Adult post-mortem imaging in traumatic and cardio-respiratory death and its relation to clinical radiological imaging

Invited Review

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Abstract

The use of post-mortem imaging is expanding through-out the world with increasing use of advanced imaging techniques, such as contrast enhanced Computed Tomography and Magnetic Resonance Imaging. The questions asked of post-mortem imaging are complex and can be very different, for example for natural sudden death, investigation will focus on cause, whereas for trauma the cause of death is often clear, but injury patterns may be very revealing in investigating the background to the incident. Post-mortem imaging is different to clinical imaging as regards both the appearance of pathology and the information required, but there is much to learn from many years of clinical research in the use of these techniques. Furthermore, it is possible that post-mortem imaging research could be used not only for the investigation of cause of death, but also as a model to conduct clinically relevant research. This article reviews challenges to the development of post-mortem imaging for trauma, identification and cardio-respiratory death, and how they may be influenced by current clinical thinking and practice.

Introduction

Generally post-mortem investigation is carried out to ascertain four basic principles of who the deceased was, where they died, when they died and by what means (why) they came to their death. Imaging is normally only pertinent to the 'whom' and 'why' they died, and the emphasis on these questions may be completely different; for example a case of a witnessed natural death at home compared with a mass fatality traumatic incident. A consistent theme however is that investigation should be carried out quickly and efficiently; for the sake of both the family and legal services.

Imaging in post-mortem investigation is as old as radiography (X-rays) itself but there has recently been a massive expansion in the use of imaging techniques to

assist or supplant traditional autopsy techniques in post-mortem investigation. Whilst there are few who doubt the ability of Post-mortem Computed Tomography (PMCT [1]) to demonstrate fractures, foreign bodies and major hemorrhagic injuries [2], there have been many false dawns in this field. What is clear is that an 'unenhanced' PMCT scan can only go so far in the investigation of death [3-5] and the emphasis is now moving from non-invasive techniques to minimally-invasive techniques, 'enhancing' the scan [6;7]. Similar to development in the clinical world, many new imaging techniques struggle to live up to their hype [8]. However, by incremental progress, imaging has transformed clinical management in the living, and it is also likely to do so in the investigation of cause of death.

This article looks into a few areas where research is ongoing to develop these techniques. The article concentrates on 3 main themes: The role of imaging in traumatic death, specifically relating to mass fatalities and disaster victim identification (DVI); the lessons that can be learnt from clinical imaging practice to inform the investigation of cardiovascular death; and finally the importance of other techniques being introduced, such as ventilation scans, dual source CT and MRI techniques.

Traumatic death and Identification

Radiography is particularly useful for traumatic or suspicious deaths and for many years this has proved satisfactory to help with identification (whom), particularly if accompanied by previous dental radiographs, or dental records. Although DNA analysis and fingerprinting are preferred identification strategies, forensic odontological / dental examination has many unique markers that may be compared with previous dental records or preferably radiographs. Other radiographic imaging is classified as a secondary identifying system, but is recognized and may be necessary if dental assessment is not possible. These tests are particularly useful in a 'closed' situation where the task is identification of bodies from a known list of victims (e.g. from a passenger manifest). This approach exploits the principle that many people have unique pre-existing injuries that may be visible to a plain radiograph, such as a fracture. This is particularly useful when x-rays can be compared with those taken in life, such as used by Singleton who managed to identify 24 of the 119 victims of SS Noronic fire disaster in 1949, by the sole use of radiology [9]. However with standard radiography this can be a big task, such as for the Oklahoma City bombing response [10], which used 60 radiographers and 10 radiologists over a 10-day period to do full skeletal surveys, giving 6 positive identifications where other techniques were inconclusive.

PMCT can offer all this from a single scan giving multiple potential identification options including odontology [11], medical implants, fractures and sinuses [12]; with new approaches still being identified. Even though previous radiographs are more likely to be available than CT, PMCT images can be compared with previous radiographs using image manipulation [13;14]. PMCT has a further

advantage over plain radiographs in the assessment of the soft tissues. This can be particularly useful for detecting visceral abnormalities, particularly as a result of surgery such as cholecystectomy, which would not be detectable on standard radiography and could be used to identify the body.

