERSITÉ
DE GENÈVE**
FACULTÉ DE MÉDECINE

DOCTORAT EN SCIENCES BIOMEDICALE MENTION MEDECINE LEGALE

Thèse de :

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Originnaire de Bruxelles/Belgique

Intitulée :

Postmortem CT Angiography in Fetuses and Children: Development, Systematic Review, and Forensic Insights from Pediatric Cases

La Faculté de médecine, sur les préavis du Comité directeur du PhD, autorise l'impression de la présente thèse, sans prétendre par-là émettre d'opinion sur les propositions qui y sont énoncées.

Genève, le 20.02.2026

Thèse n° 8

Antoine Geissbühler
Doyen

N.B. - La thèse doit porter la déclaration précédente et remplir les conditions énumérées dans les "Informations relatives à la présentation des thèses de doctorat à l'Université de Genève".

The dead teach the living – Hic mors gaudet succurrere vitae

What cannot be visualized cannot be understood – Anonymous

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Scientific communications

Publications

- **Jessica Vanhaebost**, Nicolas Michoux, Xavier de Spiegeleire, Silke Grabherr, Emmanuel Coche, Development of a technique for postmortem CT angiography of fetuses with a lipophilic contrast agent, *Forensic Imaging*, Volume 37, **2024**, 200593, ISSN 2666-2256, <https://doi.org/10.1016/j.fri.2024.200593>.
- **Vanhaebost J**, Scholzen T, Coche E, Grabherr S. Postmortem CT angiography of fetuses, infants and children up to 12 years old a systematic review and conceptual decision tree. *Int J Legal Med*. Volume 139, pages 2829-2836, **2025** Jul 4. doi: 10.1007/s00414-025-03556-5. PMID: 40613835.

Submitted articles

Jessica Vanhaebost, Bastien Trächsel, Florian T. Fischer, Silke Grabherr, Gina Maria Bruch, Postmortem CT angiography in infants and young children (PedPMCTA): Technical feasibility and emerging forensic insights from a 30-case study, submitted on 15 October **2025** in *Int J Legal Med*.

Oral communications

08/04/2022: TWGPAM Workshop Munich 2022 April 7th/ 8th: Fetal postmortem angiography

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Other publications and communications during the study period not directly related to the thesis topic

Kerschen A., Schmit G., De Boosere E., Palmiere C. and **Vanhaebost J.**, Black esophagus as an autopsy discovery: a challenging interpretation. Egyptian Journal of Forensic Sciences (2020) 10:4. Review.

Schmit G, Lelotte J, **Vanhaebost J.**, Horsmans Y, Van Bockstal M, Baldin P. The Liver in COVID-19-Related Death: Protagonist or Innocent Bystander? Pathobiology. 2020 Oct 27:1-7. doi: 10.1159/000512008.

Kerschen, A., Aydin, S., Marbaix, E., Gérin, V., Haufroid, V., Daudon, M., & **Vanhaebost, J.** (2022). Misdiagnosis of a primary vaginal stone leading to a suspicion of sexual assault in a heavily disabled woman. Journal of the Canadian Society of Forensic Science, 55(4), 206-212. doi:10.1080/00085030.2022.2051326

Jashari R, Van Esbroeck M, **Vanhaebost J.**, Micalessi I, Kerschen A, Mastrobuoni S. The risk of transmission of the novel coronavirus (SARS-CoV-2) with human heart valve transplantation: evaluation of cardio-vascular tissues from two consecutive heart donors with asymptomatic COVID-19. Cell Tissue Bank. 2021 Mar 9:1–10. doi: 10.1007/s10561-021-09913-z. PMID: 33687611; PMCID: PMC7941121.

Breugelmans L, Di Fazio V, Boland A, Wille S, Samyn N, Schmit G, **Vanhaebost J.** Increase of pregabalin misuse among forensic toxicological analysis in Belgium, 61nd TIAFT Annual Meeting, St. Gallen, September 2024

Completed course

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Internship

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Abstract

This thesis, entitled *“Postmortem CT Angiography in Fetuses and Children: Development, Systematic Review, and Forensic Insights from Pediatric Cases,”* explores the application of postmortem imaging techniques, with a particular focus on Postmortem CT Angiography (PMCTA), in the investigation of fetal and pediatric deaths. While cross-sectional imaging has progressively emerged as a complement, and in some contexts an alternative, to conventional autopsy in forensic pathology, its use in fetuses and young children remains an evolving field, facing both technical and interpretative challenges. The objective of this work was to develop and optimize PMCTA protocols tailored to the anatomical and physiological specificities of these vulnerable populations, while taking into account the ethical considerations inherent to postmortem imaging in minors.

The thesis is structured around three original articles that respectively introduce, synthesize and evaluate dedicated PMCTA methods. Language editing assistance was provided using ChatGPT (OpenAI, 2024–2025); however, the author remains solely responsible for the scientific content and conclusions.

The first article, *“Development of a technique for postmortem CT angiography of fetuses with a lipophilic contrast agent”* describes the design and validation of an innovative fetal PMCTA (FPMCTA) technique. Thanks to a lipophilic contrast agent, better suited to postmortem vascular changes, this protocol achieved superior vascular opacification compared to previous water-soluble approaches (hydrophilic contrast medium used in the living). It provided reliable visualization of major fetal vessels and offered a reproducible method for integrating angiography into the postmortem investigation of fetal deaths.

The second article, *Postmortem CT angiography of fetuses, infants and children up to 12 years old: a systematic review and conceptual decision tree*” presents a comprehensive synthesis of the existing literature on fetal and pediatric PMCTA. Beyond highlighting the current lack of standardization in clinical practice, the review led to the proposal of a decision tree designed to guide protocol selection based on age, weight, vascular accessibility and diagnostic objectives. This practical framework serves as a reference for clinicians and forensic practitioners.

The third article, *“Postmortem CT angiography in infants and young children (PedPMCTA): Technical feasibility and emerging forensic insights from a 30-case study”* empirically evaluates a weight-adapted lipophilic PMCTA protocol in 30 individuals aged 1 day to 3.6 years. Feasibility was confirmed across the entire pediatric age range studied, with consistently high arterial and venous opacification and reliable vascular access routes, particularly via the femoral approach. Arteriovenous shunts were observed in several cases and key forensic structures, including the superior sagittal sinus, bridging veins and ocular vessels, were successfully visualized in a substantial proportion of examinations. Although artifacts such as contrast extravasation and air bubbles were encountered, they did not hinder diagnostic interpretation.

Collectively, these findings demonstrate that pediatric PMCTA, when based on appropriately adapted lipophilic protocols, overcomes many limitations associated with postmortem vascular alterations and provides valuable diagnostic information, particularly for vascular injuries that are difficult to identify macroscopically, such as those encountered in non-accidental head trauma or unexplained pediatric deaths. While not intended to replace autopsy, PMCTA emerges as a powerful complementary tool that enhances the diagnostic yield of forensic investigations and may, in specific consent-based or clinical settings, serve as a less invasive alternative. This work therefore paves the way for future standardization of protocols and wider integration of PMCTA into forensic and clinical practice, with major implications for the study of fetal and pediatric mortality.

Language refinement of this manuscript was performed using ChatGPT solely for English clarity enhancement; no contribution was made to the generation of scientific content or interpretation.

Résumé

Cette thèse, intitulée « *CT-angiographie postmortem chez le fœtus et l'enfant : développement, revue systématique et apports médico-légaux à partir de cas pédiatriques* », explore l'application des techniques d'imagerie postmortem, en particulier l'Angio-CT postmortem (PMCTA), dans l'investigation des décès fœtaux et pédiatriques. Alors que l'imagerie en coupe s'est progressivement imposée comme complément, voire, dans certains contextes, comme alternative, à l'autopsie conventionnelle en pathologie médico-légale, son utilisation chez le fœtus et le jeune enfant reste un domaine émergent, marqué par des défis à la fois techniques, anatomiques et interprétatifs. L'objectif de ce travail était de développer et d'optimiser des protocoles de PMCTA adaptés aux spécificités de ces populations vulnérables, tout en tenant compte des considérations éthiques propres à l'imagerie postmortem des mineurs.

La thèse repose sur trois articles originaux qui développent, synthétisent et évaluent des méthodes dédiées. Une assistance à la relecture linguistique a été réalisée à l'aide de ChatGPT (OpenAI, 2024–2025) ; cependant, l'auteure demeure seule responsable du contenu scientifique et des conclusions.

Le premier article, consacré au « *Développement d'une technique de CT-angiographie postmortem du fœtus avec un agent de contraste lipophile* », décrit la mise au point et la validation d'un protocole innovant permettant, grâce à un agent lipophile mieux adapté aux modifications vasculaires postmortem, d'obtenir une opacification vasculaire supérieure à celle des produits de contraste solubles dans l'eau utilisés chez les patients vivants (produits de contraste iodés hydrophiles). Ce protocole s'est révélé reproductible et fiable pour la visualisation des principaux vaisseaux fœtaux, offrant ainsi une base solide pour l'intégration de l'angiographie dans l'investigation des décès fœtaux.

Le deuxième article, intitulé « *CT-angiographie postmortem des fœtus, nourrissons et enfants jusqu'à 12 ans : revue systématique et arbre décisionnel conceptuel* », propose une synthèse structurée de la littérature existante sur la PMCTA pédiatrique. Au-delà du constat de la faible standardisation des pratiques, cette revue a abouti à la proposition d'un arbre décisionnel guidant le choix des protocoles selon l'âge, le poids, l'accessibilité vasculaire ou encore les objectifs diagnostiques. Ce cadre pratique constitue un outil de référence pour les praticiens.

Le troisième article, « *CT-angiographie postmortem chez le nourrisson et le jeune enfant (PedPMCTA) : faisabilité technique et apports médico-légaux à partir d'une série de 30 cas* », a évalué empiriquement un protocole lipophile adapté au poids chez des sujets âgés de 1 jour à 3,6 ans. La faisabilité a été confirmée sur l'ensemble de la fourchette d'âge pédiatrique étudiée, avec une opacification artérielle et veineuse constante et des voies d'accès vasculaires fiables, en particulier la voie fémorale. Des shunts artérioveineux ont été observés dans certains cas, tandis que des structures cruciales en médecine légale, telles que le sinus sagittal supérieur, les veines ponts ou les vaisseaux oculaires, ont pu être visualisées dans une proportion substantielle des examens. La présence d'artefacts, tels que l'extravasation ou les bulles d'air, n'a pas compromis l'interprétation diagnostique.

Dans l'ensemble, les résultats de ces travaux démontrent que la PMCTA pédiatrique, lorsqu'elle repose sur des protocoles lipophiles adaptés, permet de surmonter nombre de limitations liées aux altérations vasculaires postmortem et fournit des informations diagnostiques précieuses, notamment dans l'identification de lésions vasculaires difficiles à mettre en évidence macroscopiquement, comme dans les traumatismes crâniens non accidentels ou les décès inexpliqués. Sans prétendre remplacer l'autopsie, la PMCTA s'affirme comme un outil complémentaire puissant, susceptible d'améliorer le rendement diagnostique des investigations médico-légales et, dans certains contextes cliniques ou reposant sur le consentement, de constituer une alternative moins invasive. Ce travail ouvre ainsi la voie à une future standardisation des protocoles et à une intégration élargie de la PMCTA dans la pratique médico-légale et clinique, avec des implications majeures pour la compréhension et l'analyse des décès fœtaux et pédiatriques.

Enfin, l'anglais scientifique de ce manuscrit a été affiné, exclusivement pour des ajustements linguistiques, à l'aide de ChatGPT ; aucune contribution à la création du contenu ou à l'interprétation scientifique n'a été réalisée par cet outil.

Abbreviations

AI : Artificial Intelligence

CA : Contrast Agent

CT : Computed Tomography

ESPR : European Society of Pediatric Radiology

FPMCTA : Fetal PostMortem Computed Tomography Angiography

ISFRI : International Society of Forensic Radiology and Imaging

MDCT : Multi-Detector Computed Tomography

MRI : Magnetic Resonance Imaging

NAHT : Non Accidental Head Trauma

MPMCTA : Multiphase PostMortem Computed Tomography Angiography

PedPMCTA : Pediatric PostMortem Computed Tomography Angiography

PEG : PolyEthylene Glycol

PM : PostMortem

PMFMRI : PostMortem fetal MRI

PMCTA : PostMortem Computed Tomography Angiography

PMI : PostMortem Interval

PMMR : PostMortem Magnetic Resonance imaging

PMUS : PostMortem Ultrasonography

TWGPAM : Technical Working Group Post Mortem Angiography Methods

Outline

This thesis investigates the development and application of PMCTA in fetuses and children, a field that remains underexplored due to significant anatomical, technical, and ethical challenges. The manuscript is structured around three original scientific articles, each addressing a distinct but complementary aspect of this imaging technique, with the overarching aim of contributing to a more standardized and effective use of PMCTA in pediatric forensic practice.

The thesis begins with a general introduction that provides an overview of postmortem imaging in fetal and pediatric populations. It outlines the current state of the art, identifies the technical and interpretative challenges associated with PMCTA in small bodies, and presents the rationale and objectives of the research.

Following the introduction, a methodological contribution details the candidate's specific involvement in each study, including protocol design, data collection and analysis, image interpretation, and manuscript preparation. Ethical considerations related to the use of postmortem specimens and clinical data are also addressed.

The first article reports on the development of a FPMCTA protocol using a lipophilic contrast agent (CA). It introduces a practical two-phase injection method, demonstrates feasibility in a series of 25 fetuses, and evaluates image interpretability through a structured vascular scoring system.

The second article presents a systematic review of the literature on PMCTA in fetuses, infants, and children under 12 years of age. It identifies major methodological variations, highlights diagnostic applications and synthesizes current practices into a conceptual decision tree that can help guide age-appropriate case management.

The third article describes a prospective case series of 30 pedPMCTA procedures, assessing technical feasibility, vascular opacification scores, and emerging diagnostic insights. Special attention is given to spontaneous arteriovenous shunting, practical thresholds for image interpretation and the visualization of forensic structures such as bridging veins, ocular vessels and coronary arteries.

The thesis concludes with a comprehensive discussion integrating the findings of the three studies. It emphasizes the methodological contributions and forensic implications of fetal and pediatric PMCTA, acknowledges current limitations and outlines perspectives for future

research, particularly regarding protocol optimization, standardization and multicenter validation.

A complete bibliography and appendices provide supporting material for the studies presented.

Introduction

Over the past decades, pathology has witnessed a growing demand for less invasive, more acceptable alternatives to traditional autopsy, particularly in pediatric and perinatal cases. Postmortem imaging has emerged in response to this need, offering tools that are not only diagnostically useful but also socially and ethically more acceptable [1-3]. This thesis explores how PMCTA, an advanced imaging technique, can be adapted to the specific technical and interpretative demands of fetal and pediatric pathological cases, and how it may serve as a viable tool in forensic investigations.

Overview of Postmortem Imaging

Postmortem imaging, as a subspecialty of (forensic) pathology and radiology, has undergone rapid development over the past two decades [3-7]. Although it has evolved in parallel with clinical imaging, its objectives, workflows and interpretive criteria differ fundamentally from those applied in living patients [8]. Current practice relies primarily on multidetector computed tomography (MDCT) and high-field MRI (Magnetic Resonance Imaging) (3 Tesla or higher), which have demonstrated utility across a wide range of forensic and pathological investigations [9-11]. However, the degree of validation varies considerably between adult and pediatric populations, with the latter remaining comparatively understudied.

While traditional autopsy remains the diagnostic gold standard for postmortem examination, imaging techniques are increasingly used as non-invasive, minimally invasive alternatives, or complementary tools to conventional autopsy [12]. Numerous studies have demonstrated the utility of PMCT (PostMortem Computed Tomography) in visualizing fractures, foreign bodies, gas distribution and gross anatomical structures [13]. However, the limitations of PMCT are well documented [14,15]. Without vascular contrast, PMCT fails to visualize vascular pathologies such as thrombosis, dissections, or occlusions and offers limited sensitivity for soft tissue or cardiac abnormalities. These shortcomings highlight the need for contrast-enhanced techniques capable of reliably assessing vascular integrity in postmortem settings.

To overcome these shortcomings, PMCTA was developed in the early 2000s [16-18]. By introducing CA into the vascular system under controlled perfusion, PMCTA enables detailed

evaluation of the arterial and venous trees and improves detection of vascular lesions, hemorrhages, perfusion defects and cardiac pathology [19-22]. Validation studies in adult populations have demonstrated its value, particularly in cardiovascular, traumatic and iatrogenic deaths, where it provides information comparable to, and sometimes superior to, conventional autopsy [23-25]. Thus, although PMCTA does not replace autopsy, it now stands as a powerful complementary modality with growing acceptance in routine casework.

Beyond CT-based techniques, PMMR (PostMortem Magnetic Resonance imaging) has also been explored as an alternative or complementary modality within the postmortem imaging spectrum. Introduced in the early 1990s, PMMR was initially investigated as a potential adjunct or alternative to conventional autopsy, particularly in cases where consent was limited or autopsy was declined [26]. Early pilot studies demonstrated its ability to identify major cranial, thoracic, and abdominal abnormalities, while conventional autopsy remained superior for subtle or microscopic lesions. Although its clinical adoption has been more limited than PMCT [27], mainly due to scanner availability and technical complexity, PMMR remains a powerful tool for detecting otherwise occult findings, particularly in soft tissues and the central nervous system.

Nevertheless, the mere diversification of imaging modalities has not been sufficient to secure widespread adoption; sustained institutional support and structured coordination have been essential in transforming experimental tools into accepted forensic practice. This increasing professionalization has been accompanied by sustained efforts from organizations such as the International Society of Forensic Radiology and Imaging (ISFRI) and the European Society of Pediatric Radiology (ESPR), which have contributed to the development of standards, reporting guidelines and collaborative research frameworks [28]. In this context, future progress will rely not only on technical refinement but also on harmonized implementation strategies. Looking forward, the evolution of postmortem imaging will depend on wider standardization, the integration of developing technologies such as AI-assisted interpretation and the establishment of training pathways that bridge both radiological and pathological expertise.

Fetal and Pediatric postmortem imaging techniques

Postmortem imaging in fetuses, neonates, and young children presents distinct technical, anatomical, and interpretative challenges. These differences arise from body size, developmental physiology, and the fragile condition of the deceased. Unlike adult imaging, pediatric and perinatal postmortem imaging must account for high variability in anatomy and rapid postmortem changes.

The application of postmortem imaging in fetal, perinatal and pediatric settings has gained increasing interest, particularly as an alternative in cases where parents decline invasive procedures. In hospital-based deaths, such as miscarriage, termination of pregnancy or neonatal loss, pediatric postmortem imaging has demonstrated diagnostic value, especially when interpreted in conjunction with clinical history, antenatal imaging and placental examination [10, 29-33].

Within this postmortem context, radiography [34], ultrasound (PMUS) [35], (micro-)CT [36, 37] and PMMR have emerged not only as diagnostic tools but also as ethically acceptable alternatives that respect bodily integrity [33, 38-40]. Rather than being simple technological innovations, these modalities reflect a broader societal shift towards parental autonomy and transparency in postmortem care.

Radiography and arteriography were already evaluated as adjuncts to autopsy in stillborn and neonates as early as 1989 [41], leading to the recommendation of routine X-ray imaging for bone and soft tissue assessment, with arteriography reserved for suspected vascular malformations.

PMUS is similarly employed as a readily accessible modality that can assist autopsy by visualizing internal organs, although cardiothoracic anomalies remain difficult to assess [42, 43]. Comparative studies have shown that PMUS and 1.5 T PMMR achieve more than 85% concordance with final perinatal autopsy diagnoses when image quality allows reliable interpretation [44]. However, the relatively high rate of non-interpretable examinations, particularly for the brain and heart, limit PMUS to a screening role, with PMMR preferred when cardiothoracic anomalies are suspected.

PostMortem fetal MRI (PMFMRI) and PMMR of children therefore warrants further evaluation as access improves and standardized protocols become available. MRI can match conventional autopsy in identifying causes of death, particularly in fetuses, although it is less reliable for detecting infectious lesions in older children, supporting its selective use in combination with targeted PMMR [45]. PMFMRI is increasingly accepted by parents declining autopsy, given its rapid acquisition, permanent archiving and ability to guide targeted tissue sampling while preserving external integrity [46]. Nevertheless, its broader implementation remains limited by scanner availability, the requirement for radiographers and radiologists specifically trained in postmortem imaging and a higher rate of non-diagnostic scans in early gestational fetuses [29]. Even experimental gadolinium-formaldehyde staining has not yet yielded substantial contrast improvement in ≤ 16 week fetuses on 3 T PMMR, highlighting the need for further development and comparison with methods such as micro-CT [47].

Experimental techniques have also been explored in very small specimens, including solvent-based clearing for high-resolution 3D embryo reconstruction and iodine-enhanced micro-CT for improved soft tissue contrast, although the latter remains ineffective in larger fetuses due to insufficient contrast penetration [48].

