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Assessing the use of Magnetic Resonance Imaging Virtopsy as an alternative to Autopsy: A Systematic Review and Meta-Analysis

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MUA & MRSS planned, supervised and carried out the study. KAS and HQ carried out the literature and data search. All authors contributed to the writing of the manuscript.

ABSTRACT

Background: The post-mortem examination or autopsy is a trusted method to identify the cause of death. Patients and their families may oppose an autopsy for a variety of reasons; including fear of mutilation or religious and personal beliefs. Imaging alternatives to the autopsy have been explored; which may constitute a viable alternative to autopsy.

Objective: This paper explores the possibility of using magnetic resonance imaging (MRI) virtopsy to establish the cause of death as an alternative to the traditional post mortem examination or autopsy.

Methods: Systematic review of all studies up to December 2016, without language restriction were identified from MEDLINE, Cochrane (1960–2016), and EMBASE (1991–2016). Further searches were performed using the bibliographies of articles and abstracts. All studies reporting on the diagnosis of the cause of death by both MRI virtopsy and traditional autopsy were included.

Results: 5 studies with 107 patients, contributed to a summative quantitative outcome in adults. The combined sensitivity MRI virtopsy was 0.82 (CI:0.56-0.94) and diagnostic odds ratio (DOR) of 11.1 (CI:2.2-57.0). There was no significant heterogeneity between studies (Q=1.96, df=4, p=0.75, I2=0). 8 studies, with 953 patients contributed to a summative quantitative outcome in children. The combined sensitivity of MRI virtopsy was 0.73 (CI:0.59-0.84) and diagnostic odds ratio (DOR) of 6.44 (CI:1.36-30.51). There was significant heterogeneity between studies (Q=34.95, df=7, p<0.01, I2=80).

Conclusion: MRI virtopsy may offer a viable alternative to traditional autopsy. By using MRI virtopsy, a potential cost reduction of at least 33% is feasible, therefore ought to be considered in eligible patients.

Key words: Virtopsy; Autopsy; Imaging; MRI

Main Messages:

Use of MRI virtopsy can reduce costs by a minimum of 33%.

MRI virtopsy offers a less invasive and quicker alternative to conventional autopsy.

Eligible patients should be considered for MRI virtopsy.

Research Questions:

Alternatives to MRI virtopsy such as CT virtopsy should be explored.

The sensitivity of combined imaging virtopsy needs to be looked at.

MRI virtopsy has not been established completely, this needs to be studied.

INTRODUCTION

Rationale

The post-mortem examination or autopsy has been a trusted method to help identify the pathology, which was the cause of death, which is also very important in detecting unnatural or suspicious deaths. This tool is also very important in criminal inquiries as well as for quality control in healthcare. In modern day medicine, autopsy provides meaningful information contributing to databases that generate important feedback and statistics [1].

There are other reasons as to why an autopsy is of value to healthcare professionals as it adds to medical knowledge, offers an avenue for medical training while continuing to offer important feedback on care and insights on any judgments made [2]. However, there are also many disadvantages to having an autopsy.

In many countries, permission for the procedure must be sought from the patient's next of kin, in which case some may refuse. Patients and their families may oppose an autopsy for a variety of reasons; these include fear of mutilation of the deceased or even religious and personal beliefs [3, 4]. In modern day medicine, patient autonomy is one of the first principles considered when treating the patient; therefore, their decisions and choices should be respected during any procedure [4].

For these reasons, alternatives to the autopsy have been sought. New imaging techniques, such as magnetic resonance imaging (MRI) in perinatal autopsy and image guided tissue biopsies have been developed as a substitute [5]. Forensic specialists have optimised these modalities therefore offering a viable alternative to autopsy.

Objective

This paper explores the possibility of using magnetic resonance imaging virtopsy to establish the cause of death as an alternative to the traditional post mortem examination or autopsy.

METHODS

Protocol & Registration

The title, methods and outcome measures were stipulated in advance and the protocol is available in the PROSPERO database [6].

Types of studies

All comparative studies reporting on the use of post mortem MRI virtopsy and autopsy were identified. There were no regional or publication date restrictions on studies. All study designs were considered for inclusion (Table 1). All animal studies were excluded. Articles that only assessed the use of X-Ray Computed Tomography, minimally invasive autopsy or did not use both MRI virtopsy and autopsy were excluded. Further studies, which were specific to an organ system, were also then excluded.