Identification is much more difficult in an 'open' disaster resulting in the death of unknown individuals, or where there are no prior data or records available for comparison. In this situation basic anthropological data is the starting point to establish the age, gender and sometimes help with ethnicity of the victim. Standard anthropological examination often depends on osteology, which may require defleshing of bones, which is time consuming and also destructive and against many religious and cultural beliefs [15]. PMCT 3D reconstructions are particularly useful for assessment of bone architecture and are reliable for anthropological assessment and potentially answer most anthropological questions without the need to strip bones [15-17]. PMCT may also be useful in re-uniting body parts in mass traumatic mortality [18].

Radiography and fluoroscopy also help with the 'by what means' question by locating fractures and foreign bodies including bullets [2]. In many cases the cause of death is all too obvious in trauma. However patterns of injury may be important to reconstruct details of how the traumatic death came about, or to locate evidence. CT is very good in this aspect, as shown for road traffic collisions [19]. PMCT has also proven to be useful in dealing with unlawful death, such as reconstructing bullet or stab wound trajectories [20-23].

PMCT also has potential in the speed and efficiency of examination. Replacing traditional dental, fluoroscopic and standard x-ray equipment in a mass fatality temporary mortuary could cut the examination time considerably and replace multiple radiation sources in a complex environment, improving radiation protection for staff [24]. PMCT, as a single mobile machine, can be moved anywhere, run on a generator and data can be handled and sent anywhere in the world [25].

PMCT does have disadvantages compared with radiography. Intra oral metal dental work can cause artifacts. These artifacts can be ameliorated to some extent with modern equipment using an extended CT scale, or with post processing. However, very dense material such as dental mercury amalgam can cause irrecoverable artifact due to photon depletion. Rigor mortis, or deformity due to exposure to severe heat, can delay scanning if displaced limbs cannot easily fit through the CT aperture. Soft tissue release can be performed in cases of burning [26].

It is likely that PMCT will become the primary advanced imaging modality for traumatic death for adults [27]. The PMCT and PM Magnetic resonance imaging (PMMR) balance is different in children for reasons relating to size and the types of relevant pathology suspected [28]. However new roles are being discovered for MRI, for example MRI spectroscopy of the brain, which has been shown to correlate to time from death [29]. Other changes to the body that may occur after death, such as cooling, will also change the appearance of PMMR, and need to

be considered [30]. PMMR also has a role in investigation of trauma, not only due to its superior soft tissue contrast resolution, but also to assess bone fractures. Clinical scanning with MRI can detect marrow edema in the absence of a radiologically visible fracture [31;32], and it is now being used in post-mortem investigation and can be useful to 'date' fractures [33;34]. MRI is also particularly appealing for the forensic examination of strangulation in the living, due to its good soft tissue contrast resolution and lack of radiation exposure [35;36].

The biggest challenges to the scientific community to provide a rapid and efficient service are firstly logistical & financial. Running a CT scanner is expensive in terms of both capital outlay and staff costs. Furthermore until PMCT is more widely available, bodies may need transporting to a PMCT centre as part of their investigation. For mass fatalities a mobile CT scanner can be taken almost anywhere, but having such an expensive resource continually available has considerable requires planning.

The second major task will be making sure the evidence provided by imaging is believed. For example plain film skeletal survey is a standard procedure for investigation of sudden unexpected death in infancy [37], but it is easy to propose that PMCT could replace this entirely, as well as adding extra information [38]. The principle of radiographic skeletal survey to detect evidence of non-accidental injury predates the age of multi-detector CT scanners [39-41]. However the evidence is lacking that PMCT can do this; simply showing the ability of PMCT to detect bony trauma in general is not enough, as specific injuries such as characteristic 'bucket handle' metaphyseal fractures must be *confidently excluded* [42]. MRI may be sensitive to these metaphyseal fractures [31,43] and it is therefore unlikely that CT would be used in living patients due to radiation exposure. This scenario demonstrates that all indications of PMCT in legal investigations should be clearly defined, and should have their accuracy tested and validated by scientific review. Establishing the evidence for each indication and presenting it to the legal profession will become an important part of on-going research [44;45].