Nevertheless, MDCT stays an accessible alternative, being cheaper, faster and more widely available in both pathological and forensic settings. It is particularly effective for detecting skeletal trauma, gas-related findings (e.g. putrefaction gas, air embolism, pneumothorax) and gross anatomical injuries [49-53]. However, its limited soft tissue contrast restricts its utility for visceral or subtle pathological changes.

In pediatric and perinatal cases, PMCTA offers a promising extension of these benefits. It is particularly relevant when invasive autopsy is limited or declined, as it can provide insights into congenital malformations, perinatal complications or trauma-related vascular injuries [9, 30, 54-57]. Nevertheless, its implementation in children remains technically demanding and has not yet been standardized, making it an emerging rather than routine practice [58].

Despite these advances, PMCTA remains insufficiently documented in fetal and pediatric populations. Existing approaches are heterogeneous in methodology, timing and injection protocols, hindering reproducibility and comparison across centers. Yet, its ability to provide

detailed assessment of vascular structures and hemorrhagic sources positions it as a promising complementary tool to conventional autopsy. Establishing standardized protocols and shared reference databases through international collaboration will be essential to enable reliable interpretation, particularly in children, where normal postmortem vascular patterns are age-dependent and poorly defined.

Challenges in Pediatric and Fetal PMCTA

From a technical standpoint, small body size and low vascular volume complicate both image acquisition and contrast perfusion. In MDCT, reduced attenuation differences in soft tissues limit contrast resolution [59]. Moreover, decomposition processes, particularly autolysis and maceration, progress more rapidly in infants and fetuses, degrading anatomical integrity and increasing the risk of artifacts. Intrauterine deaths often present with severe maceration, making the distinction between pathology and postmortem changes difficult. Standard radiological protocols designed for adults often require significant adaptation in pediatric cases.

The adaptation of PMCTA to pediatric and fetal cases adds another layer of complexity. In adults, PMCTA relies on stable vascular structures, large-caliber vessels and predictable hemodynamic behavior. In infants and fetuses, the vascular system is underdeveloped, fragile and sometimes difficult to identify due to anatomical variations or postmortem collapse. The small size of arteries and veins requires the use of extremely fine catheters and precise injection techniques, often under real-time image guidance such as ultrasound. Achieving a homogeneous vascular opacification without inducing extravasation is technically challenging and requires meticulous control. In fetuses, traditional vascular access is often not feasible, prompting the development of alternative perfusion strategies, such as cardiac, umbilical or even percutaneous approaches using modified CA and low-pressure systems [60, 61].

Moreover, the choice of carrier substance used in PMCTA may significantly impact postmortem tissue and vascular characteristics, thus affecting image interpretation. Bruch et al. compared the effects of a lipophilic oil-based mixture and a hydrophilic polyethylene glycol (PEG 200) carrier, and found markedly different postmortem changes: specimens in PEG solidified rapidly, whereas specimens in oil exhibited earlier and more pronounced

putrefactive alterations [62]. However, the study's in-vitro design did not permit definitive extrapolation of these effects to full-body angiography in forensic cases. Therefore, awareness of such potential artefactual changes remains essential when selecting a PMCTA protocol.

Interpretation of pediatric postmortem images also requires specialized knowledge of developmental anatomy and postmortem physiology. Structures such as the thymus, non-aerated lungs, patent ductus arteriosus or elements of persistent fetal circulation may mimic pathological changes if not correctly identified. Intraosseous hematopoiesis, incomplete ossification, and organ immaturity may further blur the diagnostic line between normal variants and disease particularly in the context of suspected trauma or congenital malformations [63]. The absence of life-sustaining physiological parameters (e.g., blood flow, oxygenation) also means that imaging findings must be interpreted in a fundamentally different context than in the living patient.

Finally, despite increasing interest in pediatric and fetal postmortem imaging, the evidence base remains limited. Most existing studies are small-scale, retrospective or methodologically heterogeneous. Few protocols have been standardized across institutions, and comparative validation studies between PMCTA and autopsy findings in children are scarce. This lack of multicenter data makes it difficult to establish normative reference values or to generalize conclusions across age groups and imaging protocols.

While much of the current literature addresses technical feasibility and diagnostic performance, it is equally important to acknowledge the societal drivers that have fueled the adoption of postmortem imaging in perinatal and pediatric settings [3].

Addressing these challenges requires interdisciplinary collaboration among forensic pathologists, pediatric radiologists, imaging physicists and technologists. Progress will depend on the development of optimized protocols, age- and weight-adapted contrast strategies and standardized interpretive frameworks to improve diagnostic accuracy and reproducibility in this technically demanding field.

Ethical and Methodological Considerations

Methodological Considerations

Postmortem imaging studies, particularly those involving pediatric and fetal cases, present unique methodological challenges. Unlike prospective clinical research, postmortem studies often rely on retrospective analyses or opportunistic data collection, which leads to heterogeneity in protocols, equipment and inclusion criteria. This issue is especially pronounced in pediatric cohorts, where case numbers are small and standardization remains limited [56, 64-67].

Most published studies are single-center and retrospective, restricting the generalizability of findings. Technical differences, including scan parameters, contrast injection protocols and postmortem intervals, further affect reproducibility. Recent initiatives have therefore emphasized the importance of multicenter collaboration and shared databases to establish reference values, particularly in children where age-dependent anatomical variation is considerable.

Methodological rigor requires detailed reporting of inclusion criteria, imaging protocols and the comparison standards used, whether for autopsy, histology or clinical diagnosis. The ISFRI guidelines provide a useful framework for quality assurance in forensic radiology and encourage methodological transparency across institutions [28].

Ethical and Regulatory Aspects

Research involving postmortem imaging in children and fetuses must navigate complex ethical and regulatory frameworks [68]. Although the deceased are not considered legal subjects of consent, ethical review by institutional committees is required in most jurisdictions. This applies even to anonymized or retrospective studies.

In hospital-based, non-forensic settings, parental refusal of conventional autopsy has led to growing interest in imaging alternatives. While imaging may be more acceptable to families, especially when it preserves the body's integrity, even minimally invasive techniques such as PMCTA typically require specific institutional approval and, in some cases, parental consent.

Professional organizations such as the Royal College of Pathologists and the ESPR have issued guidance promoting respectful communication and informed consent in these contexts [28].

Data protection and anonymization are central to ethical compliance. Imaging data used for research must be fully anonymized, and care should be taken to avoid indirect identification, particularly in rare or recognizable cases. No patient-identifiable information was included in the datasets used for the studies described in this thesis.

Each component of the present research complied with ethical requirements. The fetal PMCTA study used anonymized specimens donated for research and education, under institutional approval. The pedPMCTA series consisted of retrospective analysis of legally authorized postmortem examinations conducted under standard institutional protocols. The systematic review was based exclusively on data already published in peer-reviewed literature and required no ethical approval.

Research Objectives and Thesis Overview

The overarching aim of this thesis was to contribute to the development, validation and critical assessment of PMCTA in fetal and pediatric populations. It addressed the technical and interpretative challenges of vascular imaging in small and immature bodies and seeks to promote standardization and ethically sound implementation in forensic and clinical settings.

Three complementary research axes were explored:

- Development of a tailored fetal PMCTA protocol using a two-phase injection technique with a lipophilic CA. This method was designed to maximize vascular opacification while minimizing technical complications. Its feasibility and diagnostic yield were evaluated in a prospective series of 25 fetuses of varying gestational ages.
- A systematic review of the literature on PMCTA in fetuses, infants and children up to 12 years of age. This work synthesized current evidence, highlighted methodological heterogeneity and proposed a conceptual decision tree to guide age-appropriate protocol selection.
- A prospective analysis of 30 pediatric PMCTA cases, assessing technical feasibility, vascular opacification quality and emerging forensic insights. Particular attention was

given to spontaneous arteriovenous shunting, diagnostic thresholds and interpretation challenges.

These three axes are not only complementary but also interdependent. The development of a fetal protocol provided the technical foundation for applying PMCTA to real pediatric cases, while the systematic review contextualized both approaches within the broader literature. Together, they form a coherent body of work aimed at advancing both methodology and interpretive reliability in ped PMCTA.

The thesis is organized as follows:

- A methodological contribution section outlines the candidate's involvement in each study and discusses ethical considerations specific to postmortem imaging of minors.
- This is followed by the three original research articles, presented in their published or submitted form.
- A general discussion synthesizes the findings, identifies limitations and outlines perspectives for future research.
- The manuscript concludes with annexes and a comprehensive reference list.

Beyond academic significance, this work also aims to provide practical impact. By supporting less invasive approaches to fetal and pediatric autopsy, it may improve the acceptance of postmortem investigations among bereaved families and clinicians. At the same time, it seeks to equip medicolegal stakeholders with more precise tools for determining cause of death in vulnerable populations.

Through the development of original protocols, the synthesis of existing evidence and the practical application to real pediatric cases, this thesis helps establish fetal and pediatric PMCTA as a feasible, interpretable and ethically responsible tool in postmortem investigations.

Articles

Overall methodological contribution of the Thesis

This doctoral thesis is based on three original scientific articles, each addressing a specific aspect of PMCTA in fetuses and children. My contribution to this thesis was multidimensional and covered several key methodological aspects throughout the research process. I played an active role in coordinating and contributing to all stages of conceptualization, development, analysis, and drafting of the scientific articles. My contribution is detailed below for each article.

Conceptualization and Development of the Methodology:

I was involved in conceptualizing the various imaging methods used in this thesis, particularly in developing FPMCTA technique with a lipophilic CA. My work consisted of defining the methodological objectives, selecting the appropriate imaging technologies and adapting protocols for each group of cases (fetuses, infants, and children).

Study Design and Investigation:

I was actively engaged in designing the experimental protocols for data collection and in selecting the methods for analyzing the results. This included evaluating post-mortem imaging techniques and analyzing the data obtained from different types of cases, whether fetal, infant or postpartum placental. My role was essential in preparing the cases, acquiring the images and conducting preliminary data analysis.

Formal Analysis and Data Curation:

I led the formal analysis of the data obtained from CT scans and post-mortem angiographic images. This involved processing, organizing and interpreting the results aided by a board-certified radiologist while ensuring their quality and consistency. I was also responsible for data curation, which included managing the data sets, validating them and preparing the data for manuscript writing.

Writing the Articles:

As the primary author, I wrote the initial drafts of each article, developing the methodology, incorporating our findings and presenting the analyses. I also coordinated the revision and editing of the articles, ensuring that the structure and clarity of the text adhered to scientific standards and research objectives. This task involved close collaboration with my co-authors and supervisors to integrate their feedback and enhance the sections of each article.

Review, Analysis, and Editing:

As corresponding author of the three articles, after the initial drafting of the articles, I participated in their revision and formal editing, ensuring that the methods, results, and conclusions were clearly presented and understandable to the reader. I also took charge of the formal review of the manuscripts in collaboration with my co-authors, making adjustments based on the reviewers' comments and strengthening the presentation of the data.

Collaboration with Co-Authors:

In collaboration with my co-authors, I played a key role in integrating various perspectives and methodological expertise.

Statement on Artificial Intelligence (AI) Assistance :

ChatGPT (OpenAI, 2024-2025) was used solely for academic English language refinement. The conception, analysis and interpretation of the content remain entirely the author's own work.

Article 1 - Development of a technique for postmortem CT angiography of fetuses with a lipophilic contrast agent

Vanhaebost J, Michoux N, de Spiegeleire X, Grabherr S, Coche E. Development of a technique for postmortem CT angiography of fetuses with a lipophilic contrast agent. Forensic Imaging. 2024;37:200593.

Methodological contribution

I initiated this research project to explore the feasibility of fetal PMCTA using a lipophilic CA. I developed the injection protocol, performed or supervised the catheterizations and coordinated the imaging acquisitions. I also designed the scoring system for vascular opacification and participated in all stages of image analysis together with a radiologist. I conducted the statistical analysis, interpreted the findings and wrote the manuscript while managing revisions with the co-authors.

Nicolas Michoux primarily contributed to the statistical analysis. He brought essential expertise in data processing and the development of analytical methods.

Xavier de Spiegeleire was instrumental in visualizing the results, contributing to the interpretation of the visual data obtained and optimizing the analytical methods. He was also actively involved in the conceptualization of the studies and in the validation of the findings.

Silke Grabherr supervised the research, ensuring that the methodologies used adhered to clinical and ethical standards. She played a pivotal role in validating the methods and directing the project, while also reviewing the writing to ensure scientific rigor.

Emmanuel Coche supervised the validation of the methods and results, providing his expertise in radiology and visualization. He also provided resources for data collection and actively participated in reviewing and editing the articles.

Thus, my methodological contribution was crucial at each stage of the project, from conceptualization to finalizing the articles. This interdisciplinary collaboration allowed for the development of innovative methods and ensured a rigorous and scientific approach to pedPMCTA and FPMCTA.



Development of a technique for postmortem CT angiography of fetuses with a lipophilic contrast agent

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ABSTRACT

Background and objectives: Postmortem examinations of fetuses play a crucial role in confirming abnormalities, especially vascular and cardiac malformations leading to fetal demise. This study aims at developing and assessing a method for acquiring Post-Mortem CT-Angiography (PMCTA) with the injection of a lipophilic contrast agent (CA) to better visualize the great vessels of the trunk and head.

Materials and methods: 25 human fetuses (gestational age at death between 106 days and 28 weeks) were included. Examinations were performed using a dual-energy Multidetector Computed Tomography (MDCT) scanner. Three imaging sequences were acquired, before CA injection, after injection of 7 mL of CA through umbilical artery (arterial phase), and after an injection of 15 mL of CA through umbilical vein (venous phase). CA-induced vascular opacification was scored per-vessel in both phases as follows: 0 = none, 1 = partial, 2 = complete. Total opacification was defined as the sum of the per-vessel opacification scores.

Results: In 23/25 subjects, CA injection into the umbilical vessels was feasible manually using flexible catheters. After the first injection, at least a partial opacification of the arterial network was achieved in 15/23 (65%) subjects. After the second injection, a complete opacification of the venous network was achieved in 18/23 (78%) subjects. Failures occurred in 10/25 (40%) subjects and were mostly due to the preservation status.

Conclusion: PMCTA performed with a two-phase intra-umbilical injection of a lipophilic CA enabled to visualize the vascular network, even after a significant postmortem interval. This protocol may help in detecting vascular malformations, improving clinical diagnoses and prenatal counselling.

Introduction

Fetopathology involves the examination of fetuses to identify abnormalities, particularly vascular or cardiac malformations that contribute to fetal death. The autopsy remains the gold-standard examination for evaluating the deaths of fetuses and stillborn children, after termination of pregnancy, miscarriage or unexpected intrauterine fetal death [1,2]. The addition of less invasive radiological examinations improve the results obtained during the autopsy by the pediatric

pathologist and gives a better acceptance of the invasive procedure by the parents [3,4].

X-ray examination of stillbirths refines the results of the autopsy by allowing good visualization of the bone skeleton and by allowing better genetic guidance [5,6]. Whole body radiography remains an important diagnostic tool in adjunction to the fetal autopsy [7] but according to other studies, standard X-ray would not add diagnostic value to conventional autopsy of the fetus [8,9]. It is therefore difficult to justify the practice of routine post-mortem radiography in all cases of fetal

Abbreviations: CA, Contrast Agent; CRT, Cinematic Rendering Technique; MDCT, Multidetector computed tomography; MIP, Maximal Intensity Projection; MRI, Magnetic Resonance Imaging; NA, not assessable; PMCTA, Post-Mortem CT angiography; PMI, postmortem interval; VRT, Volume Rendering Technique.

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autopsies. However, it remains essential in cases of intrauterine growth retardation and syndromes involving skeletal abnormalities. Nevertheless, traditional autopsies for fetuses are often challenging due to the small size of most vessels, making dissection laborious or even impossible for some cases.

Postmortem ultrasound was developed because it is more available, even in developing countries, and it is cheaper [10]. The downsides of this method are that the cardiac anatomy is more difficult to evaluate and that artefacts resulting from the presence of air in the cardiac chambers are frequently encountered after fetocide by intracardiac injections. In addition, there are operator-dependent artefacts.

Numerous studies [11–16] have demonstrated the benefit of post-mortem Magnetic Resonance Imaging (MRI) and have also compared it to conventional autopsy. MRI has been proposed as an alternative method of investigation to conventional autopsy in certain cases. This technique allows an accurate determination of congenital developmental malformations of the central nervous system, in particular in cases involving a limited contribution of autopsy analysis such as cases where advanced autolysis can be presumed. However, for fetuses with a gestational age < 20 weeks, MRI performance is poor [10].

MultiDetector Computed Tomography (MDCT) has also garnered attention for postmortem examinations due to its rapid acquisition, availability, and post-processing capabilities [11,17,18]. 3D images of human embryos (smaller specimens than fetuses) by combining solvent-based clearing methods were also proved effective to analyse nervous system development [19]. Diffusible iodine-based contrast-enhanced CT increase the soft-tissue visualization using a micro-CT but appears to be difficult in large fetuses, due to insufficient penetration of Lugol [19]. By injecting a contrast agent (CA) into the vascular system, the vascular lumen becomes visible, and organ parenchyma becomes contrasted, a technique known as Post-Mortem CT Angiography (PMCTA). This approach enables visualization of lethal malformations and provides answers to specific clinical queries raised by requesting clinicians [20–22].

While PMCTA in adults is well-established in the scientific literature [20,21,23–27], its application in pediatric cases, especially in fetuses, remains poorly explored, with only one study conducted on a porcine model [28]. A significant challenge encountered in PMCTA is that the contrast agent used in living patients cannot be utilized during the postmortem period due to extravasation through the vessel's porous wall resulting from postmortem alterations [29,30]. In 2015, Sarada-Quarello et al [31] described the feasibility and interest of performing perinatal postmortem angiography in order to provide additional information to prenatal investigations. More recently, Tumanova et al [32] demonstrated the importance of a radiological examination with angiography for a better diagnosis of vascular pathologies. This technique allows the separate study of arterial and venous vessels and makes it possible to identify both congenital anomalies of the heart and blood vessels, as well as their acquired pathologies in newborns. However, the method used was limited in time (no earlier than 12 h and no later than 48 h after the death of the newborn) due to the postmortem alterations undergone by the organs and tissues, more particularly the changes in the composition and properties of blood and the permeability, elasticity and integrity of vessels.

This study aims at assessing the efficiency of a CT acquisition protocol based on a postmortem injection of a lipophilic contrast agent to visualize the great vessels of the trunk and head. For this purpose, successes and failures in the procedure of injection were documented. Then the frequency of a vascular opacification score (defined as complete, partial or none) was assessed *per-vessel* and *per-phase* (arterial and venous). The presence of imaging artefacts and quality of the radiological examination were also assessed. Finally, the overall feasibility of the protocol and interpretability of images in routine clinical practice was discussed.

Materials and methods

Study population

This study was carried out in accordance with the declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans for medical research purpose local and the protocol was approved by the local Ethics Committee. Anonymised specimens from the Department of Anatomy, donated for scientific research were included. The study prospectively included 25 human fetuses of gestational age at death between 106 days and 28 weeks (Table 1). The postmortem interval (PMI) varied between 5 days and 20 years and their weight varied between 39 g and 1498 g. Selection and exclusion criteria were established before the study: no previous autopsy performed on the fetus prior donation to the department of anatomy, stage of fetal development and residual length of the clamped umbilical cord. The gestational age of one fetus could not be determined because of its too small size and was noted NA (not assessable). Of the 25 fetuses examined, 21/25 (84 %) were frozen, 1/25 (4 %) was preserved in formalin and 3/25 (12%) were fresh (neither frozen nor preserved in formalin). Each fetus presented a state of more or less advanced post-mortem alteration (e.g. skin maceration, gas throughout all anatomic spaces as the result of putrefaction, brain liquefaction).

Data collection

Each fetus was photographed and measured before the MDCT examination. Gestational age (in days) was assessed by obstetricians at the time of fetal death before donation to the anatomy department. The fetus was then measured, weighed, and its cranial perimeter measured, before the radiological examination. The length of the feet was also recorded. For each fetus, the interval between expulsion and examination was also recorded.

Imaging

Imaging examinations were performed on a dual-energy MDCT (Definition As Edge 128, SiemensTM Healthcare, Forchheim, Germany). The fetuses were placed on supine position. A scout-view (256 mm length) was first performed in order to determine the MDCT acquisition. Thereafter, unenhanced spiral acquisition was performed using the following parameters: 128 slices / rotation, collimation of 16 x 0.3 mm, reconstructed with a slice thickness of 0.4 mm, tube voltage: 80 kVp and a fixed tube current time product of 168mAs, field-of-view (FoV) depending of the size of the fetus. The kernel, a reconstruction algorithm used in computed tomography, was standard, and included smooth reconstruction kernel (U30) and sharp reconstruction kernel (U70). Three imaging sequences were performed during the same examination: before contrast agent injection (unenhanced MDCT), during the arterial phase (in order to better visualize the arterial opacification without superimposition with the venous network), and during the venous phase (after the vascular opacification) [33].