Types of participants

Patients who had undergone both post mortem MRI virtopsy scans and an autopsy to establish the cause of death were required; therefore, articles that included these patients were selected for this review [7-19]. Patients selected were of an unknown cause of death and were of any age or gender.

Hypotheses and Types of outcome measures

Our primary hypothesis was that there is no significant difference between the use of post mortem MRI virtopsy and conventional autopsy to establish an unknown cause of death. The outcome measure was the cause of death; there were no secondary outcome measures. Results are presented using forest plots and diagnostic odds ratios.

Information sources

The studies reviewed, examined the ability of a post mortem MRI virtopsy scan to diagnose the cause of death. We searched the MEDLINE, EMBASE and CINAHL databases available through the NHS National Library of Health website, the Cochrane library and PubMed available online, up to December 2016. The last search was performed on 29th December 2016. There was no language restriction in place and articles in other languages were translated if required.

Searches

Text words were used in combination with Medical Subject Heading (MeSH) Terms. Text words used were “Post Mortem”, “Necropsy”, “Pathological Examination”, “Autopsy”, “Virtual”, “Non-invasive” “Imaging”, “Visual”, “CT Scan”, “MRI”, “Traditional”, “Clinical”, “Surgical”, “Medical”, “Pathological”, “Conventional”, “Regular” and “Classical”. MeSH terms used were “Autopsy”, “Magnetic Resonance Imaging”,

"Tomography, X-Ray Computed" and "Pathology". Articles relating to other imaging modalities, irrelevant articles, reviews, meta-analyses evident from the titles and abstracts were excluded. Relevant articles referenced in these publications were obtained and the references of identified studies were searched to identify any further studies. A flow chart of the literature searches according to PRISMA guidelines [20] is shown in Figure 1a and 1b.

Study selection & data collection process

Each included article according to our review criteria (Table 1) was reviewed. This was performed independently and where more specific data or missing data was required, the authors of manuscripts were contacted. Data was entered onto an Excel worksheet ready for analysis.

Data items

Patient demographics and study characteristics were extracted from the relevant studies. The study characteristics were year, country of origin, imaging and autopsy protocol along with experience of the investigator (Table 2). An expert was defined as anybody with at least 3 years' experience in the respective field. Patient demographics included total number of patients and mean age at death (Table 3). Two authors independently (M.U.A & M.R.S.S) collected the data, before being compared; in the event of discrepancies in the collected data, this was to be reviewed by a different author.

Risk of Bias & Quality assessment

The methodological quality of the trials included for meta-analysis was formally assessed using the QUADAS scale [21]. Assessment was performed by two authors (M.U.A. & M.R.S.S.) independently (Table 4).

Summary Measures & Data Synthesis for summative and comparative meta-analyses

Statistical analyses were performed using widely available computer software [22], where 0.5 was added to each cell frequency for trials in which no event occurred, according to the method recommended by Deeks et al [23]. The study was undertaken in accordance to reported guidance for diagnostic test meta-analyses [24-26]. In the studies examined, the gold standard was physical autopsy. The numbers for true positives were identified as those patients who were found to have identified a cause of death on MRI and physical

autopsy. Patients in which neither method identified a cause of death or pathology were defined as true negatives. False positive rates were those patients in which MRI scan were able to identify a cause of death whilst post-mortem findings were negative. False negative rates were those patients in which MRI did not pick up a cause of mortality but was later found to have a cause on autopsy.

Sensitivity (true positive/[true positive+false negative]) and specificity (true negative/[true negative+false positive]) pooling were calculated with 95% confidence intervals using the random effects model. Forest plots were used for the graphical display. Interaction between sensitivity and specificity was assessed using summary receiver operating characteristic (SROC) analyses described by Littenberg and Moses [27, 28]. The diagnostic rigour of MRI over study groups was assessed using diagnostic odds ratios (DOR).

Data for sensitivity and specificity was used to calculate the DOR (frequency of true positives/frequency of false positives)/(1–frequency of true positives/1–frequency of false positives). The diagnostic accuracy of our virtopsy tests is proportional to the value of the DOR. A DOR of 1 indicates that a test is unable to discern between patients with or without a specified cause of death [29].

Heterogeneity between studies was assessed using Cochran's Q statistic, which is a type of Chi squared test instituted to establish the application of SROC meta-regression curves over our dataset.