Cardio-vascular imaging

The subject of vascular imaging and specifically coronary vascular imaging is discussed elsewhere in this edition. However this is a key issue, being the most common cause of sudden death in adults, and has relevance even if the specific cause of death is non-cardiac, such as for a driver in a head-on road crash. Traditional autopsy and post-mortem imaging deliver a static view of tissue morphology and previous studies have shown that luminal examination of the coronary arteries with PMCTA can be equivalent to autopsy [46-49], but highlight that PMCTA does not provide intra-plaque pathology such as plaque rupture or hemorrhage [47] and cardiomyopathy [50]. However, plaque rupture when present is often associated with other critically stenosed lesions. Also, sudden death from coronary artery disease can be difficult to diagnose even at autopsy *with absolute certainty*, if death is caused by immediate causes such as

arrhythmia, even in the presence of stenosis or thrombus [51;52]. Therefore cause of death is more commonly attributed to 'ischemic heart disease' on the 'balance of probabilities', if no other cause of death is ascertained [53;54], and pathologists often use an arbitrary 75% cut-off to define critical stenosis [55]. This is demonstrably a flawed approach because, for example, although the cause of death as shown in Figure 3a (introduced later) is clearly a ruptured abdominal aortic aneurysm, the degree of coronary artery disease in this case was more severe than in many cases of documented ischemic heart disease death.

One specific finding using targeted coronary PMCTA is that contrast injection under pressure can show luminal patency in regions of calcification where autopsy reports 'critical stenosis' [47;56]. The benefits of examining vessels under pressure at autopsy, and therefore mimicking normal physiological conditions, are well recognized but rarely performed in standard pathological practice [57].

This raises a major question to post-mortem practice; how to interpret the significance of stenosis of the coronary arteries at PM examination? A narrowing of a vessel appears to be a simple straightforward issue but the full implications of stenosis are not yet fully understood. Even in clinical cardiac angiography qualitative assessment of stenosis does not necessarily correlate with clinical significance [58;59], although there is no doubt that severe coronary artery disease does predict for coronary occlusion [60]. It has been acknowledged that the functional significance of vessel narrowing is more important than the actual narrowing; but as symptoms and clinical consequences vary between patients gaining a full understanding of this is difficult. This is a key clinical question when assessing patients for suitability for a coronary artery stent. Current clinical investigations are now focused on the physiological impact of a stenosis [61;62]. Recently direct measurement of pressure changes across a stenosis has become possible using a 'pressure wire' to measure the pressure gradient across a stenosis (fractional flow reserve, FFR). It has been shown that FFR is more predictive of clinical benefit from coronary artery stent than luminal narrowing alone, and only 80% of 70-90% diameter stenoses are functionally significant [63]. Treatment can therefore be targeted to functionally significant stenoses [64]. These techniques can be translated into PM investigation, particularly if the coronary arteries are examined under controlled pressure [56]. It is possible to insert catheters into the coronary arteries in cadavers, including a 'pressure wire' to measure intra-luminal pressure and an optical coherence tomography (OCT) catheter to provide high resolution 'virtual histology' coronary images [65]. Intra vascular ultrasound could also be used. Catheter insertion is difficult in a minimally invasive manner similar to clinical practice, as there is no circulation to guide catheters into the arterial orifices and the shapes of the unpressurised vessels are different so more work is required to perfect this (Figure 1).

It is unlikely that these techniques will become routine, but they may contribute to a better understanding of coronary stenoses seen in post-mortem imaging. In clinical cardiology, FFR values may not directly correlate with maximal luminal narrowing but they do correlate well with full 3D analysis of a stenosis [66].

Therefore better mapping of stenoses in 3 dimensions may provide better assessment of its likely impact. Performing this type of research in the post-mortem setting will improve our ability to asses the significance of lesions but may also provide a useful model to inform clinical practice.

Post-mortem imaging does not lend itself to the type of functional imaging used in clinical cardiac stress studies, but if tissue perfusion can accurately be shown then its deficit may indicate significant coronary artery stenosis [67] (figure 2). However this has yet to be shown in an autopsy controlled study and may provide too many false positives to be a useful sign as, although perfusion loss in myocardial tissue may imply a significant stenosis, there is no way of knowing whether this is old or new, or caused by technical reasons such as air bubble or post-mortem clot (as opposed to pathological thrombus).