Injection of the contrast agent

Once unenhanced MDCT images were acquired, a 10 mL syringe was filled with a contrast medium specifically designed to avoid the problem of postmortem extravasation (AngiofilTM, Fumedica, Switzerland) [29]. This product was mixed with paraffin oil of low viscosity (at 20 °C relative density between 0.810 and 0.875, dynamic viscosity between 25 mPas and 80 mPas and refractive index between 1.462 and 1.472) with a 6 % ratio. In order to avoid a sedimentation phenomenon, the syringe was heavily shaken before proceeding with the injection. Due to the physical properties of the contrast agent mixed with low viscosity paraffin oil, the contrast medium was manually injected at ambient temperature.

Table 1

Study population. Data about the anonymised subject reference (ASR), Gestational age (GA), weight, height, cranial perimeter (CP), sex, postmortem interval (PMI) equivalent to the period between time of expulsion and PMCTA examination, and scoring. When a parameter was not assessable it was noted NA.

ASR	GA (days)	Weight (gr)	Height (cm)	CP (cm)	Sex	PMI (months)	Scoring arterial	Scoring venous	Scoring total	Failures (F) Interpretable (I)	Fresh (V) Frozen (O) Fixed (X)
69/98	168	548.7	32	19.7	M	240	0	6	6	F	O
80/05	NA	868	38	25.5	F	168	0	0	0	F	X
P03/16	106	39.2	13.5	8.5	NA	NA	0	0	0	F	O
P07/16	146	268.4	26.1	16.3	M	23	0	14	14	F	O
P09/16	154	524.5	29.4	19.4	M	21	25	10	35	I	O
F10/16	140	192.8	21.5	14.7	M	20	23	14	37	I	O
F12/16	175	345.8	26.6	19.1	M	20	28	16	44	I	O
F16/16	112	58.4	14	9.7	M	15	2	0	2	F	O
F18/16	151	117.5	23.5	14.4	M	21	0	0	0	F	O
P06/17	149	271.5	26.5	16.7	F	10	3	10	13	F	O
F14/17	159	316.5	27	16.5	F	18	0	10	10	F	O
F15/17	143	371.9	27	17.4	M	8	23	15	38	I	O
F16/17	133	212.6	23.5	14.8	M	7	28	15	43	I	O
F01/18	142	249.3	24.7	15.9	F	1	27	13	40	I	O
P03/18	173	696	32.5	21	M	16	20	4	24	I	O
P05/18	115	80.9	15.3	10.9	M	0.33	23	13	36	I	O
P08/18	154	295	25.4	16.8	M	0.63	1	0	1	F	O
P09/18	154	397.5	29.2	19.3	F	0.63	25	13	38	I	O
F10/18	168	551.8	32	20.5	F	0.2	28	15	43	I	V
F20/18	123	126	19	12	M	42	13	16	29	I	O
36/18	196	1498.1	38.7	29	M	0.16	27	15	42	I	V
F01/19	114	101	18.9	11.8	M	1	0	1	1	F	O
P03/19	170	645	32.4	20.5	F	0.75	13	13	26	I	O
F07/19	175	777.8	33	22.9	F	0.3	28	13	41	I	V
P02/20	156	501	30	19	M	0.5	25	13	38	I	V
Mean	149.00	402.21	26.39	17.29		26.44	14.48	9.56	24.04		
STD	23.06	325.02	6.75	4.79		56.74	12.19	6.08	17.14		
Median	152.50	316.50	25.60	16.80		9.00	20.00	13.00	29.00		

Site and method of injection

A radiographer trained in postmortem imaging [34] was dedicated to this study. When the peripheral vascular access was possible, the injection was always made using the same catheterization device (24GA 0.75IN – 0.7 mm x 19 mm – BD Nexiva™ Diffusico™, Mississauga, Canada) of the arteries and the umbilical vein as described by Sarda-Quarello [35]. The insertion needles were removed in order not to

damage the umbilical vessels and thus avoid injection artefacts. Thereafter, the catheter has been purged of any air bubbles. When catheterization of the umbilical veins was not possible, a direct intracardiac injection was performed under ultrasound guidance. For the arterial phase, a manual injection of 7 mL of the contrast mixture was performed to fill the entire arterial system. In order to avoid extravasation through the other umbilical artery, the umbilical cord was clamped with a tight flexible tie. For the venous phase, an injection of 15 mL was performed

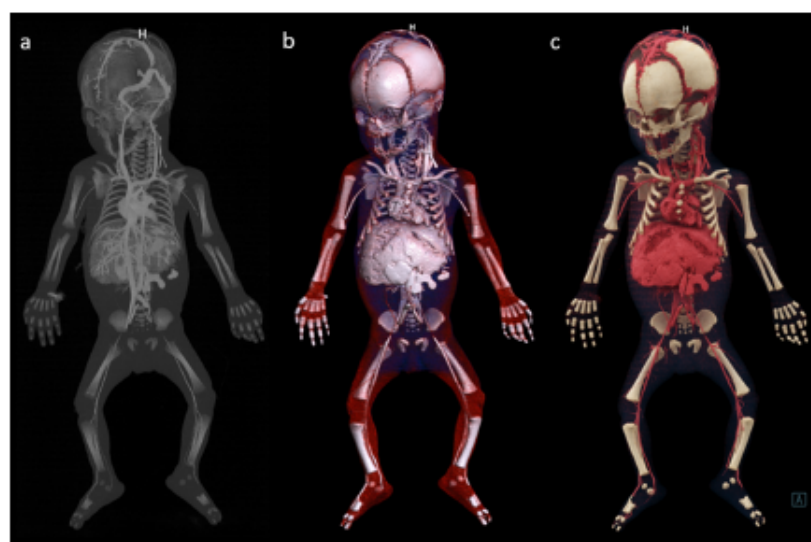


Fig. 1. Post-processing techniques: MIP - Maximal intensity projection (a) – VRT - Volume Rendering Technique (b) and CRT - Cinematic Rendering Technique (c) - anterior view.

to fill the entire venous system. The volume of contrast to be injected was determined empirically by injecting millilitre by millilitre until an optimal opacification of the vascular network was reached.

Image analysis

All MDCT acquisitions were transferred to a syngo.via workstation (SiemensTM Healthcare, Forchheim, Germany – version VB40B). Images were displayed using Maximal Intensity Projection (MIP), Volume Rendering (VRT) and Cinematic Rendering (CRT) Techniques (SiemensTM) on different projections and orthogonal axes (coronal, sagittal and transversal) (Fig. 1). A radiographer, a board-certified forensic pathologist and a board-certified radiologist reviewed images in consensus. The following features were assessed during each review using MIP: (i) the vascular opacification (scored 0 when none, 1 when partial, 2 when complete (Fig. 2) both in the arterial phase and in the venous phase, (ii) the presence of imaging artefacts, and (iii) the overall quality of the radiological examination in taking into consideration the alteration state of the fetus, technique-related artefacts and filling of the vascular system (Table 1). A total opacification score (defined as the sum of the *per-vessel* opacification scores in a given subject) was also studied (Table 2). Noteworthy, this total vascular opacification covered the main body regions including the great vessels of the cervico-cerebral and thoraco-abdominal regions. The vascularity of the limbs was also examined but was not taken into account to assess the opacification (Table 3). An examination was considered as interpretable if the opacification was at least partial.

Statistical analysis

Measures of interest were reported in terms of mean values (median values when the data distributions were non-normal according to the Shapiro-Wilk test) with their associated 95 % Confidence Interval (CI). Frequency of each of the 3 levels of opacification was reported *per-vessel* compartment and *per anatomical region*. Difference of frequency of complete opacification between vascular compartments was studied using a two-sided Exact test. Correlation between foetus' weight and the *per-vessel* opacification score, between PMI and the total opacification score, and between the method of fetal preservation (coded on a ordinal scale as follows: formol = 0, frozen = 1, fresh = 2) and the total opacification score was investigated using Kendall's tau coefficient. Strength of correlation was interpreted as follows: $\tau \geq 0.80$, strong, $0.6 \leq \tau < 0.80$, moderate, $0.40 \leq \tau < 0.60$, weak and $\tau < 0.40$, poor. A *p*-value < 0.05 was regarded as statistically significant for all tests cited above. The Statsdirect statistical software v3.3.5 was used for the analyses.

Results

Population

Clinical and morphological characteristics are given in Table 1.

Unenhanced imaging

Examples of unenhanced MDCT and post-contrast images are shown in Fig. 2. Unenhanced MDCT provided visualization of the fetal skeleton, but no differentiation of the soft tissues.

Procedure of injection

In two cases, the fetuses were too small, and the umbilical cord was mummified; thus, it was not feasible to inject the vessels. An intracardiac injection was performed under ultrasound guidance, but many artefacts appeared, such as filling of the pericardium, mainly resulting from heart slippage and its very small size (Fig. 3). In 23/25 (92 %) cases, an

injection into the umbilical vessels was performed manually using flexible catheters (without the insertion needle).

Correlation between subject's characteristics and opacification score

Results are given in Table 4. A weak positive correlation between weight and opacification score was observed in 3 vessels only: iliac arteries ($\tau = 0.39$, $p = 0.0067$), renal arteries ($\tau = 0.34$, $p = 0.0198$), and descending aorta ($\tau = 0.32$, $p = 0.0293$). A moderate negative correlation between PMI and total opacification score was observed ($\tau = -0.53$, $p = 0.0073$). A moderate positive correlation was also observed between the method of fetal preservation and the total opacification score ($\tau = 0.49$, $p = 0.0007$).

Opacification after the first injection

Even after a long postmortem interval causing an alteration of the fetus (Fig. 4a), after catheterizing an umbilical artery, the aorta was visible following the injection only 1 mL of the mixture (Fig. 4b). After injection of 7 mL, even microscopic arteries such as coronary arteries became visible (Fig. 5). In all succeeded cases, large vessels of the body were visible, such as the pulmonary arteries, the aorta, the renal arteries and the iliac arteries (Fig. 6a). The process also makes visible small vessels, such as the digital arteries of the upper and lower limbs (Fig. 6b). Additionally, vessels of the neck and the head, such as the polygon of Willis and the facial arteries and lingual arteries, were visible (Fig. 6c).

After the first injection phase, the arterial network appeared in 15/25 (60 %) subjects. In addition, it became visible in the limbs of 12/23 (52 %) fetuses.

Among the 10/25 (40 %) subjects considered as failures, 3/10 (30 %) fetuses still presented an interpretable opacification of large vessels such as the pulmonary arteries and the aortic arch. In these three failures, we observed an absence of accessibility to the vessels in the formalized fetus (Fig. 7a), a fragility of the vessels (due to postmortem alteration) and an abdominal extravasation of the contrast agent which no longer allowed the vascular analysis (Fig. 7b). Additionally, when the catheter was not properly purged, air bubbles appeared in the vessels, thereby reducing the opacification score.

Opacification after the second injection

By catheterizing the still ligated umbilical vein, an injection of 15 mL of the mixture was sufficient to opacify the entire venous system. After the second injection phase, the venous network appeared in 18/23 (78 %) subjects (Fig. 6d). Among the 7/25 (28 %) subjects considered as failures, 3 fetuses still presented interpretable opacification of the Aorta duct, jugular veins and the heart. Some injections were only interpretable in a single phase; 3 fetuses had an interpretable opacification score in venous injection, whereas arterial injection did not allow an interpretable opacification of the arterial network.

Proportions of subjects with a complete, partial and no opacification

Results are given in Table 1. For each anatomical region (head, trunk) we observed a complete opacification of the basilar trunk and the renal arteries in the arterial phase and the pulmonary veins in the venous phase in more than 14/23 (61 %) after injection.

Post processing of CT images

MIP reconstruction provided more details on the global opacification but only offered a 2D image (Fig. 1a). Volume Rendering Technique (VRT) offered a 3D image and allowed segmentation of bones and vessels in the different phases of acquisition (Fig. 1b). Cinematic Rendering Technique (CRT) provided additional information on the depth of the

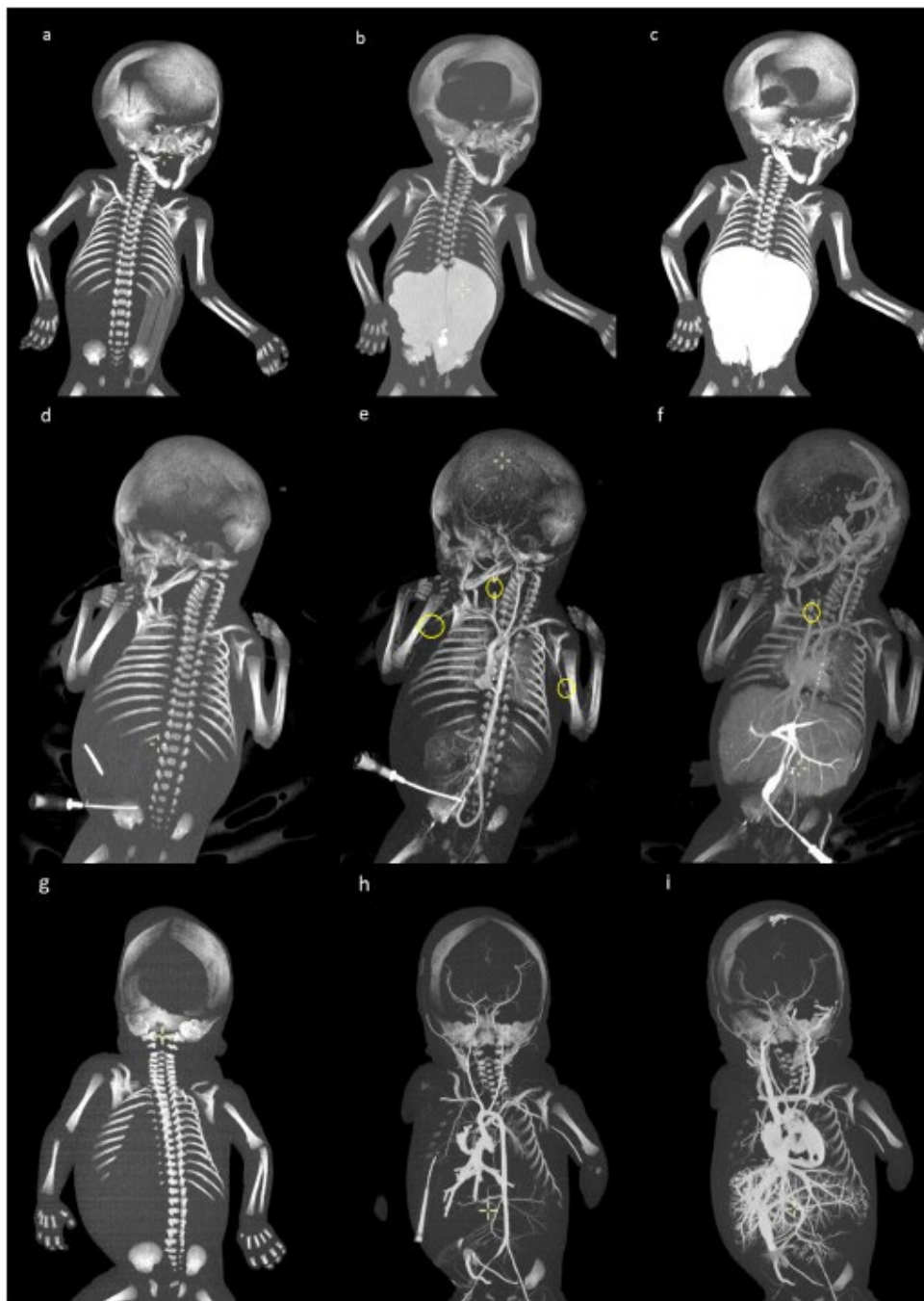


Fig. 2. Fig. 2A (a-b-c) Fetus deceased at 154 days of gestational age. CT angiography image using MIP before injection (a), after arterial opacification (b) and after venous opacification (c) show no opacification, corresponding to a score 0 and artefactual abdominal extravasation. Fig. 2B (e-f-g) Fetus deceased 170 days of gestational age. CT angiography image using MIP before injection (d), after arterial opacification (e) and after venous opacification (f) show no opacification (score 0), partial opacification (score 1 – yellow circle) and complete opacification (score 2). The yellow circles surround the brachial arteries and the right carotid artery (e) as well as the right brachiocephalic trunk (f). Fig. 2C (g-h-i): Fetus deceased 196 days of gestational age. CT angiography image using MIP before injection (g), after arterial opacification (h) and after venous opacification (i) show complete opacification (score 2) of the Willis polygon and hepatic veins.

Table 2

Proportions of subjects with a complete, partial and no opacification after the second injection of CA. Proportions are sorted per-vessel.

Complete opacification		Partial opacification		No opacification	
% of patients	Vessel	% of patients	Vessel	% of patients	Vessel
56	basilar trunk	20	anterior cerebral artery	48	posterior cerebral artery
48	middle cerebral artery	16	posterior cerebral artery	44	basilar trunk
40	anterior cerebral artery	12	middle cerebral artery	40	anterior cerebral artery
36	posterior cerebral artery	0	basilar trunk	40	middle cerebral artery
40	superior longitudinal sinus	12	cerebral veins	48	cerebral veins
52	renal artery	16	renal artery	64	aortic arch descending aorta
48	superior mesenteric artery	16	pulmonary artery	56	aortic arch descending aorta
40	descending aorta	8	iliac artery	52	pulmonary artery
40	iliac artery	8	aortic arch descending aorta	52	iliac artery
32	pulmonary artery	4	superior mesenteric artery	48	superior mesenteric artery
28	aortic arch	4	superior mesenteric artery	32	renal artery
52	pulmonary vein	44	heart	68	arantius
32	hepatic veins	8	arantius	68	inferior vena cava renal veins
28	inferior vena cava renal veins	8	hepatic veins	68	hepatic veins
28	renal veins	4	pulmonary vein	60	hepatic veins
24	heart	4	inferior vena cava renal veins	44	pulmonary vein
24	arantius	4	renal veins	32	heart

tissue and preserved the details of the MIP reconstruction (Fig. 1c).

Discussion

The first results of this study is that MDCT protocol with an intra umbilical injection of a lipophilic contrast agent mixed with paraffin oil allowed the vascular opacification of the fetal vasculature. The opacification of the large vessels of the trunk and head made it possible to obtain an interpretable radiological image in the majority of cases studied (15/23 – 65 %). Most cases showed interpretable opacification of the large vessels after one of the two injections even though the limbs were not, or partially, opacified (9/15). In view of these findings, it was decided that the opacification of the trunk and the cephalic extremity were sufficient to consider that the opacification was interpretable. Analysis of the vascular opacification of the limbs should be considered in future studies.

The second result is that the limitations in time for fetal postmortem CT angiography described in the literature [32] can be compensated for by the use of an oily contrast product, and the technique can therefore be applied in the event of a post-mortem delay of more than 48 hours. This procedure with oily contrast agent was already described for the post-mortem CT angiography of preterm neonate [36] and newborns [37].

The study showed that arterial and venous opacification of the fetal vascular network is achievable by injecting a mixture of 6 % Angiofil™ contrast medium with low viscosity paraffin oil by umbilical vascular

Table 3

Descriptive table of the vascular elements studied in the various anatomical sectors in order to judge the vascular opacification quality. Each anatomical segment reviewed was evaluated by an individual score of 0 (no opacification) - 1 (partial opacification) - 2 (complete opacification). The vascularity of the limbs was also examined but was not taken into account to assess the overall quality opacification. The results are shown in Table 1. All vessels analyzed are abbreviated in brackets and included in the supplementary material.