Verification bias occurs when one test determines the choice of subsequent tests [30]. Because every patient in our analyses who underwent MRI also had a physical autopsy, the primary-endpoint verification bias is zero. All statistical analysis was performed using the OpenMetaAnalyst software [22].

Publication bias

There is likely to be inherent publication bias although this was not formally tested due to the low numbers of studies.

Funding

There are no funding declarations related to this study.

RESULTS

Study selection

8488 articles were screened for relevance (Figure 1a). The electronic databases searched (Medline, Cochrane, EmBase) yielded 24984 citations and 16 citations were identified through bibliographies and conference proceedings. After the removal of duplicates, 8488 unique records were left. Records were excluded if they were deemed irrelevant or not related to comparative imaging and autopsy. A total of 39 studies were then reviewed for eligibility, after which 25 were excluded. 1 further study was then excluded from the qualitative analysis as the data was repeated in a more recent study; the remaining studies were then used for qualitative analysis (Table 5). The remaining studies were chosen based on our inclusion criteria (Table 1). There was no data from any unpublished or grey literature.

Study characteristics

Study types

All study characteristics are shown in Table 2. All 13 studies were published in English. 5 studies were adult studies and 8 studies were paediatric. From the 5 adult studies, 1 study selected was from an Australian centre, 1 study from the USA and 3 based in European centers. 7 paediatric studies selected for this review were from European centres, with 1 study coming from the USA.

Participants

A total of 1060 patients were included in this review. There were 107 adult patients and 953 paediatric patients. Due to the disparity in the large variance of total patients, the results were categorised into adult and paediatric studies. Data for the cause of death was collected for each study; true positives, false positives, true negatives and false negatives were noted, as shown in Table 3. The definitions for these have been described in the section *summary "Measures & Data Synthesis for summative and comparative meta-analyses".*

Quality assessment

The studies were assessed using the QUADAS tool in Table 4 [21].

Qualitative and Quantitative synthesis of ability of MRI to identify cause of death in adults

5 studies [7-11] contributed data to the meta-analysis. Sensitivity (95% CI) for MRI virtopsy against the gold standard physical autopsy was 0.82 (0.56-0.94), specificity (95% CI) was 0.57 (0.29-0.82) and diagnostic

odds ratio was 11.1 (2.2-57.0). These are shown in forest plots in figures 2a, 2b and 2c respectively. There was no evidence of heterogeneity Chi^2 1.96 (4 DF), p=0.75; I^2=0.

Qualitative and Quantitative synthesis of MRI to identify cause of death in children

8 studies [12-19] contributed data to the meta-analysis. Sensitivity (95% CI) for MRI virtopsy against the gold standard physical autopsy was 0.73 (0.59-0.84), specificity (95% CI) was 0.71 (0.28-0.94) and diagnostic odds ratio was 6.44 (1.36-30.51). These are shown in forest plots in figures 3a, 3b and 3c respectively. There was evidence of significant heterogeneity Chi^2 34.95 (7 DF), p<0.01; I^2=80.

DISCUSSION

When this meta-analysis was conducted, there were no other meta-analyses to assess the use of MRI virtopsy as an alternative to traditional autopsy. There has been a similar systematic review conducted by Blokker et al [31], where a range of modalities were reviewed.

Main findings

In traditional medicine, there is always the aim to have the best practice implemented all over the globe, based on the strongest evidence. However, there are some inaccuracies when it comes to autopsies. It has been reported that one in four autopsies are conducted to a poor or unacceptable standard, with one in five the cause of death stated appears to be questionable [32].

One of the biggest factors to play a part in this is the cost of the services provided. Within the United Kingdom's National Health Service (NHS) a routine medico-legal autopsy, with histological examination is around £471.80, at the very minimum, in fees [33]. Currently, a full body MRI scan which images more than 3 areas, costs £197 plus a reporting fee of £29, therefore a total fee of £226 [34]. The sensitivity of 81.5% as shown within the adult population means big costs could be saved. If 100 patients underwent a routine autopsy with histological examination, the cost would be £47,180.00. Alternatively, 100 patients undergoing MRI virtopsy would cost £22,600.00, as the sensitivity is 81.5%, 18.5% of patients would then have to undergo a traditional autopsy at a cost of £8728.30, therefore costing an overall £31,328.30. Therefore, an MRI virtopsy at a sensitivity of 81.5% would save £15,851.70 per 100 patients. An MRI virtopsy with a sensitivity of 73.0% as shown within the paediatric population would still save £11,841.40

per 100 patients. MRI virtopsy has the potential to reduce the costs by over one third at least when compared to traditional autopsy.