Dynamic imaging methods, including contrast studies, are becoming possible in the post-mortem setting using pressure injectors and contrast agents of differing molecular weights with different carrier molecules. However it is rapidly becoming clear that the information obtained is not directly related to that from standard clinical studies and that the significance of tissue perfusion has to be assessed in the post-mortem setting and for all types of contrast agent. There is more flexibility in the use of contrast agents in PMCT as toxicity is not a concern, although some consideration has to be taken of the effect of any contrast medium on subsequent toxicology or DNA examination [68-70]. Generally these can be lipophilic agents (dissolved in oil), barium particles in suspension or water-soluble iodinated chelates [6]. Agents such as air or fat, that lower x-ray attenuation and appear black on traditional CT images, may also be used as negative contrast agents (figure 3).

All of these agents have their advantages and disadvantages. The key issues are related to their molecular size, viscosity, density and osmolality, which all dictate how they disperse in the body (pharmacokinetics). Currently 2 broad approaches are used: the first is based on standard water-soluble agents in aqueous medium; the second uses water soluble agents in a larger carrier solution such polyethyleneglycol (PEG) or lipophilic agents in oil. In clinical practice water soluble agents disperse rapidly from the intravascular space into the extravascular extracellular space (or interstitial space). This provides good tissue contrast particularly where this vascular leak is rapid in one area compared with the adjacent tissues. This however requires rapid (dynamic) imaging after contrast agent delivery or there will be general dispersal in the tissues, reducing this early 'contrast'. This is particularly important if purely vascular information is required. Contrast agents have been developed for clinical MRI scanning that leak more slowly into the extravascular extracellular space. Similar leak into the interstitial space is noted in post-mortem contrast enhanced imaging, although the pharmacokinetics are unlikely to be identical. Although this potentially allows imaging of tissue perfusion (figure 2) it also presents two problems, particularly for whole body imaging, firstly considerable dispersal will occur during the time required to pump the tracer around the body reducing contrast in the image and secondly this leak may cause alterations in osmolality in the interstitial space

causing edema and histological changes that would affect subsequent autopsy results. This has been observed in whole body studies but not localized targeted studies, presumably due to the lower amount of agent used [48;49;71]. In order to overcome this extravasation into the surrounding tissues, in whole body studies polyethylene glycol has been added as a solvent [72;73] or alternatively a lipophilic iodinated contrast agent dissolved in paraffin oil. Using different solvents viscosity can be changed allowing the agent to enter capillaries and changing the information gained [74].

However to enable post mortem contrast enhanced imaging to follow clinical practice it is important that more is understood about the dispersal patterns of these contrast agents and what this means in a patho-physiological sense. For example contrast enhancement in normal tissues is common using water soluble media but is exceptional using contrast in oily carriers where the contrast agent does not access the capillary bed as a result of the increase of viscosity (figure 2b). However exceptional soft tissue enhancement does occur in the brain, the renal cortex and in the left ventricular myocardium and may indicate dilatation of precapillary arterioles at the time of death [72;73]. It is possible that these contrast enhancement patterns will reveal information as regards physiology such as left ventricular hypertrophy but this will require confirmation specific to the type on contrast agent and carrier it is injected with (figure 4).

Another avenue that may indicate the significance of cardiac ischemia is to use MRI imaging. Early work was not autopsy controlled [75] and later papers were less optimistic [4] but more recently, changes on T2-weighted images have been shown in animal models and clinical studies [76-78]. Clinical MRI scanning tells us there may be more complex contrast enhancement changes that may be seen, such as delayed myocardial enhancement occurring in region of myocardial infarction [79] and whole body contrast angiography is possible [80] and there is no reason that targeted techniques cannot be translated to MRI, except cost and time. Interestingly information on coronary arteries has also been obtained without angiography, by using the absence of 'chemical shift' artifact as a sign of a stenosed vessel [81]. Whether this turns out to be a helpful post-mortem or clinical sign [82] remains to be seen but a clear message arising from this section is that post-mortem imaging has a lot to learn from advanced clinical imaging techniques. Furthermore clinical imaging potentially has a lot to learn from post-mortem imaging, which may provides a good research model of human disease with which to test clinical paradigms.

Respiratory imaging and Ventilation

Clinically most chest CT scanning is performed during breath-hold after inspiration to clear atelectasis and 'dependent' changes. This makes interstitial or nodular changes more apparent. Occasionally both inspiration and expiration scans are performed to obtain functional information, such as for emphysema and air trapping [83;84]. Post-mortem scans may have obscuration of lung pathology due to increase in pulmonary opacification (livor mortis), which can be

mistaken for aspiration, pulmonary edema or pneumonia [85]. These changes build up with greater delay from death to scan [86] and the best interpretation of lung pathology has been shown within 2 hours of death [87;88]. Pulmonary diagnosis is therefore perceived to be difficult in most cases [38].