Region	Arteries	Veins
Cervico-cerebral	Anterior cerebral artery (aca)	Superior longitudinal sinus (sls)
	Middle cerebral artery (mca)	Jugular veins (jv)
	Posterior cerebral artery (pca)	
	Basilar trunk (bt)	
	External carotid artery (eca)	
	Internal carotid artery (ica)	
	Vertebral arteries (va)	
	Common carotid arteries (cca)	
	Aortic arch (aa)	Pulmonary arteries (pa)
	Descending aorta (da)	Heart
Thoracic, abdominal and pelvic	Pulmonary veins (pv)	Inferior vena cava (ivc)
	Superior mesenteric artery (sma)	Hepatic veins (hv)
	Renal arteries (ra)	Renal veins (rv)
	Common iliac arteries (cia)	Arantius ductus (ad)
	Brachial arteries (ba)	Axillary vein (av)
Upper limbs	Radial/ulnar arteries (rda/ua)	Basilic/cubital vein
	Palmar arches (pas)	Palmar arch (pa)
Lower limbs	Femoral arteries (fa)	Femoral vein (fv)
	Tibial arteries (ta)	Tibial veins (tv)
	Plantar arches (plas)	Plantar arch (pla)

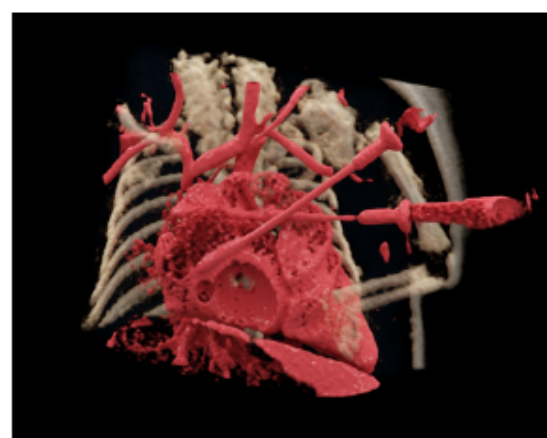


Fig. 3. PMCTA of a deceased fetus at 112 days of gestational age. Injection performed in the cardiac chambers under ultrasound guidance. CT angiography image in the anterior view using Cinematic Rendering Technique (CRT) highlight the visualization of the heart and large vessels but extravasation of the contrast product is also observed. The needles used for the injection are still in place.

access. The arterial injection of 7 ml then the injection of 15ml into the vein was sufficient for the complete opacification of the vascular network. The injection in the venous phase allowed an increase of the opacification score of the vessels, especially at the cardiac and hepatic

Table 4

Correlation between subject's weight and opacification score (a) and postmortem interval and arterial opacification (b).

(A)		
Vessel	p-value	tau
Iliac artery	0.0067	0.39 [0.05; 0.63]
Renal artery	0.0198	0.34 [-0.04; 0.58]
Descending aorta	0.0293	0.32 [-0.06; 0.59]
Anterior cerebral artery	0.0630	-
Middle cerebral artery	0.1304	-
Superior mesenteric artery	0.1424	-
Basilar trunk	0.1814	-
Posterior cerebral artery	0.2801	-
Aortic arch	0.3185	-
Pulmonary artery	0.3922	-
Total artery	0.1411	-

(B)		
Postmortem interval in months	p-value	tau
9.00 [0.72; 20.0]	0.0055	-0.40 [-0.61; -0.08]

Kendall's tau is reported only when the correlation is significantly different from 0

Significance level $p < 0.05$

95 %CI is given into brackets

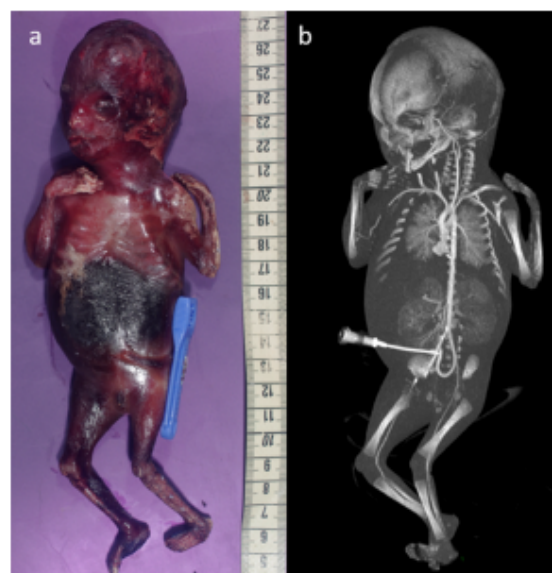


Fig. 4. Fetus deceased at 146 days of gestational age. The postmortem interval between expulsion and examination is 23 months. The stage of postmortem alteration is advanced (a), however CT angiography image in anterior view using Maximal Intensity Projection (MIP) after arterial opacification consecutive to the injection of 1 mL already demonstrates a good opacification of great vessels (b).

level. Nevertheless intravenous injection could not be carried out alone given that the arterial network was then not highlighted. The liver vessels were filled via the ductus Arantius - Ductus Venosus, connecting the umbilical vein to the terminal part of the inferior vena cava. This venous conduct allows some of the oxygenated blood to pass from the placenta through the umbilical vein to go almost directly into the right atrium of the fetal heart without passing through the liver. The Arantius canal stops functioning a few minutes after birth. It will spontaneously close again during the first week of life and remain in the form of a residue: the venous ligament of the liver. The venous phase allowed, through the ductus Arantius, an interpretable opacification of the heart

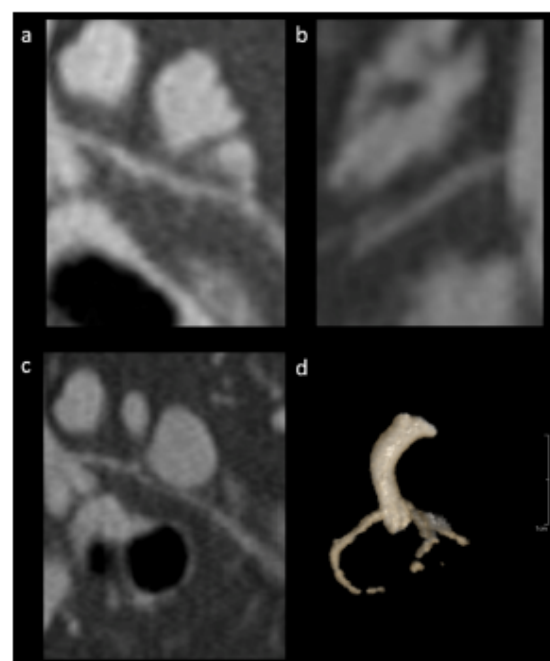


Fig. 5. Fetus deceased at 175 days of gestational age. The post-mortem interval between the expulsion and the examination is 20 months. CT angiography image using MIP after arterial opacification shows very small caliber arteries such as left anterior descending artery (a), right coronary artery (b) and circumflex artery (c). The CT angiography image using the Cinematic Rendering Technique (CRT) makes it possible to visualize the sinuses of Val-salva as well as the coronary arteries (d).

chambers by opacifying more particularly the right chambers of the heart.

Concerning the post-processing techniques used to assess CT images, MIP reconstruction allowed rapid assessment of vascularity and completeness of the vascular network and the scoring of opacification. The high dynamic range lighting of CRT ensured that the natural illumination of the rendered data generated a more realistic and visually attractive 3D image, which affects and improves the perception of depth and shape. In this way, the method provided anatomy models of the fetus and, therefore, improved predictive power [38,39].

The two-phase intra-umbilical injection method developed in this study allows visualizing the main vascular trunks, which may help pathologists to diagnose cardiovascular malformations. Further studies linked to autopsy findings should make it possible to assess the extent to which diagnosis is facilitated.

Our protocol resulted in umbilical injection failures in 40 % of cases. These failures were due to the small size of some fetuses (2/25) requiring a cardiac injection. Even without taking into account the risk of artefacts, the intracardiac injection was a difficult technique due to the location of the heart even when performed under ultrasound guidance. Other failures (8/25) were due to an inadequate method of preservation (freezing or formalin). We therefore recommend performing this examination on fetuses that have not undergone prolonged postmortem storage.

Imaging artefacts, already described in the literature [25], were observed, such as the sedimentation of the contrast product with paraffin oil, layering in the lumen of arterial system, and the incomplete opacification of certain veins.

The main limitation of our study was the limited sample size, which was due to the lack of donations to the department of anatomy. Since

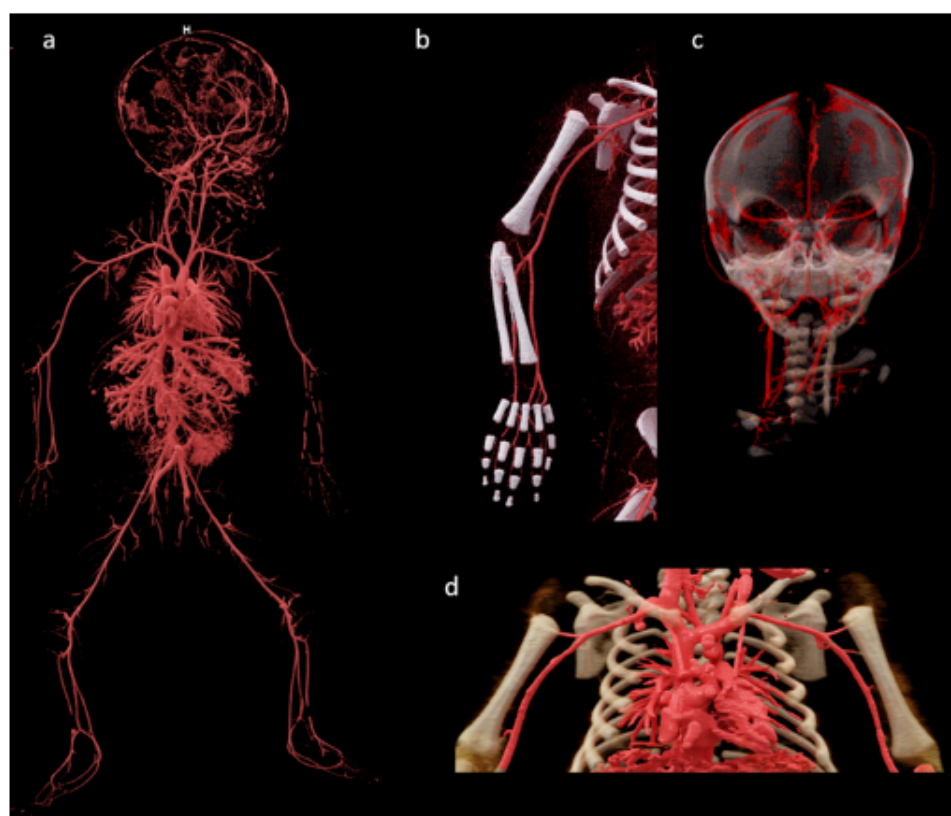


Fig. 6. Fetus deceased at 175 days of gestational age. CT angiography image after injection of 7mL in the arterial system shows opacification of the entire arterial system using Cinematic Rendering Technique (CRT) (a) highlighting small arteries such as digital arteries (b) Willis circle (c) in anterior view. Venous opacification after injection of 15 mL optimizes cardiac chambers opacification (d).

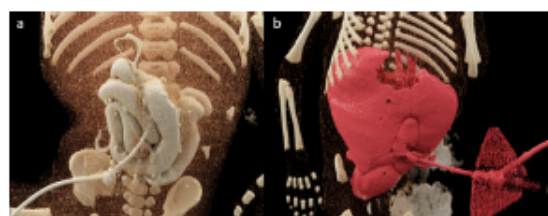


Fig. 7. Example of failures: CT angiography image using the Cinematic Rendering Technique (CRT) showing bowel injection in formalized fetus (A) and abdominal extravasation (B).

many fetuses were donated to the anatomy department after autopsy, radiological examination with injection of a contrast agent was therefore not feasible. Methodological limitations were also encountered. The fetuses studied were mostly frozen before examination and therefore did not represent an appropriate population.

Other future goals are the accurate mapping of abnormalities, which could be obtained by a systematization of the radiological reading. It has been shown that the development of adjacent brain structures and the appearance of the gyri induce changes in the position, path and relationship of brain arteries [40]. It is also necessary to study and establish an accurate mapping of the intrahepatic portal venous system to optimize the prenatal counselling and postnatal care due to fetal

abnormalities of the umbilical-portal-systemic venous shunts [41]. Likewise, it will be essential to analyse the placenta with the same method to help figure out more causes of death due to placental causes such as abruption, fetal-maternal haemorrhage, cord accident, etc... [42].

Conclusion

PMCTA of the fetus is possible by manually injecting a lipophilic contrast agent mixed with paraffin oil into the umbilical vessels. The procedure takes place in two phases and requires a first intra-arterial injection and then a second intravenous injection. The technique allows visualization of the fetal vascular network, even after long post-mortem intervals. By providing detailed vascular images and contributing to a more comprehensive understanding of fetal vascular abnormalities, PMCTA could significantly advance medical knowledge and improve clinical practice in the field of fetal medicine. With continued further research and development, PMCTA may become an invaluable tool in the diagnostic and counselling process for affected families, offering hope for improved outcomes and a better understanding of fetal vascular pathologies.

Supplementary material captions

Appendix: anatomical diagram of the arteries (a) and veins (b) analyzed during the procedure, abbreviated according to table 3.

CRediT authorship contribution statement

Jessica Vanhaebost: Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. Nicolas Michoux: Writing – review & editing, Software, Formal analysis. Xavier de Spiegeleire: Visualization, Methodology, Investigation, Formal analysis, Conceptualization. Silke Grabherr: Writing – review & editing, Validation, Supervision. Emmanuel Coche: Writing – review & editing, Visualization, Validation, Supervision, Resources.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.fri.2024.200593](https://doi.org/10.1016/j.fri.2024.200593).

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Article 2 - Postmortem CT angiography of fetuses, infants and children up to 12 years old a systematic review and conceptual decision tree

Vanhaebost J, Scholzen T, Coche E, Grabherr S. Postmortem CT angiography of fetuses, infants and children up to 12 years old a systematic review and conceptual decision tree. *Int J Legal Med* 139, 2829–2836 (2025). <https://doi.org/10.1007/s00414-025-03556-5>

Methodological contribution

For this article, my involvement covered various essential stages of the research, including conceptualization, methodology development, data extraction and analysis, as well as the drafting and revision of the manuscript.

I designed and conducted this systematic review independently, under the supervision of my thesis advisors. I defined the inclusion and exclusion criteria, conducted the literature search across four databases, selected and analyzed the relevant publications and synthesized the technical and clinical information. I developed a conceptual decision tree to help guide case management based on anatomical and age-related parameters. I wrote the entire manuscript and was responsible for integrating peer-review feedback prior to publication.

Conceptualization and Methodology

I led the conceptualization of the study design using the recommendation of my supervisors, defining the research objectives and establishing the methodology. I also developed the systematic approach to reviewing the existing literature and organizing the data for subsequent analysis, ensuring the methods were robust and systematic.

Literature Research

I conducted the literature search, systematically identifying relevant studies on PMCTA in fetuses, infants and children. I focused on collecting studies that would provide valuable insights into current methodologies and outcomes, contributing to the development of the decision tree for fetal and pediatric PMCTA (PedPMCTA).

Data Extraction and Analysis

I was responsible for extracting the relevant data from the selected studies. This involved organizing the data according to key themes, evaluating study quality and performing a comprehensive analysis. The goal was to synthesize existing knowledge and identify gaps in the field that could be addressed through the proposed decision tree.

Writing – Original Draft

I wrote the original draft of the manuscript, presenting the conceptual framework, literature review, methodological approach and results. I carefully structured the content to ensure clarity and coherence, particularly in presenting the decision tree and its implications for future research and clinical applications.

Writing – Review & Editing

After completing the original draft, I contributed to the review and editing process, incorporating feedback from co-authors and refining the manuscript to enhance its scientific quality. I focused on improving the flow of the text, ensuring that the methodology and results were clearly communicated and that all references were accurately cited.

Contributions from Co-Authors

Tristan Scholzen contributed significantly to the literature search, assisting in identifying relevant articles and conducting the data extraction. He also provided visualization support, ensuring that the figures and diagrams were clear and effectively illustrated the findings.

Emmanuel Coche played an essential role in reviewing the manuscript and providing guidance during the supervision process. His insights helped ensure that the study adhered to high scientific standards and that the methodology was rigorously applied.

Silke Grabherr provided critical input during the writing, reviewing and editing stages. She supervised the project, ensuring that the manuscript met the required scientific and clinical standards. She also offered valuable feedback to refine the methodology and presentation.



Postmortem CT angiography of fetuses, infants and children up to 12 years old a systematic review and conceptual decision tree

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Abstract

Background Postmortem CT angiography (PMCTA) enhances traditional autopsy by enabling detailed visualization of vascular structures and sources of hemorrhage. However, its application in fetuses and children remains limited due to small vessel size and the lack of standardized techniques. This systematic review critically evaluates existing literature on PMCTA in decedents under 12 years old, with the aim of identifying current practices and methodological variations to assist practitioners in selecting appropriate protocols based on age and anatomical characteristics.

Materials and methods A systematic literature research was conducted following PRISMA guidelines using PubMed, Scopus, Embase and Google Scholar from 2004 to 2024. Eligible articles investigated PMCTA in fetuses and children up to 12 year old. Extracted data covered technical protocols, vascular access, contrast preparation, perfusion parameters and imaging outcomes. A decision tree was constructed to illustrate potential approaches by age group and anatomical features.

Results Ten studies met inclusion criteria: five focused on fetal PMCTA, four on children, and one on both populations. Considerable heterogeneity was found across protocols, especially regarding contrast media preparation and injection techniques. A conceptual decision tree was developed based on reported practices. This framework is not a validated algorithm and should be applied cautiously, with attention to individual anatomical and contextual factors.

Conclusion This review underscores the lack of standardized fetal and pediatric PMCTA protocols. It offers structured guidance while highlighting the need for further research to develop and validate consistent approaches in this vulnerable population.

Keywords PMCTA · Pediatric imaging · Postmortem imaging · Fetal imaging · PedPMCTA

Introduction

Postmortem CT angiography (PMCTA) has been developed over the past two decades as a valuable complement to traditional autopsy, particularly for detailed visualization of vascular structures and potential sources

of hemorrhage. In adults, it has proven useful in both clinical and forensic settings [1–4]. However, PMCTA practices remain heterogeneous, with different institutions adopting varying techniques based on available resources, case types and expertise. Its primary advantage lies in its ability to address questions regarding the

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vascularization of the deceased and potential sources of hemorrhage. In Europe, several PMCTA protocols have been described. In Switzerland, Grabherr et al. proposed a multiphase postmortem CT angiography (MPMCTA) technique involving sequential arterial, venous, and dynamic phases with dedicated perfusion equipment and contrast protocols, laying the groundwork for a standardized approach [1]. A more recent Swiss feasibility study also demonstrated the potential of a low-cost immersion pump system, assembled using 3D-printed components, which may enhance accessibility in resource-limited environments [5, 6]. In the United Kingdom, targeted cardiac PMCTA has been developed and successfully applied in the investigation of sudden cardiac death. The Leicester group demonstrated the feasibility of both air-based and contrast-enhanced coronary PMCTA using minimally invasive methods [7–10], while the Oxford forensic institute contributed to broader postmortem imaging integration in routine medico-legal practice with a novel method of coronary PMCTA. In Japan, Iizuka et al. proposed a chest-compression-based PMCTA technique as a simplified and cost-effective method to visualize the vascular system postmortem [11]. In France, Jolibert et al. reported the use of ultrasound-guided vascular access and injector-based perfusion in Marseille [12]. These examples reflect the growing interest in PMCTA worldwide, but also illustrate that no universally adopted protocol currently exists, with techniques varying widely depending on infrastructure, objectives, and funding. Despite these developments, PMCTA remains underused in fetal and pediatric autopsies, largely due to anatomical limitations—such as small-calibre vessels—and the absence of validated, adapted protocols. Most angiographic assessments in these populations still rely on radiography [13, 14] or MRI [15] rather than computed tomography, with or without the use of contrast agents, specifically in fetal autopsies [16]. Comparisons of these different methods have already been the subject of published research [17].

This systematic review was conducted to critically evaluate the existing literature on PMCTA in fetuses and children up to 12 years of age. Its aim is to synthesize current evidence, identify methodological variability and knowledge gaps and inform future clinical and forensic applications. While this review does not propose a standardized protocol, it offers a conceptual framework based on existing practices to support decision-making. This decision tree is intended as a descriptive tool, not a validated algorithm, and should be interpreted in light of case-specific and institutional factors.

Materials and methods

The review design is consistent with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 [18] statement and checklist, graphically reported in Fig. 1.

Search strategy

The systematic review was carried on the four electronic databases: PubMed, Scopus, Embase and Google Scholar to answer the question. The primary outcome of the review was the visualization of vascular structures according the clinical or forensic question. The main search string included: (“Computed Tomography Angiography”) AND (“Autopsy” OR “Postmortem Imaging”) AND (“Pediatrics” OR “Fetus” OR “Infant” OR “Child” OR “Infant, Newborn” OR “Stillbirth”). For Google Scholar the terms were: Autopsy, OR Postmortem OR Imaging, OR Pediatric, OR Fetus, OR Infant, OR Child, OR Newborn, OR Stillbirth “Computed Tomography Angiography”. In Scopus, the search was conducted in Article, Title, Abstract and Keywords. MeSH was also explored but yielded no additional results. In PubMed the search string used was: (“Computed Tomography Angiography”) AND (“Autopsy”[Mesh] OR “Postmortem Imaging”[Mesh]) AND (“Pediatrics”[Mesh] OR “Fetus”[Mesh] OR “Infant”[Mesh] OR “Child”[Mesh] OR “Infant, Newborn”[Mesh] OR “Stillbirth”[Mesh])

Literature search was guided by the PICO framework: Population – human fetuses from 10 GA to children up to 12 year old; intervention and comparisons: PMCTA, compared to autopsy; outcome: visualization of the vascular system.