Summary & Appraisal of evidence

A total of 13 studies used in this meta-analysis signify the potential that MRI virtopsy has in relation to determining the cause of death. Due to the evident differences in between adult and paediatric populations, the results have been split. However, due to demographical data and there are more adults in the world compared to children; the adult results are potentially more significant.

Within the studies used, two specific studies observed seemed anomalous, despite using the random effects model for meta-analysis. Bisset et al [10] only used 6 patients of their own, with the rest of the data being secondary data, only showing a sensitivity of 50% (Figure 2a). The second study to show an anomaly is Alderliesten et al [15] from the paediatric category, whilst coming from an obstetric practice. The study initially assessed 58 cases, of which 26 patients consented to both MRI virtopsy and traditional autopsy. From this, a comparison at autopsy was only available for 11 patients. Again, whilst not affecting the overall results due to the small patient sample, the sensitivity of 36.4% is anomalous.

With regards to the sensitivity, the point estimates suggest some reassuring statistics. However, there are still wide confidence intervals for the pooled estimates, which suggests that there is still some variability in the effectiveness of MRI virtopsy.

Strengths of this study

The value of this study is in two principle aspects. Firstly, due to the combination of the data from different studies, it allows this study to be able to evaluate the sensitivity of MRI virtopsy in a larger cohort of patients. Subsequently the power of the study is also drastically improved, making the results and interpretations of the study more applicable to clinical practice.

Limitations and heterogeneity of this study

The first assumption to be made by this study was that autopsy is assumed to the gold standard. However, there are limitations with the autopsy, with our results also showing that there are occasions where MRI virtopsy was able to confirm a diagnosis where autopsy was not able to do so (Table 2). This was

particularly evident in the paediatric setting and occurred in 110 cases, therefore indicating imaging was a better modality than autopsy in 13.3% of cases [12-16].

Whilst no regional restrictions placed on the studies, there should not have been any limitations because of this. Cohen et al [13] reported patient numbers of 250, however the results were given in percentages, which meant after rounding only a total of 249 patients were accounted for. A request for the results with patient numbers was made to the authors, however this was unsuccessful. Most of the studies used in this meta-analysis were from Europe and North America, which may demonstrate some disparity in the way an autopsy is conducted, therefore potentially affecting the way a diagnosis is made concerning the cause of death.

From this study, there is an overall sensitivity of over 73.0% in paediatric studies, with this being higher at 81.5% in the adult population. Whilst being an overall sensitivity, this could vary depending on the different techniques used along with what body system is being assessed, with MRI virtopsy inevitably varying in the sensitivity. Another key point to note is the MRI system that is used, in comparison to a 1T system; a newer 3T system may offer better sensitivity for post-mortem imaging.

In addition, another limitation, which may have introduced bias into the study, was that of blinding. None of the studies specifically discussed methods of blinding; therefore, there is a possibility of bias in how sensitive MRI virtopsy is.

Importance and implications for practice

There are two major implications, which concern clinical practice. The first is that of costs which can be saved within the healthcare service. Potentially, a minimum of at least 33% can be saved if MRI virtopsy is to be carried out. Whilst cost may not be the biggest factor in healthcare provision, this may affect policies and protocols that are followed. Secondly, the benefits of MRI virtopsy as an alternative to traditional autopsy include that of patient autonomy and the wishes of the relatives. Avoiding the traditional autopsy may help to prevent distress and anxiety caused by bereaving relatives [3, 4].

Implications for research & further studies

Further research is still required to offer better evidence, especially concerning adult studies. There have been no major studies with a large patient cohort investigating MRI virtopsy in comparison to autopsy. Studies have also lacked controlled blinding; therefore, further blinded studies are required to eliminate bias.

CONCLUSION

MRI virtopsy offers an alternative to traditional autopsy with additional benefits. The process could save both time and money, with potential cost reductions of at least 33%. MRI virtopsy may also help to reduce stress and anxiety within the relatives of the patient. Virtopsy is a good clinical tool to help diagnose the cause of death in patients.