Being able to mimic ventilation in PMCT is therefore appealing to improving both the visibility of pathology and to provide functional information. Germerott et al published a novel method, called Ventilation-PMCT (VPMCT), using a portable home care ventilator delivering intermittent pressures up to 40mBar [89-91]. Although these papers demonstrated the diagnostic advantages of applying such a technique particularly clearing background lung changes, they reported a number of potential problems ranging from the method of ventilation, to movement artifact and gastric dilation. We now routinely use this technique, but have developed a technique for using supraglottic airways in all cases and use a ventilator set at 40mBar constant pressure to avoid motion artifact [92]. The images are appealing as they clear background pulmonary changes without affecting significant pathology (Figure 5).

We anticipate that this approach may be useful in the diagnosis of traumatic and 'natural' respiratory disease but also as a useful 'dynamic' model to study diseased lung to aid clinical practice.

Other approaches

There are many developments occurring in clinical imaging. Clearly those related to targeted injectable tracers, such as nuclear medicine studies cannot be translated to the post-mortem setting. We have already discussed that where translation is possible in the case of injected contrast agents, circulation the pharmacokinetics may be different and require systematic re-evaluation for every new agent and setting. New cardiac imaging techniques such as optical coherence tomography and intravascular ultrasound can be exploited. Two further new imaging modalities currently being tested in the post-mortem setting are dual source CT and developments in MRI scanning.

a) Dual source CT

Dual source CT was developed mainly to increase scan speed but it does have the advantage of easily allowing 'dual energy' CT. However, as the major obstacle to dual energy CT for single scanners is movement, dual energy PMCT can be performed on most 'single source' modern scanners. The advantage of using dual energy is that if x-ray attenuation is known for two x-ray energies, the information gained is much more specific to the type of material. Dual energy CT can therefore separate materials with similar appearance such as calcium and contrast agents and identify foreign bodies. This makes contrast perfusion patterns more reliable and is being used clinically for both cardiac and lung perfusion studies. However a key advantage for general indications is better discrimination of soft tissues, a weakness of CT compared with MRI [93-95]. Whether dual source imaging becomes an essential component of post-mortem

investigation is unclear, but it is likely to become an option on all clinical scanners and therefore for PMCT.

b) MR-Spectroscopy and Diffusion weighted MRI

Magnetic resonance imaging allows morphological information to be obtained, in a similar fashion to CT. The great advantage of MRI, and possibly its curse in terms of cost and complexity, is the ability to image using multiple tissue contrast mechanisms. These contract mechanisms in the post mortem setting are well reviewed elsewhere in this issue [96]. Two specific methods of MRI, MR spectroscopy (MRS) and 'diffusion weighted imaging' (DWI), provide potential information related to physiology and function in clinical practice. Although developed some time ago their clinical utility is still increasing due to advancing technology and both techniques are now becoming available in all parts of the body and are simpler to use. MR spectroscopy can give information related to molecular concentrations in a selected region and this information can be registered with the anatomical images. Common metabolites that can be measured are lactate and choline, which link to ischemia and cancer proliferation. More complex clinical MRI systems can test concentrations of metabolites related to other nuclei such as phosphorous. Considering these tools have been available to clinicians for many years they are not widely used outside very narrow indications. However MRS is becoming easier to perform and will become available to forensic investigators using clinical MR scanners. It remains to be seen whether these techniques will be useful and justify their cost and complexity.

Diffusion weighted MRI is sensitive to microscopic water diffusion and therefore to tissue structure and cellularity. The technique can also use the asymmetry of diffusion caused by nerve sheaths (diffusion tensor imaging) to create maps of these nerve tracts (Diffusion weighted tractography). Clinically DWI has multiple applications relating to ischemia, cancer and discrimination of other pathologies, and its use is increasing because it is becoming easier to use in all parts of the body, not just the brain. There is evidence that these techniques can be used in the post-mortem setting, although the normal post-mortem appearance is radically different to the clinical normal, but may help with both time from death and cause, particularly in relation to brain [29;97-99].