Eligibility criteria

Articles published in a peer-reviewed journal in English and within the last 20 years (to ensure relative currency of research) were considered for the review. All studies (original article, case report, retrospective and prospective case series) were included if they enrolled (a) human fetuses from 10 weeks GA till children up to 12-year-old, (b) deceased, (c) underwent PMCTA attempts.

Data extraction and quality appraisal

The search results were managed using EndNote 21 (The EndNote Team. 2013, Clarivate: Philadelphia, PA), to remove duplicates. Titles, abstracts and full texts were screened based on predefined inclusion criteria. The screening process was conducted by a single investigator (JV), and data from the included articles were extracted into an Excel spreadsheet (Microsoft

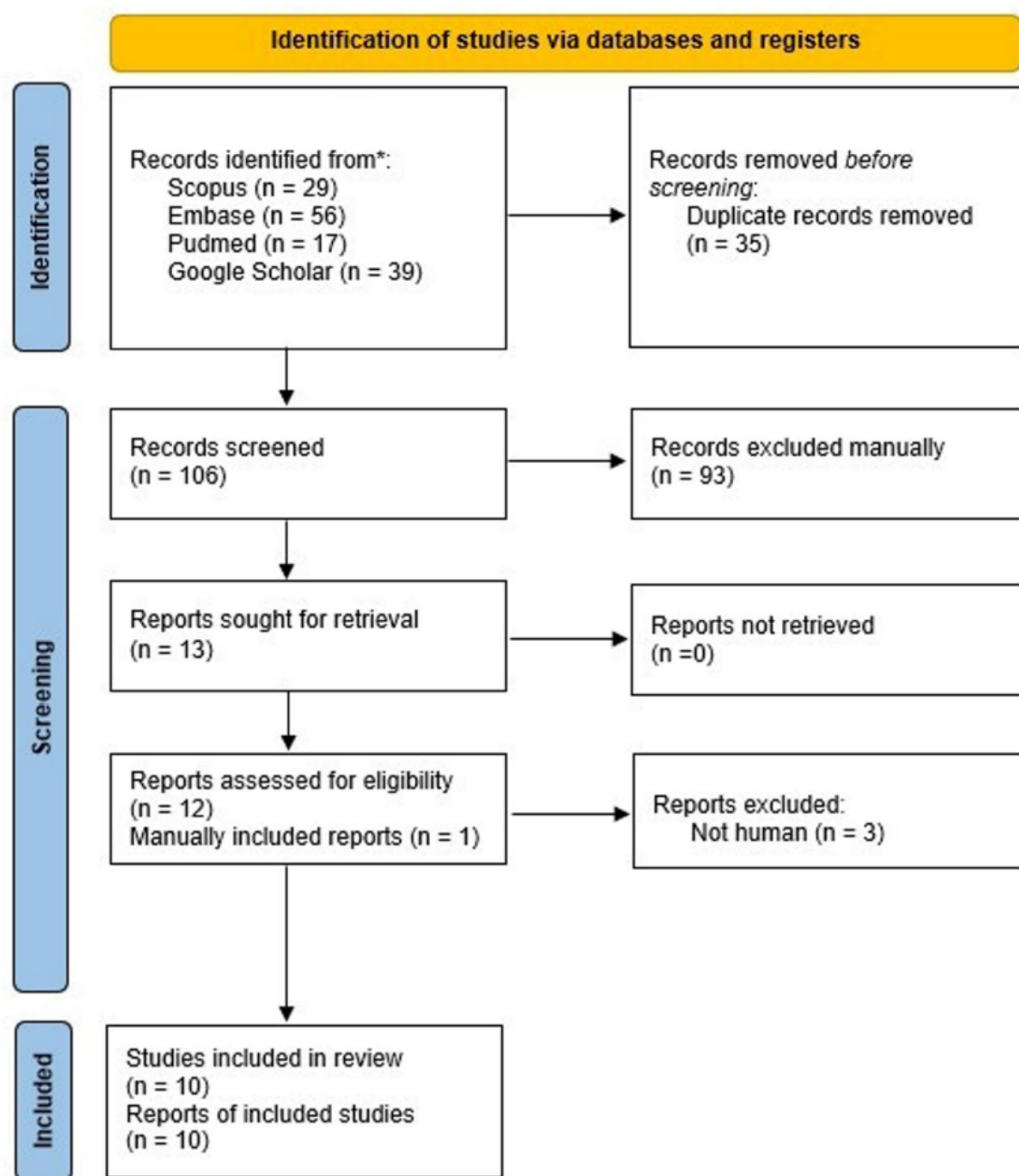


Fig. 1 PRISMA flowchart of the present review

Excel, 2010 Microsoft Corporation, Redmond, WA, USA). The following variables were collected from each article: publication details (authors, title, journal, and year), population characteristics (sample size, age, and postmortem interval), CT scan parameters and PMCTA procedure details (vascular access,

contrast agent, volume, catheter and protocol specifications). ChatGPT (OpenAI, 2023) was used to assist in refining and improving the clarity and linguistic quality of the manuscript. Final content and interpretation remain the responsibility of the author.

Results

The study selection process is visualized in Fig. 1 and the results of the literature search are summarized in Table 1.

Of 139 articles initially identified, 35 duplicates were removed. Following title, abstract, and full-text screening, 91 articles were excluded for addressing antemortem CT angiography, MRI or living subjects. Three additional studies were excluded due to non-human subjects (e.g., piglets) [29–31].

Discrepancies regarding inclusion were resolved by consensus between two reviewers (JV and TS). One article required specific deliberation due to its inclusion of both pediatric and adult cases, and its comparative analysis of PMCTA and MRI [21]. Ultimately, 10 articles met the inclusion criteria and were included in the review. All studies were assessed using the MMAT tool [32, 33], comprising 7 original research papers, 2 case reports (one described as methodological) and 1 technical note.

Key limitations included small sample sizes (typically <30 subjects) [20, 23, 28], limiting generalizability; heterogeneity in methodologies [19] (e.g., products, volumes), preservation conditions [26], and imaging parameters; and selection bias through exclusion of certain pathological cases [21], affecting applicability. Additionally, most studies lacked sufficient statistical rigor, precluding meta-analysis.

Fetal cases predominated, with GA ranging from 106 days [26] to 39 weeks [27]. Neonatal and pediatric cases extended up to 7 years [20], with one study including adults for comparison, albeit without distinguishing age groups [21]. The postmortem interval varied widely, from 3 h [21] to over 20 years [26]; in the latter, advanced formalin preservation precluded PMCTA. Data were further analyzed by subgroup: fetal PMCTA (including stillbirths) and pediatric PMCTA (newborns and children up to 12 years).

Fetal PMCTA (including stillbirth)

Five studies investigated fetal PMCTA [19, 22, 23, 26, 27]. A total of 81 fetuses underwent PMCTA attempts. The preferred injection route was umbilical vessel cannulation, while cardiac injection was used when umbilical access was unfeasible due to small fetal size or vessel closure.

Injection methods

Intra-umbilical injection was the primary approach for PMCTA in fetuses, generally involving sequential injection into the umbilical artery (7–20 mL) followed by the vein (15–40 mL), or up to 60 mL/kg via the vein alone [22,

26, 27]. Catheter sizes ranged from 22 to 24 G (artery) and 16–22 G (vein) to preserve vessel integrity.

Cardiac injection, though less frequently used, was considered when intra-umbilical access was not feasible due to fetal size limitations [26, 27]. This technique requires the direct injection of contrast into the fetal heart under ultrasound guidance to ensure precision and minimize the risk of artifacts. A 26 G needle and volumes of 5–10 mL were recommended, adjusted to fetal size [27].

Contrast agents

Both lipophilic (6% lipophilic contrast agent Angiofil™ combined with paraffin) [19, 26] and water soluble iodinated contrast agent [22, 23, 27] were employed. Lipophilic agents may allow for extended postmortem intervals [26].

Technical considerations

Proper fetal positioning (e.g., supine or prone with rotation) optimized vascular filling and minimized artifacts [22, 23]. Pre-injection flushing with physiological saline (e.g., Hartmann's solution) improved contrast perfusion by clearing postmortem clots [27]. Ultrasound guidance confirmed catheter placement and reduced the risk of misperfusion [23], with some protocols including a pre-injection test [19].

PedPMCTA (newborns and children up to 12 years old)

Six studies [19–21, 24, 25, 28] reported on 57 pediatric cases. Femoral access was most commonly employed (4/6 studies), with additional techniques including umbilical [19, 28], transfontanellar [24], and intraosseous injection [19]. One study combined pediatric and adult cases without age distinction and included MRI [21].

Peripheral (femoral) injection

Femoral catheterization was reported in four studies. In a child of 7 year, femoral access was achieved using 16–17 F catheters and a modified adult multiphase PMCTA protocol [20], delivering 6% Angiofil™ with paraffin oil in three phases: 600 mL (arterial), 900 mL (venous), and 250 mL (circulating), at flow rates of 400 mL/min (arterial/venous) and 100 mL/min (circulating). This method requires an adaptation of the size of the tubes (cannulas) to the size and age of the children. For smaller children, 14 G (artery) and 18 G (vein) needles were used with gradual injection until full vascular opacification was achieved [19]. In cases where peripheral catheters were placed during life, they were reused to inject iodinated water-soluble contrast agents [25].

Table 1 Characteristics of the 10 included studies—light grey concerning fetal PMCTA—white concerning newborn and children PMCTA (in alphabetical order)

Publication information (Authors, year)	Population details (sample size, age, PMI)	CT scan parameters and specifications	Angiography procedure (access, contrast agent, catheter and specifications)
Bruch et al. 2024 [19]	5 fetuses (22–37 GA), PMI <48 h	CT Somaton Emotion 16 S® (HealthCare Erlangen, Germany) 120–130 kV, 50–100 mAs, 50 eff.mA, tilt 0.0, slice 0.75 mm.	Manual gradual injection of contrast medium mixture umbilical vessels (4/5)/tibia bone marrow (1/5), 6% Angiofil™ (Fumedica AG, Muri bei Bern, Switzerland) diluted with paraffin oil, through 14 G PVC into artery and 20 G PVC into vein.
	4 children (3 h–16 mo), PMI <48 h	CT Somaton Emotion 16 S® 120–130 kV, 50–100 mAs, 50 eff.mA, tilt 0.0, slice 0.75 mm.	Gradual injection in umbilical vessels/femoral vessels/tibia bone marrow, of 6% Angiofil™ diluted with paraffin oil, umbilical: 14 G PVC in artery and 20 G in vein/femoral: 14 G PVC in artery and 18 G PVC in vein/bone: 15 mm 15 G bone needle, umbilical vascular access if possible.
Chevallier et al. 2015 [20]	1 child (7 y), PMI NA	8-row CT unit (GE Lightspeed Ultra; GE Healthcare, Milwaukee, Wis), 120 kV, 160–200 mAs, slice 1,2 mm.	Injection in femoral vessels, of 6% Angiofil™ mixed with paraffin oil, of 600 mL arterial, 900 mL venous and 250 mL circulating, through tubes 16 F and 17 F, at a flow rate 400 mL/min for arterious and venous, 100 mL/min for circulating phase.
Pluchinotta et al. 2015 [21]	10 (3 d–45 y), median PMI 15 h	64-detector CT scanner (Sensation 64; Siemens, Erlangen, Germany), 80 kV, 100 mAs, 0,75 mm thickness, 0,8 pitch, 64×0,6 mm collimation, 0,5 s rotation. Fuji Synapse work station (Fujifilm Medical Systems, Stamford, CT, USA) and 3D reconstructions using Voxar software (Voxar, Toshiba Medical Systems, Tochigi, Japan).	Injection in femoral vessels - venous (8 mL/kg body weight) or arterial (5 mL/kg body weight) - of iodinated contrast (Isovue 370, Bracco Diagnostics, Monroe Township, NJ, USA) diluted 1:8 with a 50% aqueous solution of polyethylene glycol 200 (Acros Organics, Thermo Fisher Scientific Inc., Waltham, MA, USA)/ECMO cannula if present.
Sarda-Quarello et al. 2015 [22]	17 fetuses (16–37 GA), PMI NA.	Definition 64 (Siemens, Erlangen, Germany), 100 kV, 250 mAs, collimation 64×0,6, rotation time 0.5s.	Manual injection of 60 mL/kg of a mixture of water (50%) and iodine contrast (50%, Iobitridol 300 mg/L - Xenetix, laboratoires Guerbet, Villepinte, France) through a 22 GA peripheral catheter in the umbilical vein.
Sarda-Quarello et al. 2016 [23]	1 fetus (37 GA), PMI 15 h (after expulsion)	MDCT dualsource 64-slice (Siemens Definition, Siemens Medical System, Erlangen, Germany). Imaging parameters included: 100 kV;250 mAs; collimation 64×0,6, rotation time: 0.5 s.	Injection in umbilical vessels of 180 mL mixture of 30% water and water soluble iodated contrast medium (Iobitridol 300 mg/L), through peripheral venous catheter 22 G, visual control by ultrasound.
Stein et al. 2006 [24]	11 children (2 d–19 mo), PMI 12 h–4.5d	CT scanner (Siemens Somatom Plus-S, Erlangen, Germany).	Injection in the fontanel membrane, of 5–65 ml iodine-based contrast medium (e.g., Ultravist 300 or Imeron 300), through 21-G-needle, punctured in a head-down position, inserted under aspiration.
Tumanova et al. 2020 [25]	30 newborns (12 min–18 d), PMI 12–48 h	Toshiba Aquilion ONE 640 - Pediatric 0.5 software, Abdomen Baby protocol - CT reconstructions: software Myrian Expert (Intrasense).	Injection through catheters and probes installed during life of iodine-containing water-soluble radiopaque drug containing at least 250 mg of iodine per 1 ml, calculated based on body weight: CV=1.5×body weight (g)/100 (1,4 if edema).
Vanhaebost et al. 2024 [26]	25 fetuses (106 d–28 GA), PMI 5d–20y	Dual-energy MDCT (Definition As Edge 128, Siemens™ Healthcare, Forchheim, Germany) – 80 kV 168 mAs, 128 slices/rotation, collimation of 16×0.3 mm.	Manual injection of 6% Angiofil™ mixed with paraffin oil of low viscosity, 7 mL artery – 15 mL vein, through 24 GA insertion needle in the umbilical vessels (23/25)/heart (2/25), in two phases, first arterial then venous.
Votino et al. 2012 [27]	33 fetuses (18–39 GA), PMI 0–11d	64-row multidetector CT scanner (SOMATOM Sensation 64, Siemens Medical Solutions, Forchheim, Germany). 3D volume data set using a Vitrea workstation (Vital Images, Minnetonka, MN, USA) or IntelliSpace Portal workstation (Philips Healthcare, Cleveland, OH, USA).	Injection in umbilical vessels of 20 to 40 mL in umbilical (8/33) and 5 to 10 mL into heart (25/33) according to fetal size, through 22-G catheter for the artery and a 16–18-G catheter for the vein/under ultrasound guidance, directly into the left ventricle through the ventricular septum, and into the right ventricle using a 26 G needle, using Iomeprol (Imeron®, Bracco UK Ltd., High Wycombe, UK), at a concentration of 140 mg/mL.
Woźniak et al. 2015 [28]	1 newborn (40 GA), PMI ~38 h	CT Somaton Emotion 16 S®, kVp 130, mAs 50 and 240, reconstructed slice thickness 0.75 and 1.5, collimation 16×0.6, and pitch 0.85 and 0.55.	Injection in the umbilical vessels, of 60 mL venous and 60 mL arterious, of 6% paraffin oil solution of Angiofil™, through 1,2 mm needle.

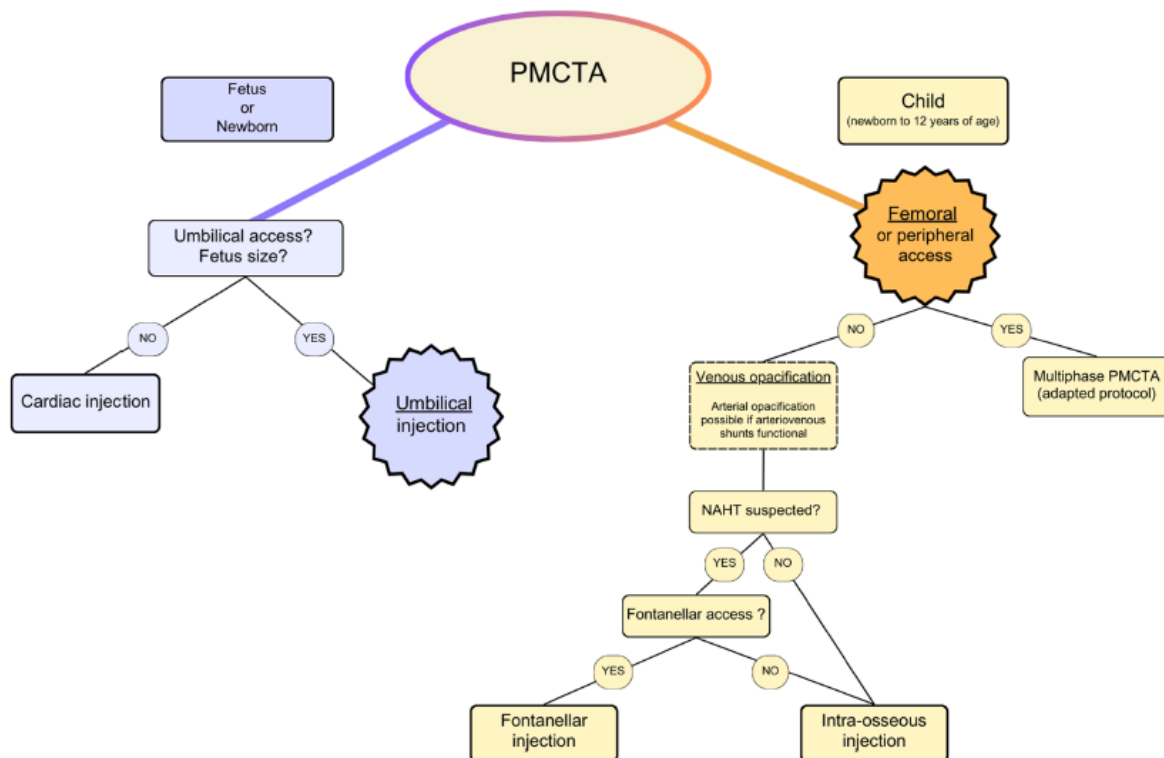


Fig. 2 Conceptual decision tree for the application of PMCTA in fetuses, newborns, and children up to 12 years of age

Alternative methods

Umbilical access remained feasible in neonates shortly after birth, using the same contrast as femoral access [19]. *Fontanel* [24] and *tibial bone marrow access* [19] may be considered when umbilical or femoral access is not possible.

Regarding the *fontanellar access*, a mixture of 6% Angiofil™ and paraffin oil can be injected through a small catheter inserted via the fontanelle to access the cranial vasculature. Flow rates should be adjusted according to the infant's size. This technique is particularly useful when cranial visualization is required, such as in forensic investigations of Non Accidental Head Trauma [34].

Tibia bone marrow injection can be applied when arteriovenous shunts exist or venous-only imaging are required. If the umbilical vessels are unavailable, bone marrow access is preferable due to its ease of use in the presence of a physiological or pathological arteriovenous shunting. Intraosseous access, particularly in smaller infants, is suitable for venous imaging, whereas fontanelle access is preferred for cranial vascular studies. However, bone marrow contrast injections

have been reported as ineffective in newborns and infants weighing less than 2.5 kg.

Special considerations

Contrast volume should be adjusted in cases of edema. If the child is on ECMO, cannula-based injections can be performed, with volumes adapted to body weight [25].

Proper positioning is crucial to facilitate vascular access: a supine position prevents umbilical vessel compression; slight leg abduction eases femoral catheterization; and head stabilization is required for fontanelle access [24].

Decision tree synthesis

Based on the extracted data, we synthesized a conceptual decision tree (Fig. 2) that outlines reported vascular access strategies and contrast administration techniques across different age groups. This figure summarizes practices reported in the literature but should not be interpreted as a validated clinical guideline.

Discussion

This systematic review critically assessed existing studies on PMCTA in fetuses and children under 12 years of age. The findings highlight a limited but growing body of evidence with significant methodological heterogeneity. Key variables across studies include patient age, vascular access, contrast media, and imaging protocols, all of which influence image quality and diagnostic value.

Clinical relevance of tailoring techniques to anatomy and age

One consistent theme across the literature is the necessity of adapting PMCTA protocols to the size, vascular anatomy, and developmental stage of the deceased. Optimal image quality depends on appropriate selection of vascular access routes, contrast agents, and injection parameters. This is particularly critical in fetuses and stillbirths, where vessel diameter is minimal and postmortem changes may compromise opacification.