Table 1 - Inclusion Criteria

All studies reporting on use of magnetic resonance imaging and autopsy
All studies reporting on diagnosis of cause of death
All study designs, of any age, any gender and any languages
All studies reporting on an adult or paediatric population

Table 2 – Study Characteristics

STUDY	YEAR	COUNTRY OF ORIGIN	NUMBER OF PATIENTS	MRI PROTOCOL			AUTOPSY PROTOCOL	RADIOLOGIST EXPERIENCE	PATHOLOGIST EXPERIENCE
				System	Sequences	Best Slice Thickness			
					Adult				
Puranik	2014	Australia	17	1.5T	T1, T2	Unknown	Standard + Toxicology + Histology	Expert	Expert
Patriquin	2001	USA	8	1.5T	T1, T2	4mm	Standard + Histology	Expert	Expert
Ross	2012	Switzerland	40	1.5T	T1, T2	5mm	Unknown	Expert	Unknown
Bisset	2002	UK	6	Unknown	Unknown	Unknown	Unknown	Expert	Unknown
Thali	2003	Switzerland	36	1.5T	T1, T2	4mm	Standard	Expert	Expert
					Paediatric				
Thayyil	2013	UK	406	1.5T	T2	3mm	Unknown	Expert	Expert
Cohen	2007	UK	250	1.5T	T2	2mm	Standard + Toxicology + Histology + Microbiology + Virology	Expert	Expert
Alderliesten	2003	Netherlands	25	1T	T1, T2	3mm	Unknown	Expert	Expert
Cohen	2008	UK	100	1.5T	T2	2mm	Unknown	Unknown	Unknown
Breeze	2011	UK	44	1.5T	T2	2mm	Standard + Histology	Expert	Expert
Arthurs	2016	UK	82	1.5T	T2	Unknown	Standard + Histology + Virology + Microbiology	Expert	Expert
Leadbetter	2016	USA	24	1.5T, 3.0T	T1, T2	3mm	Standard + Histology	Expert	Unknown
Vullo	2016	Europe	22	1.5T	T1, T2	2mm	Standard + Histology	Expert	Unknown

Table 3 – Patient Characteristics from the selected studies

STUDY	YEAR	NUMBER OF PATIENTS	MEAN AGE AT DEATH (YEARS)	MALE (%)	BODY HABITUS	MEAN TIME TO AUTOPSY (HOURS)	MEAN TIME TO MRI (HOURS)	IMAGING TIME (MINS)	TYPE OF DEATH
					Adult				
Puranik	2014	17	22.7	71	MEAN BMI 25.6	56.1	Unknown	Unknown	Sudden Death
Patriquin	2001	8	64	50	MRI adjusted	<12	Unknown	<40	Unknown
Ross	2012	40	32	70	MRI adjusted	Unknown	38	94	Trauma, RTA
Bisset	2002	6	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Thali	2003	36	46	83	Unknown	46	32	120-180	Trauma, RTA, Drowning
					Paediatric				
Thayyil	2013	406	Unknown	Unknown	Unknown	96-120	108	60-90	Unexpected
Cohen	2007	250	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Alderliesten	2003	25	Unknown	65	Unknown	Unknown	<96	Unknown	Unknown
Cohen	2008	100	0.49 (25.5 Weeks)	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Breeze	2011	44	Unknown	Unknown	Unknown	Unknown	Unknown	22.5-31.5	Unknown
Arthurs	2016	82	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown	Unknown
Leadbetter	2016	24	Unknown	52	Unknown	Unknown	10	30	Unknown
Vullo	2016	22	Unknown	Unknown	Unknown	Unknown	72	20-30	Unknown

Table 4 - Methodological qualities of studies according to the QUADAS criteria

	Quality Variable								
Study	**Representativeness of interest group**	**Control group selection**	**Ascertainment of disease**	**Demonstration of absence of outcome at start of study**	**Comparability of cohorts (2 points)**	**Assessment of outcome**	**Autopsy and scan time**	**Suitable time to imaging or autopsy**	**Total score (9)**
Puranik et al	+	+	+	+	++	+	-	+	**8**
Ross et al	+	+	+	+	++	+	+	+	**9**
Thali et al	+	+	+	+	++	+	+	+	**9**
Bisset et al	+	+	+	+	++	+	-	-	**7**
Patriquin et al	+	+	+	+	++	+	+	+	**9**
Thayyil et al	+	+	+	+	++	+	+	+	**9**
Breeze et al	+	+	+	+	++	+	+	-	**8**
Cohen et al (A)	+	+	+	+	++	+	-	-	**7**
Cohen et al (B)	+	+	+	+	++	+	-	-	**7**
Alderliesten et al	+	+	+	+	++	+	-	+	**8**
Arthurs et al	+	+	+	+	++	+	-	-	**7**
Leadbetter et al	+	+	+	+	++	+	+	+	**9**
Vullo et al	+	+	+	+	++	+	+	+	**9**