Conclusions

What is clear from the multitude of research avenues is that the scientific community is still a long way from understanding the detailed post-mortem physiological changes that dictate tissue changes, contrast dispersal patterns and complex imaging findings. However much has been learnt and there is no doubt that imaging should be used in many different indications in the investigation of death. There is also no doubt that post-mortem imaging can be used to inform clinical practice, not just in the traditional manner of reviewing the medical care of an individual death, but as a model to investigate epidemiology, human disease processes and their treatment. Research will undoubtedly continue in testing the diagnostic ability of new techniques, and hopefully use

these strategies to impact on clinical care. However, probably the most difficult type of research is to show that new techniques have an impact on public heath [100]. This needs to be done by specifically validating techniques for all the indications they are required for.

<u>Figures</u>

Figure 1: An image from a fluoroscopic series showing a catheter inserted into the orifice of the right coronary artery (RCA) of a cadaver (white arrow) and pressure wire inserted into the RCA (black arrows). Pressure changes in the RCA secondary to pump injection of air / contrast in the ascending aorta can then be measured.

Figure 2: Cardiac images, in 2 different cases, of autopsy proven myocardial infarction, using (a) water soluble contrast agent and (b) lipophilic contrast agent in paraffin oil. The water-soluble agent 'enhanced' the normal myocardium showing perfusion deficits (*) relating to ischemia, whereas the normal myocardium is not enhanced by the lipophilic agent and at autopsy no oil was identifiable in the capillaries.
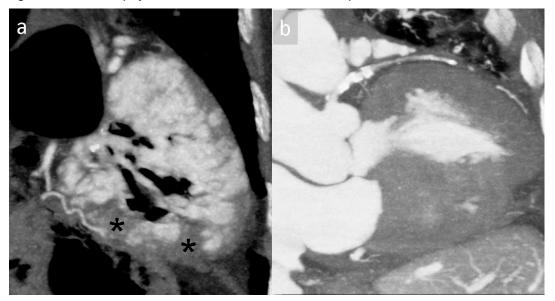
Figure 3: Whole body angiography using (a) lipophilic contrast in paraffin oil (case of ruptured aortic aneurism and (b) air (no vascular abnormality).
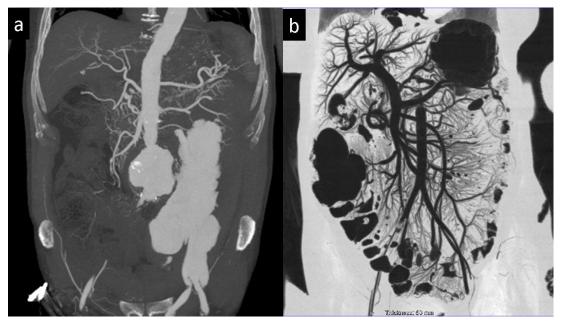

Figure 4: Images of the heart pre (a) and post (b) lipophilic contrast in paraffin oil showing atypical myocardial enhancement in a case of death due to hypertensive heart disease and obesity.
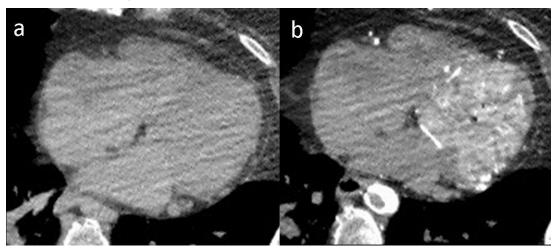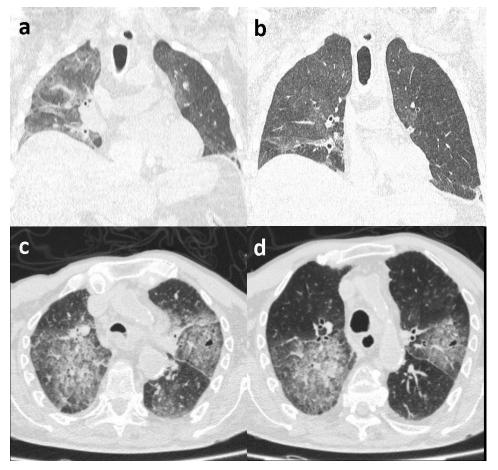
Figure 5: PMCT studies in two cases; normal (a & b) and with pneumonia documented at autopsy (c& d). The second image of each case (b & d) is after lung ventilation using a supra-laryngeal airway and continuous ventilation pressure of 40mBar and shows clearing of normal background lung changes (b) but not pneumonia changes (d).

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