Vascular access strategies based on developmental stage

Age emerged as a central criterion for guiding access route selection. Umbilical access is recommended for fetuses and newborns with an intact umbilical cord [19, 22, 23, 26–28], allowing sequential injection into the umbilical artery and vein. When this is not feasible, intracardiac injection under ultrasound guidance may serve as an alternative [26, 27]. In older children, femoral access following the multiphase PMCTA protocol is commonly reported [20], with flow rates adapted from adult techniques. In special cases such as suspected Non Accidental Head Trauma, alternative routes—such as fontanellar or intraosseous access—may be considered depending on weight and anatomical context [19, 24].

Contrast agents and imaging quality

Several studies emphasize the utility of lipophilic agents such as Angiofil™ mixed with paraffin oil (6%) for their capacity to reduce putrefactive artifacts and allow delayed imaging. Aqueous iodine-based solutions are also used, although their diffusion characteristics may differ. Regardless of the agent, injection volumes and flow rates must be

adjusted according to the patient's size to avoid overdistension or poor perfusion.

Conceptual framework and its limitations

Based on the patterns observed across the reviewed studies, a conceptual decision tree (Fig. 2) was developed to support technique selection according to age and anatomical feasibility. This tool summarizes existing practices but should not be interpreted as a validated clinical algorithm. Its utility depends on institutional capabilities and case-specific factors. The limited number and quality of available studies underscore the need for caution in its application.

Limitations of the evidence base

This review is limited by the small number of eligible studies, most of which are descriptive and lack standardized outcome reporting. The absence of control groups, detailed methodology, and histological correlation in many cases introduces a risk of bias. There is also a significant underrepresentation of fetal and neonatal PMCTA, likely reflecting broader institutional reluctance or legal constraints regarding pediatric autopsies.

Future directions

Future research should prioritize multicentric prospective studies with standardized protocols tailored to pediatric and fetal populations. Investigations comparing contrast agents, injection systems, and image post-processing techniques would enhance reproducibility and diagnostic reliability. Ultimately, the development of validated, evidence-based guidelines could promote broader adoption of PMCTA in clinical and forensic pediatric pathology.

Conclusion

This systematic review critically evaluated the existing literature on PMCTA techniques applied to fetuses and children up to 12 years of age. The review identified a limited number of studies, with substantial methodological heterogeneity. These findings informed a conceptual framework designed to assist technique selection based on age and anatomical considerations. While further validation is needed, this synthesis may help guide future research and support case-by-case decision-making in clinical and forensic contexts.

Author contributions JV (conceptualization, methodology, literature research, data extraction, data analysis, writing– original draft, writing– review & editing)– TS (literature search, data extraction, visualization), EC (Review & supervising), SG (Writing - Review & Editing– Supervising).

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Declarations

Conflict of interest None of the authors has a conflict of interest.

Clinical trial number Not applicable.

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Article 3 - Postmortem CT angiography in infants and young children (pedPMCTA): Technical feasibility and emerging forensic insights from a 30-case study

Jessica Vanhaebost, Bastien Trächsel, Florian T. Fischer, Silke Grabherr, Gina Maria Bruch, Postmortem CT angiography in infants and young children (pedPMCTA): Technical feasibility and emerging forensic insights from a 30-case study, submitted on 15 October 2025 in Int J Legal Med.

Methodological contribution

This study was designed as a retrospective observational series of 30 pediatric PMCTA cases. All angiographic exams were performed by Gina Maria Bruch at the Institute of Forensic Medicine, Ludwig-Maximilians-University Munich, Germany. My methodological contribution began with the systematic scoring and extended throughout the interpretation and publication process.

Methodology and Data Handling

The raw data from the cases were collected and organized in an Excel database by Gina Maria Bruch. I implemented the vascular opacification scoring system, applying it consistently across all 30 cases. I also complemented the dataset where necessary, ensuring completeness for subsequent analysis.

Data Analysis and Interpretation

I performed the semi-quantitative scoring of arterial and venous opacification and contributed to the interpretation of forensic relevance, with emphasis on bridging veins, ocular vessels and coronary ostia. I also analyzed and contextualized the occurrence of spontaneous arteriovenous shunts and reflected on their methodological implications.

Writing – Original Draft

I was the main and corresponding author of the manuscript. I structured the paper, drafted the introduction, methods, results and discussion, and integrated the tables and figures. I ensured that the manuscript highlighted both technical feasibility and diagnostic potential.

Writing – Review & Editing

I coordinated the revision process, incorporated feedback from supervisors and co-authors. I refined methodological descriptions, clarified forensic interpretations and ensured scientific accuracy.

Contributions from Co-Authors

Gina Maria Bruch performed all PMCTA procedures in Munich, created the Excel database and contributed to manuscript review.

Bastien Trächsel contributed to statistical analysis and methodological validation.

Florian T. Fischer supervised the PMCTA acquisitions in Munich, ensured data quality, supported case documentation and revised the final manuscript.

Silke Grabherr supervised the preparation of the final manuscript and critically revised it for scientific rigor.

Collaborative Context

This project was made possible through the TWGPAM [69], an international network that fosters methodological development and collaborative studies in postmortem angiography. Through TWGPAM, expertise from Switzerland, Belgium and Germany was brought together, enabling the successful design, analysis and publication of this pediatric series.



Postmortem CT angiography in infants and young children (pedPMCTA): Technical feasibility and emerging forensic insights from a 30-case study

Jessica Vanhaebost^{1,2,3} · Bastien Trächsel⁴ · Florian T. Fischer⁵ · Silke Grabherr⁶ · Gina Maria Bruch^{5,7}

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Abstract

Background & objectives Postmortem CT angiography (PMCTA) is increasingly used in forensic imaging but remains underexplored in pediatric populations. This study assesses the feasibility of pediatric PMCTA (pedPMCTA) using a weight-adapted manual protocol with a lipophilic contrast agent and explores its forensic application, particularly for investigating abusive head trauma.

Materials & methods Thirty pediatric cases (0–3.6 years; 2.2–25.4 kg) underwent PMCTA prior to autopsy. A biphasic protocol (arterial and venous) was applied using Angiofil™ diluted in rapeseed oil or paraffinum perliquidum. Vascular access included femoral, intraosseous, umbilical and peripheral routes. Vascular filling was assessed using a semiquantitative score for arteries (max 34) and veins (max 24). Diagnostically sufficient opacification was defined as >17/34 for arteries and >12/24 for veins. Access types, scores and technical success were analyzed.

Results PMCTA was technically feasible in all cases. Diagnostically sufficient arterial opacification was achieved in 23/30 cases (76.7%), and venous opacification in 24/30 (80.0%). Femoral venous access yielded the highest venous scores. In some cases, arterial opacification occurred despite venous-only injection, suggesting passive filling via arteriovenous shunts. Opacification scores showed no significant correlation with age or postmortem interval and only weak correlation with weight despite the weight-adapted protocol.

Conclusion PedPMCTA with a lipophilic contrast agent is feasible and diagnostically informative, including in neonates. It may complement forensic autopsy, especially in cases involving vascular lesions or suspected abusive injuries. These findings highlight the forensic value of pedPMCTA in determining causes of death in infants and young children.

Keywords Postmortem CT angiography · Forensic imaging · Pediatric autopsy · Vascular imaging · Bridging veins · Infant death · PedPMCTA · PMCTA

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Table 1 Demographic and technical characteristics of the study population ($n=30$). Variables include age, sex, weight, postmortem interval (PMI), type of vascular access, injected volumes and contrast mixture (IV= intravenous, G= Gauge, F= French, IO= intraosseous, CVL= central venous line, h= hours, mL= milliliters, CM= contrast medium)

Case number	Age (days)	sex	PMI to autopsy (h)	Length (cm)	Weight (kg)	First Arterial injection (mL)	Second Arterial injection (mL)	Total Arterial injection (mL)	Arterial access material	First Venous injection (mL)	Second Venous injection (mL)	Total venous injection (mL)	Venous access route	venous Material	CM Mixture	Total Arterial Score	Total Venous Score
1	75.00	f	30	60	6.0	0	0	0	0	90	0	90	femoral	CVL (central vein)	4% Angiostil, Rapared oil	4	19
2	4.99.00	f	48	80	9.2	80	0	80	femoral	IV Catheter 18G	180	40	io	io 20G	4% Angiostil, Rapared oil	11	17
3	0.00	m	10	51	3.4	0	0	0	0	60	80	140	umbilical	IV Catheter 20G	4% Angiostil, Rapared oil	11	14
4	64.00	m	5	63	5.4	0	0	0	0	110	0	110	io	io 20G	4% Angiostil, Rapared oil	0	3
5	232.00	m	24	72	8.8	80	0	80	femoral	IV Catheter 20G	160	0	femoral	IV Catheter 18G	4% Angiostil, Rapared oil	34	13
6	1.00	m	38	54	3.7	35	0	35	femoral	IV Catheter 20G	60	0	femoral	IV Catheter 20G	4% Angiostil, Rapared oil	34	22
7	758.00	f	70	92	13.0	130	20	150	femoral	IV Catheter 18G	50	0	femoral	IV Catheter 18G	4% Angiostil, Rapared oil	33	10
8	31.00	f	22	52	4.0	15	0	15	peripheno - other	IV Catheter 24G	40	0	peripheno - other	IV Catheter 24G	4% Angiostil, Rapared oil	32	21
9	358.00	f	90	78	12.0	60	60	120	femoral	IV Catheter 20G	240	0	femoral	IV Catheter 18G	4% Angiostil, Rapared oil	24	16
10	937.00	m	24	88	13.0	130	0	130	femoral	IV Catheter 18G	15	0	CVL	CVL	4% Angiostil, Rapared oil	33	0
11	1055.00	f	24	94	10.4	100	0	100	femoral	IV Catheter 18G	200	0	io	io 20G	4% Angiostil, Rapared flum peptigadum	32	16
12	957.00	m	96	101	20.0	200	0	200	femoral	IV Catheter 18G	400	0	femoral	CVL	4% Angiostil, Rapared flum peptigadum	32	18
13	1316.00	m	70	91	12	0	0	0	0	120	200	320	CVL	CVL	4% Angiostil, Rapared flum peptigadum	17	14
14	13.00	m	29	49	3.5	35	0	35	femoral	IV Catheter 20G	70	0	peripheno - other	IV Catheter 20G	4% Angiostil, Rapared flum peptigadum	33	22
15	140.00	f	38	57	7.5	0	0	0	0	150	0	150	peripheno - other	IV Catheter 20G	4% Angiostil, Rapared flum peptigadum	11	21
16	853.00	m	83	95	18	180	0	180	femoral	Port 4 F	360	0	femoral	IV Catheter 18G	4% Angiostil, Rapared flum peptigadum	31	15
17	94.00	f	52	69	6.2	62	0	62	femoral	Port 4 F	124	0	femoral	IV Catheter 18G	4% Angiostil, Rapared flum peptigadum	31	13
18	101.00	m	48	48.5	2.6	0	0	0	0	50	50	100	io	io 20G	4% Angiostil, Rapared flum peptigadum	17	21
19	250.00	m	21	66	8	80	0	80	femoral	Port 5 F	0	0	0	0	4% Angiostil, Rapared flum peptigadum	31	0
20	53.00	f	26	57	4.1	80	0	80	femoral	IV Catheter 18G	0	0	0	0	4% Angiostil, Rapared flum peptigadum	30	0
21	54.00	m	53	58	4.9	50	0	50	femoral	Port 6 F	100	0	femoral	Port 8 F	4% Angiostil, Rapared flum peptigadum	29	16
22	434.00	m	27	65	6	60	0	60	femoral	Port 9 F	120	0	io	io 20G	4% Angiostil, Rapared flum peptigadum	32	17
23	103.00	f	28	61	6.2	65	0	65	femoral	IV Catheter 14G	125	0	femoral	IV Catheter 18G	4% Angiostil, Rapared flum peptigadum	31	20
24	41.00	f	66	53	3.6	35	35	70	femoral	IV Catheter 20G	0	0	0	0	4% Angiostil, Rapared flum peptigadum	32	0

Table 1 (continued)

Case number	Age (days)	sex	PMI to angio (h)	Length (cm)	Weight (kg)	First arterial injection (ml)	Second arterial injection (ml)	Total arterial injection (ml)	Arterial access	First venous injection (ml)	Second venous injection (ml)	Total venous injection (ml)	Venous access route	venous Material	CM Mixture	Total Arterial Score	Total Venous Score
25	547.00	f	8.6	81	10.8	110	0	110	femoral	IV Catheter 22G	0	220	femoral	IV Catheter 14G	4% Angioll, Panf- finam pefiquadum	32	20
26	1186.00	m	5.5	107	25.4	100	0	100	femoral	IV Catheter 30G	0	300	femoral	Port 6 F	4% Angioll, Panf- finam pefiquadum	32	13
27	88.00	m	31	64	6.2	60	0	60	periph- ic - other	IV Catheter 24G	0	120	femoral	IV Catheter 18G	4% Angioll, Panf- finam pefiquadum	31	23
28	13.00	m	30	55	3.1	30	0	30	femoral	IV Catheter 20G	0	60	femoral	IV Catheter 18G	4% Angioll, Panf- finam pefiquadum	31	14
29	5.00	m	48	57	7	60	0	60	femoral	IV Catheter 20G	100	120	io	io 20G	4% Angioll, Panf- finam pefiquadum	33	17
30	0.00	f	48	40	2.2	0	0	0	0	0	40	60	umbilical	IV catheter 20G	4% Angioll, Panf- finam pefiquadum	31	22

Introduction

Sudden and unexplained deaths in infants and young children are among the most challenging and emotionally charged cases in forensic medicine, often raising complex diagnostic, legal and ethical questions. Autopsy remains the cornerstone of pediatric death investigations, particularly in cases involving trauma, sudden unexpected death or congenital anomalies. While postmortem imaging, especially computed tomography (PMCT), is increasingly integrated into forensic workflows, its application in children should be regarded as complementary rather than a substitute for conventional forensic autopsy [1, 2]. One major challenge during pediatric autopsy is the systematic evaluation of the vascular system, as vascular dissection is technically demanding due to the small size and anatomical variability of pediatric vessels, which may hinder the identification of subtle vascular injuries. Postmortem CT angiography (PMCTA) is an advanced imaging technique in which contrast agent is injected into the vascular system of a deceased individual, enabling high-resolution CT visualization of arteries and veins to detect hemorrhage, vascular injury or circulatory pathology that cannot or hardly be visualized by preparation at autopsy. PMCTA has proven valuable in adult forensic cases, offering detailed visualization of vascular anatomy and hemorrhagic lesions [3]. However, its use in pediatric cases remains sporadic and no standardized pediatric PMCTA (pedPMCTA) protocols currently exist. One reason for this is that pediatric autopsies pose specific technical challenges: vascular dissection is difficult as in fetuses and infants' vascular calibres are minuscule compared with adults, requiring innovative catheterization methods and highly specialized contrast formulations to achieve adequate perfusion while limiting extravasation and artifacts. A recent study [4] demonstrated that virtual autopsy using PMCTA in fetuses and newborns with severe congenital heart or lung malformations provides a reliable and relatively simple method to diagnose complex cardiac and pulmonary anomalies, especially when great vessels are involved. Using umbilical vessel access, the authors reported strong concordance with prenatal diagnoses and conventional autopsy findings, suggesting that this technique may serve as a valuable adjunct in cases of induced termination of pregnancy, spontaneous delivery or neonatal death. A recent systematic review identified only six studies specifically addressing pedPMCTA in children from birth to 12 years of age [5]. Those studies primarily focused on feasibility and technical parameters, with most using femoral access, although alternative routes such as umbilical [6], transfontanellar [7] and intraosseous [8] have also been described. This lack of standardization is particularly critical in the context of suspected non-accidental head trauma

(NAHT), where bridging vein rupture is a hallmark lesion often associated with subdural hemorrhage. However, because of their caliber and anatomical delicacy, bridging veins are often extremely difficult to identify macroscopically at autopsy [9].

The aim of this study was to evaluate the feasibility of pedPMCTA using a standardised, weight-adapted protocol with a lipophilic contrast agent, and to assess its potential contribution to forensic investigations in infants and young children, particularly in cases of suspected non-accidental head trauma (NAHT), by enabling the visualisation of critical vascular structures such as bridging veins and ocular vessels.

Materials and methods

Study population & data collection

This retrospective study was conducted in accordance with the Declaration of Helsinki (revised in 2013) for research involving human subjects, and was approved by the relevant ethics and/or forensic authorities. The internal protocol was approved by the local ethics committee (approval no. 19–438). A total of 30 pediatric cases who underwent PMCTA between late 2019 and mid-2025 were included. The age of the deceased ranged from 0 day to 3.66 years (median: 120.5 days), including two neonates who died intrapartum, with a mean weight of 8.2 kg (range: 2.2–25.4 kg) and a mean length of 68.7 cm (range: 43–107 cm). The postmortem interval, defined as the time between death and the PMCTA procedure, ranged from 5 to 96 h (median: 38 h). All cases were referred to the Institute of Forensic Medicine Munich, Germany and underwent PMCTA prior to prosecutor-ordered forensic autopsy. All prosecutors agreed to the complementary procedure. Inclusion criteria consisted of deceased children undergoing medicolegal investigations by PMCT and autopsy, with an intact vascular system and adequate body preservation. Collected data included demographic information (age, sex, weight and length), postmortem interval and technical details of the PMCTA procedure. Causes of death were determined by a full forensic autopsy supported and complementary examinations when indicated (histology, toxicology, microbiology...). The cause of death included infectious diseases, congenital cardiac anomalies, trauma, perinatal complications and suspected sudden infant death syndrome but excluded confirmed NAHT cases. Injection routes were mainly femoral, but also included umbilical, intraosseous and other peripheral venous access. A complete table of demographic and technical variables is provided in Table 1.

Preparation of the vascular access – site of injection

Before the radiological examination, an external inspection of the body was performed, followed by placement of the vascular cannulas. If intravascular catheters e.g. from emergency care were already in place at the time of death and remained in situ upon arrival at the forensic institute, they were used for contrast agent injection (seven cases). Otherwise, peripheral vascular access was established, most commonly via femoral artery and vein dissection. Femoral access was preferred whenever feasible, as it allows direct vascular cannulation with minimal disruption to central anatomical structures. If no vascular access was in place, the accesses were inserted in the femoral vessels or, for venous vascular access, intraosseously according to the published scheme [8]. The peripheral arterial and venous access was established using age-appropriate intravenous catheters (14G to 24G; Vasofix® Braunüle, B. Braun Melsungen AG, Melsungen, Germany). In addition, vascular introducer sheaths (4 F to 9 F) were used depending on the subject's anatomy, for both arterial and venous access (Terumo®, Leuven, Belgium). In six cases where peripheral venous access was not feasible due to vessel fragility or anatomical constraints, intraosseous access was performed using a 20 G, 15 mm intraosseous needle (Arrow® EZ-IO®, Teleflex Inc., Morrisville, NC, USA). In some cases, due to the small caliber and previous clinical puncture attempts of the femoral vein, intraosseous access was preferred for venous contrast administration when dissection was not feasible. In two cases, the umbilical vein was still accessible and was used for venous phase injection placing intravenous catheters, as the children died during birth [Table 1].

Imaging protocol

PMCTA was performed using a GE Revolution CT 660 system in 27 cases and a Canon Aquilion Prime SP (128-slice) system in 3 cases. A native CT (120 kV, 50 mA, Tilt 0.0, Slice 1.5 mm until 2023; then 0.675 mm) preceded the angiography (120 kV, 100 mA, 50 eff.mA, Tilt 0.0, Slice 0.675 mm). Subjects were scanned in the supine position. The imaging protocol included the following phases: (a) a non-contrast CT acquisition, (b) an arterial phase, and (c) a venous phase. In some cases, only one contrast-enhanced phase (arterial or venous) was successfully performed. Scan parameters included slice thickness 0.625 mm, tube voltage 120 kVp and reconstruction algorithms such as maximum intensity projection (MIP) and multiplanar reconstructions (MPR).

Injection protocol

Once unenhanced multidetector CT (MDCT) images were acquired, the needed contrast agent mixture was created. A lipophilic contrast medium, specifically designed to minimize postmortem extravasation (Angiofil™, Fumedica, Switzerland), was combined with either rapeseed oil (10/30 cases – viscosity at 20 °C 74 mm²/s) or paraffinum perliquidum (20/30 cases – viscosity at 20 °C 36 mm²/s) at a 4% dilution ratio. The contrast mixture was prepared in advance in a container and drawn up as needed. The volume of contrast agent was calculated based on body weight: 10 mL/kg for arterial injection and 20 mL/kg for venous injection, according to the institutional protocol. After injection of the arterial volume and computed tomography imaging, the venous volume was injected. If an arterial injection was not possible, only a venous injection of contrast agent was performed. Injections were performed manually using 10 mL syringes.