Table 5 – Study Results

STUDY	YEAR	AREA	NUMBER OF PATIENTS	TRUE POSITIVES	TRUE NEGATIVES	FALSE POSITIVES	FALSE NEGATIVES
			Adult				
Puranik	2014	Australia	17	12	2	3	0
Patriquin	2001	USA	8	7	0	0	1
Ross	2012	Europe	40	39	0	0	1
Bisset	2002	UK	6	3	0	0	3
Thali	2003	Europe	36	18	7	0	11
			Paediatric				
Thayyil	2013	UK	406	222	78	6	100
Cohen	2007	UK	250	157	0	77	15
Alderliesten	2003	Europe	25	4	13	1	7
Cohen	2008	UK	100	54	10	24	12
Breeze	2011	UK	44	32	0	2	10
Arthurs	2016	UK	82	24	27	0	31
Leadbetter	2016	USA	24	14	6	0	4
Vullo	2016	Europe	22	7	8	0	0

References

1. Burton, E.C., *The autopsy: a professional responsibility in assuring quality of care.* Am J Med Qual, 2002. **17**(2): p. 56-60.
2. Lundberg, G.D., *Low-tech autopsies in the era of high-tech medicine: continued value for quality assurance and patient safety.* Jama, 1998. **280**(14): p. 1273-4.
3. Gatrad, A.R., *Muslim customs surrounding death, bereavement, postmortem examinations, and organ transplants.* Bmj, 1994. **309**(6953): p. 521-3.
4. Oluwasola, O.A., et al., *The autopsy: knowledge, attitude, and perceptions of doctors and relatives of the deceased.* Arch Pathol Lab Med, 2009. **133**(1): p. 78-82.
5. Brookes, J.A., et al., *Non-invasive perinatal necropsy by magnetic resonance imaging.* Lancet, 1996. **348**(9035): p. 1139-41.
6. *Ahmad MU, Siddiqui MRS. A systematic review and meta-analysis in the use of post-mortem imaging versus traditional autopsy. PROSPERO 2016:CRD42016033020 Available from: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016033020.*
7. Patriquin, L., et al., *Postmortem whole-body magnetic resonance imaging as an adjunct to autopsy: preliminary clinical experience.* J Magn Reson Imaging, 2001. **13**(2): p. 277-87.
8. Ross, S., et al., *Postmortem whole-body MRI in traumatic causes of death.* AJR Am J Roentgenol, 2012. **199**(6): p. 1186-92.
9. Puranik, R., et al., *Comparison of conventional autopsy and magnetic resonance imaging in determining the cause of sudden death in the young.* J Cardiovasc Magn Reson, 2014. **16**: p. 44.
10. Bisset, R.A., et al., *Postmortem examinations using magnetic resonance imaging: four year review of a working service.* Bmj, 2002. **324**(7351): p. 1423-4.
11. Thali, M.J., et al., *Virtopsy, a new imaging horizon in forensic pathology: virtual autopsy by postmortem multislice computed tomography (MSCT) and magnetic resonance imaging (MRI)--a feasibility study.* J Forensic Sci, 2003. **48**(2): p. 386-403.

12. Thayyil, S., et al., *Post-mortem MRI versus conventional autopsy in fetuses and children: a prospective validation study.* Lancet, 2013. **382**(9888): p. 223-33.

13. Cohen, M.C. and E. Whitby, *The use of magnetic resonance in the hospital and coronial pediatric postmortem examination.* Forensic Sci Med Pathol, 2007. **3**(4): p. 289-96.

14. Cohen, M.C., et al., *Less invasive autopsy: benefits and limitations of the use of magnetic resonance imaging in the perinatal postmortem.* Pediatr Dev Pathol, 2008. **11**(1): p. 1-9.

15. Alderliesten, M.E., et al., *Perinatal mortality: clinical value of postmortem magnetic resonance imaging compared with autopsy in routine obstetric practice.* Bjog, 2003. **110**(4): p. 378-82.