Image Analysis

CT images were reviewed and post-processed using OsiriX MD (version 14.0.1; Pixmeo SARL, Bernex, Switzerland). Image interpretation was performed in consensus by two board-certified forensic pathologists with expertise in forensic radiology [JV, GB]. Vascular opacification was assessed for each case and for each contrast-enhanced phase (arterial and venous), using a semi-quantitative scale as follows: 0: no opacification – 1: partial opacification ($\geq$ appx. 50%) – 2: complete opacification ($\geq$ appx. 80%). A score of “1” was also assigned when only one of two paired vessels (arteries or veins) showed complete opacification.

A total vascular opacification score was calculated for each subject across predefined anatomical regions, including the cerebral arteries (anterior, middle, and posterior cerebral arteries), ophthalmic and central retinal vessels, the basilar trunk, carotid (external, internal, and common), vertebral and jugular veins, the aortic arch and descending aorta, coronary ostia, pulmonary arteries, superior longitudinal sinus and bridging veins, abdominal vessels (superior mesenteric, renal arteries and veins, hepatic veins, inferior vena cava), and peripheral vessels (common iliac, brachial and femoral arteries and veins). Particular attention was paid to venous structures relevant to forensic assessment (e.g., bridging veins, orbital and ocular vascularization). For bridging veins, a partial score was given when only the frontal bridging veins were visualized. The central retinal vessels were considered as a single unit as it was not possible to differentiate between arterial and venous vessels postmortem by imaging. The presence of an arteriovenous communication was assessed in all cases.

Statistical analysis

The measures of interest were reported as mean values or median values, depending on whether when the data distributions were deviated from a normal distribution according to a quantile-quantile plots. For each deceased who received contrast agent, scores were computed that summed the semi-quantitative vascular opacification of the different vessels separately for arteries and veins. Linear models were used to assess the association between the weight, the mixture, the injection site, the time before the angiography and the scores. The parameters, 95% confidence intervals and associated p-values were estimated. The normality of the residuals was assessed using quantile-quantile plots. Language refinement was supported through AI-assisted copy editing using ChatGPT (OpenAI), limited strictly to improvements in grammar and style.

Results

Technical feasibility

All 30 subjects received at least one injection, either during the arterial or venous phase. The main technical limitation was extravasation at the injection site and problems during preparation due to the small vessel diameter and previous clinical puncture attempts.

Arteriovenous (AV) shunts were clearly observed in 8/30 cases. In $n=2$ cases a big open foramen ovale was observed [Figure 1], but an arterial and venous injection could be

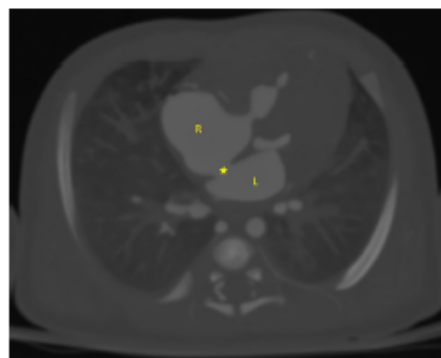


Fig. 1 pedPMCTA in a 2-week-old male infant (weight: 3.1 kg), following sequential femoral arterial and then venous injections of lipophilic contrast agent. Axial contrast-enhanced CT image showing contrast passage from the right atrium (R) to the left atrium (L) through a patent foramen ovale (yellow star), suggesting intracardiac shunting. In this case, arterial enhancement was improved following venous injection, likely due to the presence of this communication. This observation highlights the impact of physiological postnatal shunts on vascular distribution in pedPMCTA

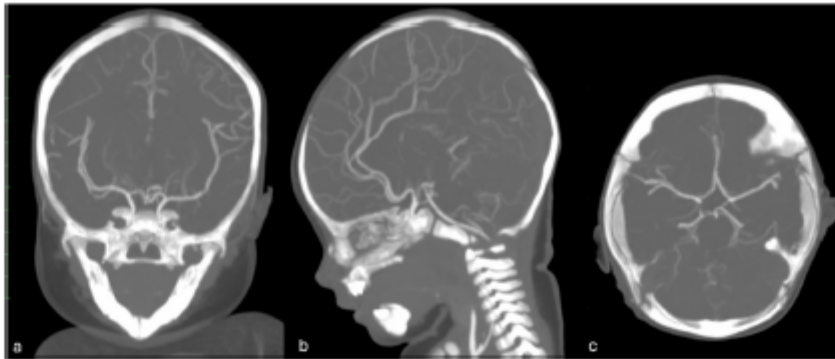


Fig. 2 Arterial-phase pedPMCTA in a 7-week-old girl, performed via femoral arterial access. Multiplanar MIP reconstructions of the head demonstrate diagnostically sufficient opacification of the internal carotid arteries, circle of Willis, basilar artery, posterior cerebral arteries, middle cerebral arteries, and anterior cerebral arteries. (a) Coronal view; (b) Sagittal view; (c) Axial view. These images illustrate the feasibility of detailed cranial vascular assessment in neonates and young infants using the pedPMCTA protocol

carried out as planned. In $n=6$ of these eight cases, due to the AV-Shunt, only a venous injection was successfully carried out to fill the arterial vessel retrogradely. In these eight cases, where there was no arterial injection, the venous injection was the first and only one. In six out of these eight cases, an arterial opacification followed due to the AV shut which resulted in a simultaneous filling of the entire vessel system.

In $n=4$, a single venous injection was sufficient to achieve satisfactory vascular opacification, also in the arterial system. In $n=1$ the only venous injection with an AV shut produced a poor arterial filling, but in one other case ($n=1$), the retrograde filling led to a nearly completely filled arterial and venous system. In $n=20$ cases a separate arterial and venous injection was possible. A total of $n=26$ cases had a fully assessable vascular system. $N=1$ had no AV shunt and no arterial injection, so in this case, the venous phase lead only to an assessable venous vessel system. In $n=3$ cases an arterial injection took successfully place but a venous injection of contrast agent mixture failed due to technical problems or extravasations.

Arterial access was achieved predominantly via the femoral artery ($n=21$), followed by other peripheral arterial access ($n=2$). Venous access was obtained through femoral ($n=14$), intraosseous ($n=6$), umbilical ($n=2$), other peripheral venous access ($n=3$) or central venous lines ($n=2$). The mean volume of contrast injected was 84,9 mL for the arterial phase (range: 15–200 mL), and 152,7 mL for the venous phase (range: 15–400 mL), yielding a total mean injection volume of 206.4 mL (range: 55–600 mL).

Vascular opacification

The mean arterial opacification score was 27,4 out of 34, and the mean venous score was 16,8 out of 24. Details of the

evaluation of the vascular opacification can be seen in Table 3. Diagnostically sufficient opacification was defined as the visualization of more than 50% of the expected vascular territory (i.e., a total score strictly greater than 17/34 for arteries and 12/24 for veins). This threshold was chosen based on the semi-quantitative scoring system, where a score of “2” reflects complete opacification and reflects diagnostically sufficient vascular filling in the pediatric postmortem setting. For instance, a score of 2 in the cerebral arteries corresponded to full delineation of the Circle of Willis [Figure 2] and its major branches. Using this definition, diagnostically sufficient arterial opacification was achieved in 23 out of 30 cases (76.7%) and diagnostically sufficient venous opacification in 24 out of 30 cases (80%). A representative whole-body arterial-phase pedPMCTA is shown in Fig. 3.

For the arteries, no significant association was found between the scores and arterial access, mixture, weight or postmortem interval. For the veins, each additional kilogram in weight was associated significantly with a decrease of 0.57 points in score ($p=0.01$). Other variables were not

Fig. 3 Arterial-phase pedPMCTA in a 2.5-year-old boy, performed by manual injection of 130 mL of contrast medium via femoral arterial access. Coronal MIP reconstruction shows excellent contrast opacification of the entire arterial system, including the aortic arch and its cervical branches, thoracoabdominal aorta, limb arteries, and cerebral vessels. A contrast leakage is visible (star) in the anatomical region of the right adrenal gland. This case illustrates the feasibility of comprehensive vascular imaging in older pediatric subjects using the pedPMCTA protocol

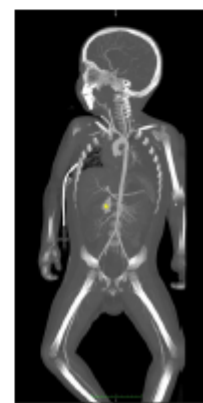


Table 2 Results of linear regression models assessing the association between vascular opacification scores and technical or demographic variables in (a) arterial phase and (b) venous phase. Coefficients, standard errors (SE), 95% confidence intervals (95% CI), and p values are shown

Parameter	Coefficient	SE	95% CI	p
(a) Arterial Phase				
(Intercept)	32.48	2.59	(27.03, 37.92)	<0.001
Arterial access (peripheral - other) (ref. femoral)	1.09	3.82	(-6.92, 9.11)	0.778
4% Angiofil, Rapseed oil (ref. paraffinum)	-2.91	2.25	(-7.64, 1.82)	0.213
Weight (kg)	0.09	0.22	(-0.36, 0.55)	0.668
PMI (h)	-0.04	0.05	(-0.15, 0.07)	0.435
(b) Venous Phase				
(Intercept)	17.53	2.56	(12.23, 22.84)	<0.001
Venous access (not io) (ref. io)	1.58	2.25	(-3.09, 6.25)	0.490
4% Angiofil, Rapseed oil (ref. paraffinum)	-3.82	1.96	(-7.88, 0.24)	0.064
Weight (kg)	-0.57	0.20	(-0.98, -0.15)	0.010*
PMI (h)	0.08	0.05	(-0.02, 0.18)	0.110

significantly associated with the venous scores [Table 2]. For bridging veins [Figure 4] no significant association was found. Coronary ostia were visualized in 26/30 cases (86.6%), bridging veins and central retinal vessels in 13/30 (43.3%), while the ophthalmic vein and artery were opacified in 21/30 (70.0%) and 8/30 (26.7%) cases.

Femoral venous access showed the highest mean venous opacification score, followed by other peripheral and intraosseous routes. Central venous lines resulted in heterogeneous outcomes, with some complete failures. Interestingly, arterial opacification was observed in certain cases despite the absence of arterial injection. In these instances, passive arterial filling from venous circulation via arteriovenous shunts was observed.

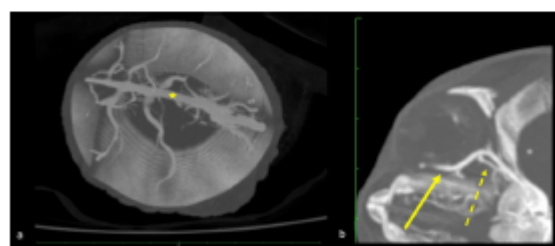


Fig. 4 Venous-phase pedPMCTA in a neonate who died in the immediate postnatal period (weight: 2.2 kg), following umbilical venous injection of 60 mL of lipophilic contrast agent. (a) Axial MIP reconstruction showing the superior sagittal sinus filled with contrast (star), from which bridging veins emerge. (b) Axial MIP reconstruction of the orbit showing opacified ophthalmic vessel (solid arrow) and central retinal vessel arising from it (dashed arrow). This case illustrates the ability of venous-phase pedPMCTA to depict cerebral and ocular venous structures relevant in forensic

Artefacts and limitations

Common artefacts [10] included extravasation of contrast agent ($n = 4$), air bubbles within vascular structures ($n = 6$), and contrast sedimentation ($n = 2$). In 7 of 30 cases, only a venous injection was performed. An arterial injection was skipped due to AV-shunt, technical failure or extravasation during attempted arterial access. In six of these seven cases the arterial system was partly or fully filled with contrast agent mixture due to an AV shunt. These artefacts variably affected the interpretability of the images, particularly in smaller or peripheral vessels. In some cases, inadequate injection technique or prolonged PMI contributed to reduced vascular filling or increased background signal. Nonetheless, none of these limitations systematically prevented the evaluation of major thoracic, abdominal or cerebral vascular structures.

Discussion

While PMCTA protocols are now well established in adults [11–13] and have shown promising feasibility in fetal applications [14–16], their adaptation to pediatric populations remains limited by anatomical and technical challenges. Those include a broad range of body sizes, tiny vascular lumen and difficulties in establishing reliable vascular access [6, 8]. The present study sought to evaluate a tailored, weight-adapted PMCTA protocol in small children and to assess its feasibility, diagnostic performance and potential forensic applications. Compared with conventional autopsy, pedPMCTA enables rapid and non-destructive visualization of vascular structures that are otherwise extremely difficult to access by dissection, such as intracranial venous pathways or small vessels. It also preserves specimen integrity, which could be important in medical autopsy cases when family consent is limited.

Feasibility and technical considerations

This study supports the feasibility of pedPMCTA using a manual, weight-adapted injection protocol with a lipophilic contrast agent across a broad range of infants, toddlers and postmortem intervals. Our approach enabled very good intravascular filling in the vast majority of cases, despite anatomical variability and the inherent small caliber of pediatric vessels. Indeed, in neonates and infants, vascular opacification can be technically challenging due to small vessel calibers. However, diagnostically sufficient arterial filling was achieved in most cases (26 out 30 cases), including very young diseased [Fig. 2]. Angiofil™ [17], diluted in rapeseed oil or paraffinum perliquidum, proved suitable

for small-body imaging. Although the type of oil mixture used in our study did not show a statistically significant association with vascular opacification [Table 2], the lower viscosity of paraffin perliquidum (36 mm²/s at 20 °C) compared with rapeseed oil (74 mm²/s at 20 °C) may indicate that paraffinum perliquidum is better suited for achieving homogeneous vascular filling.

Previous experimental studies have shown that μ Angiofil™, a polymer-based contrast agent, enables a novel postmortem microangio-computed tomography (microangioCT) approach with exceptionally high spatial resolution, allowing the visualization of very small vessels. Because it can effectively perfuse vessels across a wide range of calibers, this agent holds promise for extending postmortem angiographic applications beyond the pediatric setting [18]. Diagnostically usable images could be obtained even when the arterial opacification was obtained with retrograde filling of the arterial system.

Vascular access & injection strategies

Femoral access, although technically challenging in small children, remains the most reliable peripheral route for PMCTA. It allows direct cannulation without creating artefacts in critical autopsy areas like the thoracic inlet. Its effectiveness in adults [11, 19] gives a hint for its adaptation for pediatric use and may support future standardization efforts. In our cohort, intraosseous access was used in six cases when peripheral venous access was not feasible, offering a minimally invasive alternative [8]. Umbilical vein cannulation was successful in two neonates and should be used in perinatal cases when the umbilical cord is intact [6, 20]. Standardized access strategies adapted to age and anatomy could improve reproducibility across centers [8].

Spontaneous arteriovenous filling and shunt observation

Arteriovenous shunts were visualized in 8/30 cases [Fig. 3]. In 4 of these, a single injection yielded satisfactory arterial and venous opacification, while 2 others demonstrated partial arterial filling from a venous injection. These findings align with prior observations in perinatal imaging [21]. This suggests that under certain conditions, single-phase PMCTA protocols may be diagnostically sufficient, reducing procedure time and complexity.

Vascular opacification and trends

Diagnostically sufficient vascular filling was achieved in 76.7% of arteries and 80% of veins. This supports the robustness of our protocol across varying ages, body sizes,

and PMIs. Notably, diagnostically sufficient opacification was possible up to 96 h PMI, extending the diagnostic window beyond the previously suggested 48-hour limit [22]. Statistical analyses revealed no significant link between opacification scores and age or PMI. The absence of significant association with weight was expected, given the weight-adapted protocol. However, a negative association was observed between the children's weight and their venous system score. This suggests that the venous system may have a weight-dependent filling pattern, and future investigations should assess whether adjusting injected contrast volumes more strictly according to body weight could improve venous visualization. This trend suggests that a fixed mL/kg approach may not fully account for variations in body composition, particularly in edematous or overweight infants. Although this is not statistically proven in our cases, there is precedent for adjusting contrast volume in the context of edema [22]. Volume adaptation should be individualized and can also justify increasing the dose when appropriate. To address this, future protocols could differentiate arterial and venous injection volumes. Arterial volume might be based on expected weight (e.g., 50th percentile using height-based charts), while venous volume could reflect actual body weight. The greater compliance of the venous system may require more contrast in cases of fluid overload, whereas arterial tone remains relatively constant. Tailoring the protocol to such variables could enhance image quality and diagnostic reliability.

Assessment of forensically relevant structures

Radiologic and histopathologic evidence has emphasized the crucial role of venous injury, including sinus thrombosis, bridging vein rupture and retinal hemorrhages in the pathophysiology of NAHT [23]. To explore the potential of pedPMCTA in evaluating venous structures non-invasively, we assessed the superior sagittal sinus, the bridging veins and the ocular vascularization to understand if PMCTA could contribute to the non-invasive evaluation of venous structures in pediatric decedents.

Cerebral venous structures

We first assessed the *superior sagittal sinus*, as some authors have suggested that non-traumatic dural sinus thrombosis might mimic or coexist with NAHT-related findings [23, 24]. Among the 30 analysed cases, 15 allowed the visualization of the superior longitudinal sinus. However, it has to be noted that no deceased child older than 1.5 years or more than 12 kg body weight (each $n = 7$) had a contrasted sagittal sinus or contrasted bridging veins. This indicates that the protocol provides too little venous vessel filling with this

age/weight. We therefore hypothesise that the injected volume in these cases needs to be increased, as the visualisation of these structures is important. Although non-traumatic intracranial venous thrombosis has been proposed as a differential diagnosis in NAHT, it remains rare and is typically associated with underlying risk factors such as dehydration, infection or malignancy. Nonetheless, being able to assess venous thrombosis may add value in the evaluation of ambiguous cases.

The *bridging veins*, especially susceptible to tearing under shearing stress [25], are of particular forensic interest. A large autopsy series has shown that these veins are fragile, variable in number and mainly located over the convexities of the frontal and parietal lobes [9]. Their anatomical delicacy makes them difficult to identify once the brain has been removed, and histologic confirmation of rupture is not always feasible. While conventional autopsy may overlook them, ante mortem imaging has demonstrated that bridging veins draining into the superior sagittal sinus can be visualized by CT angiography [26]. Based on these findings, PMCTA could offer a non-destructive alternative for assessing bridging veins in deceased infants [7]. In our study, bridging vein opacification was achieved in 13 out of 30 cases (43%), supporting the technical feasibility of their depiction, though emphasizing the need for further protocol refinement [Fig. 4a]. Identifying bridging vein rupture could significantly aid in differentiating abusive from accidental head trauma in cases of subdural hemorrhage. Notably, bridging veins were visualized in 13 of the 15 cases (87%) in which the superior longitudinal sinus was also opacified, suggesting that sinus filling may be a prerequisite for their reliable depiction. However, PMCTA's spatial resolution may still be insufficient to detect subtle discontinuities, and findings have yet to be systematically validated by histology. Future research should correlate imaging with autopsy and investigate how technical factors, such as injection parameters or postmortem interval, impact venous detectability.

Ocular vessels

Retinal hemorrhages are key forensic signs but may be missed if eyes are not enucleated during autopsy. PedPMCTA offers a potential non-invasive alternative evaluation of the *ocular vascularization*. In our series, the ophthalmic veins were visualized in 70% of cases, the central retinal vessels in 43%, and the ophthalmic artery in 27% [Fig. 4b]. While PMCTA does not yet replace traditional methods, these preliminary results suggest it could contribute to postmortem evaluation of retinal hemorrhages—particularly if dedicated orbital protocols and higher-resolution acquisitions, e.g. photon-counting CT are employed. Evidence from living children indicates that magnetic resonance imaging has

shown promising results in this regard [23], whereas in the postmortem setting PMCTA may provide a complementary approach, particularly when MRI or ophthalmologic expertise is not available.

Coronary evaluation

Coronary artery anomalies, although frequently asymptomatic, are recognized causes of sudden death in infants and children [27]. In our series, coronary ostia were visualized in 26/30 cases (86.6%). The systematic identification of ostia is a promising first step toward comprehensive postmortem coronary assessment. The assessment of these important vessels will be evaluated separately. Targeted postmortem coronary angiography has already demonstrated the value of coronary imaging in neonates with congenital heart disease [28]. In the future, pedPMCTA could play a key role in postmortem cardiac imaging, especially if technical refinements allow comprehensive coronary visualization, including critical segments such as interarterial or intramural courses. These improvements will be essential to better assess the role of coronary anomalies in sudden pediatric deaths.

Study limitations

This was a single-center feasibility study with a limited sample size and heterogeneous population, precluding detailed subgroup analysis. One limitation could be seen in the fact that the interpretation of the obtained images was performed by two forensic pathologists, without a board-certified radiologist. However, as the aim of the study was just to verify the technical approach by indicating if specific vessels real filled with contrast agent or not, we considered the knowledge of the well trained for forensic pathologists was enough to obtain this goal. Indeed, no radiological interpretation of paediatric pathology was performed in the context of this study. No comparison with autopsy findings was yet performed, so it is not possible to calculate sensitivity or specificity. Prospective studies comparing PMCTA to both macroscopic and microscopic autopsy findings are needed to validate its diagnostic accuracy. Manual contrast injection could introduce variability, and vascular leakage or incomplete filling may mimic pathology. Finally, although image quality was assessed using opacification scores, interobserver variability was not measured due to consensus reading, and scoring was based on visual interpretation. The small sample also limited the power in the scores analysis. The mixture had a similar effect on the scores of arteries and veins, albeit not significant, presumably due to the limited sample size. Further studies on larger scales would be advisable.

Future perspectives

Despite increasing interest in pedPMCTA, no standardized protocol currently exists. The development of consensus-based guidelines is essential to ensure reproducibility and improve diagnostic consistency therefore allowing for robust intercenter comparisons. Future studies should focus on protocol optimization, including the adaptation of injection volumes to individual physiological variables, particularly in cases of edema or overweight infants, and the refinement of vascular access strategies based on age and body habitus. The routine use of dual-phase protocols also warrants reassessment, as their necessity may vary depending on case-specific goals and vascular anatomy. Multicenter collaborative efforts will be critical to validate the diagnostic performance of pedPMCTA, define reliable thresholds for adequate vascular filling, and better characterize normal and pathological post-mortem vascular patterns in infants and young children.

Conclusion

This study confirms the feasibility of pedPMCTA using a standardized, weight-adapted protocol and demonstrates its diagnostic value in infants and young children by manually injecting through peripheral access. The vascular access should be preferably femoral if possible, injecting 10mL/kg in the arterial phase and 20mL/kg in the venous phase of a lipophilic contrast agent diluted to 4% in oil of low viscosity. When tailored to body size, pedPMCTA produces sufficient quality vascular imaging that can supplement the findings of forensic autopsy and may substantially enhance diagnostic yield, particularly for vascular lesions that are difficult to detect macroscopically. It is not intended to replace a (prosecutor-ordered) autopsy, which remains compulsory, but rather to enhance its diagnostic yield, particularly for vascular lesions that are difficult to identify macroscopically, such as bridging-vein ruptures or subtle cardiac and retinal hemorrhages. Outside the judicial context, where a hospital (consent-based) autopsy may be declined, pedPMCTA offers a less-invasive alternative that can still provide valuable information for clinicians and families. Larger, multicenter studies are needed to validate these findings, refine pediatric protocols and define the precise role of pedPMCTA in both forensic and clinical post-mortem practice.

Parameter	Coefficient	SE	95% CI	p
(Intercept)	17.53	2.56	(12.23, 22.84)	<0.001
Venous access (not io) (ref: io)	1.58	2.25	(-3.09, 6.25)	0.490
4% Angiofil, Rapseed oil (ref: paraffinum)	-3.82	1.96	(-7.88, 0.24)	0.064
Weight (kg)	-0.57	0.20	(-0.98, -0.15)	0.010*
PMI (h)	0.08	0.05	(-0.02, 0.18)	0.110

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Data Availability The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Competing interests The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this article.

Clinical trial number Not applicable

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Discussion and perspectives

This thesis set out to advance PMCTA in fetal and pediatric populations by addressing its development, validation and practical integration into forensic and clinical workflows. This work is structured around three interdependent research axes, progressing from methodological development to feasibility assessment. The first consists in the conception and technical establishment of a FPMCTA protocol using a lipophilic CA[70]. The second is a systematic review synthesizing current fetal and pedPMCTA practices, identifying critical gaps in standardization and proposing a conceptual decision tree to support case selection and workflow planning[71]. The third presents a 30-case PMCTA series in infants and young children, providing feasibility data on access strategies, vascular opacification patterns and forensic relevance. Rather than constituting isolated investigations, these studies form a coherent and progressive framework that demonstrates how fetal and pedPMCTA could evolve from proof-of-concept applications into structured diagnostic tools. They collectively show that PMCTA in early life is not only technically achievable but also diagnostically meaningful and ethically defensible when applied under appropriate clinical or forensic governance. Beyond demonstrating feasibility, the thesis establishes the necessary foundations for the field's next phase of maturation: shifting from individual experience to shared standards, from case-based experimentation to multicenter validation, and from optional adjunct to recognized component of fetal and pediatric postmortem investigation. What follows in this discussion is not only a synthesis of the thesis' empirical contributions, but also a roadmap for the consolidation, dissemination and ethical deployment of PMCTA within both clinical and forensic pathology.

From Concept to Protocol: Establishing a FPMCTA Method

The first axis of this thesis developed a technically feasible and diagnostically informative protocol for FPMCTA based on a two-phase intra-umbilical injection of a lipophilic contrast [70]. The time-related limitations for fetal postmortem angiography reported in the literature [72] may be overcome through the use of this oily formulation, which maintains feasibility even after a postmortem interval exceeding 48 hours. Such an approach has already been described for postmortem angiography in preterm neonates [73] and newborns [74]. Unlike

hydrophilic (water-soluble) CA, which tend to leak through degraded vasculature, the lipophilic medium demonstrated strong intravascular retention, ensuring satisfactory perfusion even in markedly autolyzed specimens. Among the 25 examined fetuses, interpretable arterial opacification was achieved in 15 cases (60 %), while venous opacification was successful in 18 cases (72 %), confirming the reproducibility of the method under heterogeneous postmortem conditions.

From an imaging perspective, MIP reconstruction facilitated rapid visualization of vascular filling, assessment of network continuity, and estimation of opacification levels. The application of CRT rendering, with its high dynamic range illumination, enhanced the realism of 3D reconstructions and improved spatial depth perception, enabling the generation of detailed fetal anatomical models that strengthened the interpretative and predictive value of FPMCTA [75].

Collectively, these results indicate that FPMCTA is not merely technically achievable but capable of yielding diagnostically usable vascular information in a population previously limited to isolated case studies or small experimental series. By overcoming major challenges such as collapsed vessel lumens, advanced tissue degradation and limited perfusion tolerance, the proposed protocol provides a reproducible methodological framework applicable to both forensic and perinatal pathology settings. It bridges a longstanding technical gap between radiology and fetopathology, enabling targeted vascular assessment. Despite these advances, imaging artefacts previously reported in the literature [58] were also encountered, including sedimentation of the paraffin-oil CA, layering within arterial lumina, and incomplete opacification of certain venous structures.

Nevertheless, feasibility alone does not establish diagnostic validity. Future multicenter investigations directly correlated with conventional autopsy or histopathology will be required to determine sensitivity and specificity across different congenital malformation types. In this regard, the present protocol constitutes not only an operational technique but a foundational platform toward international standardization and future diagnostic benchmarking of FPMCTA.

Looking ahead, additional research directions should focus on the systematic mapping of fetal vascular and organ abnormalities through a standardized approach to radiological interpretation. The maturation of adjacent brain structures and the development of gyri have been shown to induce positional and morphological changes in cerebral arteries [76]. Similarly, detailed characterization of the intrahepatic portal venous system will be crucial to improving prenatal counselling and postnatal management in cases of umbilical–portal–systemic venous shunts [77]. Furthermore, extending this imaging technique to the placenta could help elucidate additional causes of death related to placental pathology, such as abruption, fetomaternal hemorrhage, or cord accidents [78].

Synthesis and Gaps: A Systematic Review of FPMCTA and pedPMCTA

The second axis of the thesis addressed the lack of standardization and the methodological heterogeneity in fetal and pediatric PMCTA through a systematic review of the literature. Ten studies were included [60, 61, 65, 70, 72, 74, 79-82], encompassing fetal, infant, and child PMCTA cases, with sample sizes ranging from single-case reports to moderate-sized series.

This analysis revealed that although fetal and pedPMCTA is increasingly reported, substantial variability persists across studies regarding CA, injection techniques, access routes, imaging timing, and reporting standards. Moreover, inconsistencies in age cutoffs and inclusion criteria hinder meaningful inter-study comparison and synthesis. A critical gap identified through this review concerns the absence of age-specific, validated protocols.

For FPMCTA, umbilical access is favored whenever the cord is intact and accessible [60, 61, 70, 79, 80]. A two-phase manual injection is commonly applied, first via the umbilical artery, followed by the umbilical vein, with optional ultrasound guidance to ensure precise vessel cannulation [79]. Peripheral venous catheters without a metal mandrin are suggested, ranging from 14G to 22G for arterial and 20G to 24G for venous access. Gradual injection facilitates full vascular opacification [80]. When umbilical access is not feasible or the fetus is too small, ultrasound-guided intracardiac injection represents a viable alternative [61, 70].

Pediatric PMCTA approaches are frequently derived from adult procedures, with insufficient adaptation to the distinct physiological and vascular characteristics of fetuses and young children. While several authors acknowledge the need for weight-adjusted contrast volumes, low-pressure perfusion systems, and alternative vascular access routes (e.g., umbilical, cardiac, or peripheral), such parameters remain rarely standardized or validated across centers.

In infants and children up to 12 years of age, femoral vessel access is generally preferred for performing multiphase PMCTA when umbilical vessels are no longer available [82]. The protocol requires injection of a contrast volume adjusted to body size, using flow rates adapted from established adult PMCTA procedures [82]. Previously placed peripheral catheters or in situ medical probes may also be reused to simplify the injection process [72]. If femoral access cannot be achieved, or when NAHT is suspected, alternative routes have been proposed. For younger children, a fontanellar approach may be adopted, consisting of a slow, controlled injection through a 21G needle inserted into the fontanel membrane according to the child's age and cranial size [65]. For children above 2.5 kg, intraosseous access offers another option, allowing venous and, when arteriovenous shunts remain patent, arterial opacification through gradual injection of contrast into the bone marrow using a 15 mm, 15G bone needle [80].

Synthesizing these heterogeneous practices, the review proposed a conceptual decision tree designed to guide clinicians and radiologists in selecting optimal PMCTA strategies according to patient age, available access routes, and the clinical or forensic context. This decision tree integrates evidence from published protocols with practical constraints such as scanner availability, operator expertise and regulatory context.

By mapping current practice and proposing a flexible framework, the review contributes to building a shared language and methodological roadmap for fetal and pedPMCTA. It further underscores the urgent need for multicenter prospective studies to assess diagnostic performance, define reference standards, and validate age-adjusted protocols across diverse forensic and clinical settings.

From Feasibility to Insight: A 30-Case Series in Infants and Young Children

The third axis of this thesis evaluated the feasibility and diagnostic yield of pedPMCTA in a prospective cohort of 30 infants and young children aged 0 to 3.6 years. Although PMCTA protocols are now well defined in adult postmortem imaging [2, 23, 83] and have shown encouraging results in fetal investigations [61, 70, 84], pediatric adaptation continues to face anatomical and technical limitations, including small vessel calibers, variable body proportions, and the difficulty of obtaining stable vascular access[74, 80]. The present work aimed to develop and evaluate a weight-adapted, lipophilic-contrast protocol specifically optimized for pediatric postmortem applications, and to examine its diagnostic contribution in a forensic setting.

Vascular access was successfully established in all subjects, mainly through femoral cannulation, but also via umbilical, intraosseous, or alternative peripheral routes when required. Using manual, weight-adjusted perfusion with a lipophilic CA (Angiofil™ diluted either in rapeseed oil or paraffinum perliquidum), diagnostically adequate vascular opacification was obtained in the majority of cases[85]. Over three-quarters of the cohort presented interpretable arterial filling and approximately four-fifths showed sufficient venous enhancement, consistent with feasibility levels reported previously. The lower viscosity of paraffinum perliquidum (36 mm²/s at 20 °C) compared to rapeseed oil (74 mm²/s at 20 °C) appeared to favor a more homogeneous vascular distribution. These findings strengthen the evidence that lipophilic contrast formulations are well suited for pediatric PMCTA, allowing visualization of small-caliber or even partially autolyzed vessels [86].

An additional methodological observation was the occurrence of spontaneous arteriovenous shunting in nearly one-quarter of cases, producing retrograde arterial opacification following venous injection alone. Such shunts, only occasionally reported in perinatal imaging[60], may have diagnostic significance, since they can imitate or obscure pathological vascular communications. Typical imaging artefacts including contrast extravasation, air entrapment, and sedimentation within dependent vessels were also observed [58], but they did not prevent interpretation of the main thoracic, abdominal, or cerebral vascular networks. Under

certain conditions, therefore, even single-phase perfusion may yield diagnostically informative data, suggesting potential simplification of existing PMCTA workflows for pediatric cases.

The study further emphasized the diagnostic potential of PMCTA for evaluating key forensic structures. Coronary ostia were recognizable in almost ninety percent of cases, corroborating earlier postmortem studies in neonates with congenital cardiac malformations [87, 88]. This result highlights the relevance of PMCTA in detecting coronary anomalies potentially linked to sudden pediatric death. Bridging veins were successfully depicted in 43 % of the series, particularly in cases where the superior sagittal sinus was also filled, echoing previous anatomical descriptions of their fragility and topographic variability [89, 90]. Their non-destructive visualization represents an important contribution to the investigation of abusive head trauma, in which bridging vein rupture and subdural bleeding remain critical diagnostic features [91, 92]. Likewise, ocular vascularization was visualized in 43 % of subjects, suggesting that PMCTA could serve as a non-invasive adjunct or substitute for enucleation in cases requiring retinal hemorrhage assessment [91].

Quantitative analysis revealed that venous opacification tended to decline with increasing body weight, implying that the standard mL/kg approach might not fully accommodate physiological variability in venous compliance or fluid retention [72]. This weight-dependent trend supports the need for refined, individualized perfusion strategies potentially distinguishing volumes based on expected weight from volumes based on actual body weight. Such differentiation could improve perfusion homogeneity, especially in edematous or overweight infants, and enhance the reproducibility of angiographic outcomes across institutions.

Collectively, these results demonstrate that pedPMCTA can be conducted reliably over a broad postmortem interval—up to at least ninety-six hours—using accessible vascular routes and simple, reproducible manual perfusion techniques. The identification of spontaneous shunts, the comparative evaluation of access routes, and the recognition of weight-related perfusion patterns provide novel methodological insight into pediatric postmortem angiography. By defining these technical determinants and confirming the feasibility of coronary and venous assessment, this work contributes essential groundwork for developing standardized, age-

specific PMCTA protocols. It also underscores the need for multicenter validation studies aimed at quantifying diagnostic accuracy, optimizing perfusion thresholds, and refining interpretive criteria for both clinical and forensic applications in early childhood deaths.

Clinical, Forensic and Ethical Implications

Fetal and pedPMCTA occupy a distinct niche at the intersection of clinical investigation, forensic evaluation and ethical mediation. From a clinical perspective, it enables targeted visualization of vascular anomalies that are difficult to access via dissection-based autopsy, particularly in the thoracic inlet, cardiac outflow tracts or intracranial venous pathways. In infants with suspected congenital heart disease or unexplained collapse, pedPMCTA can provide rapid anatomical clarification while preserving specimen integrity, allowing subsequent histological sampling without disrupting key structures. Its ability to archive volumetric datasets further facilitates interdisciplinary case review, including delayed re-evaluation without repeat intervention.

In the forensic setting, pedPMCTA may offer specific advantages in cases of suspected NAHT or unexplained sudden death. The depiction of the cerebral venous system particularly the superior sagittal sinus, bridging veins, and ocular vascularization has clear diagnostic value [91, 93], providing objective imaging evidence that can confirm or exclude traumatic vascular injury. In jurisdictions where full autopsy is contested or limited by parental refusal or cultural constraints, angiographic imaging may serve as an acceptable compromise, improving transparency without undermining legal rigor. However, it should not be construed as a replacement for forensic autopsy, but rather as a decision-support tool capable of refining dissection strategy, guiding sampling and facilitating communication with non-medical stakeholders such as magistrates or family members.

Ethically, the value of fetal and pedPMCTA lies not only in its diagnostic contribution but also in its potential to reconcile parental reluctance with investigative necessity. In perinatal bereavement contexts, minimally invasive techniques are increasingly viewed as more acceptable than full-body dissection, provided that they are applied transparently and within clear governance frameworks. FPMCTA and pedPMCTA align with this expectation by offering visual answers without visible intrusion. Nevertheless, expectations must be managed:

vascular imaging cannot detect infectious or metabolic disorders, and its limitations must be explicitly communicated to avoid misinterpretation.

In summary, the strength of fetal and pedPMCTA lies in their role as complementary, not substitutional, tools. Their contribution is greatest where dissection is constrained, suspicion is focused or structural causes of death are plausible. Their integration into routine fetopathology and pediatric postmortem practice will depend not only on technical refinement but on sustained medico-legal dialogue, ethical clarity and institutional willingness to adapt established investigative hierarchies.

Future Directions and Research Perspectives

The future of fetal and pediatric postmortem imaging will depend on four converging pillars: standardization, multicenter collaboration, technological innovation and ethical governance.

A first and urgent priority is the standardization of fetal and pedPMCTA protocols. While adult applications have benefitted from coordinated validation studies, pediatric implementations remain heterogeneous. Ongoing international initiatives are now beginning to address this gap through protocol harmonization efforts, emphasizing the need for age- and weight-adapted contrast volumes, eventually controlled perfusion pressures and clearly defined success criteria. Structured multicenter registries, supported by bodies such as the ESPR and the ISFRI [28] will be essential to ensure data comparability, particularly for rare pathologies in neonatal and fetal cohorts.

The TWGPAM [69] plays a pivotal role in this landscape. As an internationally anchored network spanning from Belgium, France, Poland, Japan, Brazil, Germany, Switzerland and beyond, TWGPAM is uniquely positioned to coordinate consensus-building, develop shared repositories, and facilitate method validation across borders. The present thesis directly contributes to this movement and should serve as a foundation for prospective joint validation studies.

Technological advances will further accelerate progress. AI [94-96] may reduce interobserver variability by assisting interpretation and highlighting subtle vascular patterns invisible to the naked eye. Photogrammetry (3D modelling from photographs), volumetric reconstructions,

and 3D printing [97] already used in forensic presentations, will increasingly support communication with clinicians, magistrates, and families. Photon-counting detector CT (PCDCT)[98-100] offers promising advantages in bone visualization and metal artefact reduction, although current implementations do not yet extend to pediatric PMCT or PMCTA, underlining the need for dedicated adaptation rather than direct transposition from adult protocols.

Beyond technology, capacity building is imperative. Few centers currently provide structured training in fetal and pediatric postmortem imaging, and formal curricula, simulation platforms and interdisciplinary fellowships in forensic radiology and pathology are urgently needed to ensure interpretative consistency. Parallel to this, open-access databases, standardized reporting templates and structured audit systems would foster reproducibility and accelerate collective expertise.

Finally, ethical safeguards must remain central. Parental consent contexts demand transparency regarding both capabilities and limitations, particularly when imaging is offered as a less invasive alternative. Future regulatory frameworks will need to define acceptable indications, communication standards and medico-legal admissibility [101] to avoid misuse or overstatement of diagnostic certainty.

In summary, FPMCTA and pedPMCTA is entering a transition phase, from feasibility research to implementation science. Future studies should validate the fetal protocol in larger cohorts, test the decision tree derived from the systematic review and further characterize shunting phenomena, opacification thresholds and the visibility of key forensic structures such as bridging veins and eye vascularization. Multicenter validation remains the final prerequisite for establishing reproducible diagnostic criteria, not only for abusive head trauma in infants [50, 51, 102], but also for blunt-force and penetrating trauma patterns in older children [49].

By combining methodological development, literature synthesis, and practical application, this thesis contributes to consolidating FPMCTA and pedPMCTA as a credible and ethically sustainable component of fetopathology and pediatric postmortem practice. The challenge for the coming decade is no longer to prove feasibility, but to ensure standardized, interoperable and justifiable implementation.

Conclusion

To conclude, this doctoral research explored the development, optimization, and forensic application of PMCTA in fetuses, infants, and young children. Through a combination of technical innovation, systematic analysis, and validation, it has contributed to the growing body of knowledge on postmortem imaging investigation in pediatric populations.

Key outcomes of this thesis include:

- *Development of a dedicated FPMCTA protocol:*
This work established a reproducible and ethically applicable method using a lipophilic CA, enabling high-quality vascular opacification in small bodies where conventional autopsy is often limited.
- *Systematic synthesis of existing FPMCTA and pedPMCTA evidence:*
The systematic review identified key technical variables, knowledge gaps, and patterns of diagnostic utility, leading to a conceptual decision tree to guide case selection and protocol choice.
- *Demonstration of PMCTA feasibility in infants and young children:*
The prospective case series confirmed the method's practicality across age and weight ranges, highlighting its capacity to visualize relevant cardiovascular and traumatic findings.
- *Refinement of diagnostic interpretation criteria:*
This research proposed objective scoring and interpretive thresholds for vascular opacification, paving the way toward standardized quality assessment in fetal and pedPMCTA.
- *Contribution to forensic and clinical practice:*
Collectively, the results support the integration of PMCTA as a complementary tool to conventional autopsy, fostering interdisciplinary collaboration and advancing non-invasive approaches to postmortem diagnosis in childhood deaths.

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