16. Breeze, A.C., et al., *Minimally-invasive fetal autopsy using magnetic resonance imaging and percutaneous organ biopsies: clinical value and comparison to conventional autopsy.* Ultrasound Obstet Gynecol, 2011. **37**(3): p. 317-23.

17. Arthurs, O.J., et al., *Comparison of diagnostic performance for perinatal and paediatric post-mortem imaging: CT versus MRI.* Eur Radiol, 2016. **26**(7): p. 2327-36.

18. Leadbetter, K.Z., et al., *The role of post-mortem MRI in the neonatal intensive care unit.* J Perinatol, 2017. **37**(1): p. 98-103.

19. Vullo, A., et al., *Post-mortem magnetic resonance foetal imaging: a study of morphological correlation with conventional autopsy and histopathological findings.* Radiol Med, 2016. **121**(11): p. 847-856.

20. Vrabel, M., *Preferred Reporting Items for Systematic Reviews and Meta-Analyses.* Oncol Nurs Forum, 2015. **42**(5): p. 552-4.

21. Whiting, P., et al., *The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews.* BMC Med Res Methodol, 2003. **3**: p. 25.

22. Wallace B.C., D.I.J., Trikalinos T.A. Lau J., Trow P., Schmid C.H., *Closing the Gap between Methodologists and End-Users: R as a Computational Back-End.* Journal of Statistical Software, 2012. **49**(5).

23. *Deeks, J. J., Altman, D. G. and Bradburn, M. J. (2001) Statistical Methods for Examining Heterogeneity and Combining Results from Several Studies in Meta-Analysis, in Systematic Reviews in Health Care: Meta-Analysis in Context, Second Edition (eds M. Egger, G. D. Smith and D. G. Altman), BMJ Publishing Group, London, UK. doi: 10.1002/9780470693926.ch15*. Publishing Group.

24. Bossuyt, P.M., et al., *Towards complete and accurate reporting of studies of diagnostic accuracy: The STARD Initiative.* Radiology, 2003. **226**(1): p. 24-8.

25. Irwig, L., et al., *Guidelines for meta-analyses evaluating diagnostic tests.* Ann Intern Med, 1994. **120**(8): p. 667-76.

26. Jaeschke, R., G. Guyatt, and D.L. Sackett, *Users' guides to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group.* Jama, 1994. **271**(5): p. 389-91.

27. Littenberg, B. and L.E. Moses, *Estimating diagnostic accuracy from multiple conflicting reports: a new meta-analytic method.* Med Decis Making, 1993. **13**(4): p. 313-21.

28. Moses, L.E., D. Shapiro, and B. Littenberg, *Combining independent studies of a diagnostic test into a summary ROC curve: data-analytic approaches and some additional considerations.* Stat Med, 1993. **12**(14): p. 1293-316.

29. Walter, S.D., *Properties of the summary receiver operating characteristic (SROC) curve for diagnostic test data.* Stat Med, 2002. **21**(9): p. 1237-56.

30. Glas, A.S., et al., *The diagnostic odds ratio: a single indicator of test performance.* J Clin Epidemiol, 2003. **56**(11): p. 1129-35.

31. Blokker, B.M., et al., *Non-invasive or minimally invasive autopsy compared to conventional autopsy of suspected natural deaths in adults: a systematic review.* Eur Radiol, 2016. **26**(4): p. 1159-79.

32. Lucas SB, C.H., Emmett S, Hargraves C, Mason M. The Coroner's Autopsy: Do we deserve better? Available at http://www.ncepod.org.uk/2006Report/Downloads/Coronial Autopsy Report 2006.pdf [Accessed on 23rd December 2016].

33. *Report from the NHS Implementation Sub-Group of the Department of Health Post Mortem, Forensic and Disaster Imaging Group (PMFDI). October 2012. Can Cross-Sectional Imaging as an Adjunct and/or Alternative to the Invasive Autopsy be Implemented within the NHS? Available at http://www2.le.ac.uk/departments/emfpu/Can Cross-Sectional Imaging as an Adjunct and-or Alternative to the Invasive Autopsy be Implemented within the NHS - FINAL.pdf [Accessed on 23rd December 2016].*

34. *NHS National Tariff Payment System 2016/17. Annex A available from https://www.gov.uk/government/publications/nhs-national-tariff-payment-system-201617.*