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A new method for the interpretation of veterinary forensic necropsy and PMCT finding with Bayesian decision theory

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ABSTRACT

This work proposes a novel approach to estimate the sensitivity of post-mortem computed tomography (PMCT) with respect to traditional necropsy (gold standard). Using concepts of Bayes theorem and the opinion of 57 veterinarians of how a relevant finding (RF) on PMCT or at necropsy can be a determinant in the animal's death, the general sensitivity was estimated. Such sensitivity can be interpreted as the probability to identify a specific RF in a necropsied animal. In the study, we included 18 animals that were subjected to traditional necropsy and underwent PMCT, which provided 48 different findings; all were assumed as a potential cause of death. This study aimed to understand the probability of death, given that a necropsied animal presented a specific RF. To estimate all contributions of the 48 RF, we designed a simple survey based on the Delphi method. In this survey, we invited veterinarians to evaluate the 48 *NF* and to assign a grade in a Likert scale from 0 to 10 for each of the RFs. In this scale, 0 (zero) indicates that the *NF* does not contribute to the animal's death, and 10 (ten) indicates that this *NF*does totally contributes to the animal's death. Therefore, each veterinarian, according to their own professional experience, assigns a grade describing how important each necroscopic finding is to the animal's death. Our results demonstrated that the problem of sensitivity analysis in the absence of a gold standard could be circumvented by the method proposed here.

1. Introduction

In general, the traditional methods for disease investigation in human and veterinary pathology diseases are necropsy, histopathology and cytopathology. In addition to these conventional methods, new procedures have emerged allowing for the expansion of pathological diagnosis, including the examination of the cadavers using computed tomography and magnetic resonance imaging prior to or without a traditional necropsy [1]. This post-mortem computed tomography (PMCT) enables the detection of macroscopic (gross) findings, and may also correlate these lesions with specific diseases.

In the past 15 years, post-mortem computed tomography (PMCT) has emerged as an important imaging procedure in forensic pathology, especially to be able to provide necropsy detection of lesions and also determination of the cause of death [2,3]. Currently, transitional necropsy is considered as a gold standard and PMCT as an adjuvant method for investigation of the cause of death in both humans and animal. However, PMCT has been previously recognized as superior to the gold standard, in the detection of micro fractures and gas in the body cavities or vascular system [4]. Traditional methods to calculate sensitivity is these cases result in values greater than one, which is not a reasonable way to compare the two approaches.

The use of PMCT in veterinary medicine is still incipient, but with a perspective of significant increase in its applicability [5,6]. The vulnerability of animals subject to accidents or mistreatment further justifies the use of forensic radiology, particularly through PMCT to detect osseous lesions which may be missed with a traditional necropsy method.

In many situations, the evaluation of the diagnostic accuracy of a test is seriously compromised by the lack of a reference standard, when

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the reference standard is imperfect or when there is no accepted reference standard [7]. These situations are called “no gold standard situations”. A review performed by Rutjes et al. [7] analyzes several solutions that have been proposed to surpass this problem.

The Bayesian approach has been largely applied in medical studies, specifically in diagnostic tests. Herein, this study will establish a parallel between the usual diagnostic test context and the necropsy process. In this analogy, the dead animals can be compared as an ill individual and a relevant finding (*NF*), taking the role of the diagnostic test, where this *NF* can or cannot be the cause of death. Therefore, the necropsy can be seen as a classification process, based on available evidence. Here, evidence is defined as the set of reported information that lead us to make a decision about the cause of death [8].

In this study, we propose a novel approach to estimate simultaneously the sensitivity of PMCT and traditional necropsy through the use of an inverse Bayes theorem.

2. Materials and methods

2.1. The Bayesian theory

In Bayesian theory, there are two important definitions. The first is *a priori probability* (*P*(*event*)), which refers to probabilities related to an event in the absence of any information explaining the presence or absence of some fact. The second is *a posteriori probability* (*P*(*event*|*evidence*)), which is the conditional probability of an event where there is some evidence related to these phenomena [8].

Here there is an illustration of those definitions using examples of the context of this study. For example, the *a posteriori probability* that an animal has died given that it presented a particular *RF* in the necropsy is given by:

$$P(dead|RF) = \frac{|dead \cap RF|}{|RF|} \quad (1)$$

where the bars indicate the number of elements in those sets. Therefore, the *a posteriori probability* given in (1) is the number of individuals who, simultaneously, have died and had a particular *RF*, divided by the total of individuals who had the particular *RF*. The expression (1) can be rewritten as (2), which is also known as a Bayes equation [8].

$$P(dead|RF) = \frac{P(dead) \times P(RF|dead)}{P(RF)} \quad (2)$$

where:

- *P*(*dead*) is the probability of observing an animal that is dead;
- *P*(*RF*) is the probability of observing a RF;
- *P*(*dead*|*RF*) is the probability of observing an animal that is dead given that the RF is true (conditional probability);
- *P*(*RF*|*dead*) is the probability of observing a RF given the animal is truly dead.

2.2. Concept of general sensitivity

Consider Table 1 below:

From Table 1, a given animal may (or may not) present lesions (RF) that are related to its cause of death (*causa mortis*). It is possible for a live animal to have potential *causa mortis* lesions however live animals were not included in this study. The focus of this study is on the presence or absence of RF in the dead animal.

Table 1
General 2 × 2 table, the relationship between the presence or absence of RF and the fact of whether the animal is dead or live is indicated.

	Dead animal	Live animal	Total
Present RF	*a*	*b*	*a* + *b*
Absent RF	*c*	*d*	*c* + *d*
Total	*a* + *c*	*b* + *d*	*a* + *b* + *d* + *c*

As in Table 1, once a specific RF is present in a dead animal, the question is how probable is this RF to contribute to the *causa mortis*. Mathematically, this probability is the relationship $a/(a + c)$ and is the sensitivity of this study design. However, because the type of necropsy technique does not matter (it is important to only confirm the presence or absence of the RF), this relationship $a/(a + c)$ can be considered a general sensitivity (GS). In other words, this GS reflects the experience of the veterinarian about the probability of death for each RF, and it represents the *P*(*dead*|*RF*).

Now, given that it was estimated *P*(*dead*|*RF*) for each *RF*, there was possible to estimate the *P*(*RF*|*dead*). Here, *P*(*RF*|*dead*) refers to the probability that a dead animal had a specific *RF*. From Eq. (1), and considering that *P*(*dead*) = 1 (since the animal has already died), it is possible to isolate the term *P*(*RF*|*dead*) as:

$$P(RF|dead) = P(dead|RF) \times P(RF) \quad (3)$$

In a practical routine, *P*(*RF*|*dead*) can be interpreted as the probability to identify a specific *RF* in a necropsied animal. This *a posteriori probability P*(*RF*|*dead*) is valid for any necropsy technique.

3. Data collection and calculation of results

3.1. Relevant findings in animals

From September 2016 to September 2017, 18 necropsies were performed on 18 animal cadavers (total number of necropsies: $n = 18$). These cadavers were collected from the Department of Parks and Green Areas of the city of São Paulo (DEPAVE) and private veterinary hospitals. Cadavers of wild animals (brown howler monkeys, lesser anteaters and opossums) and domestic dogs were included in this study.

Veterinary pathologists performed necropsies on all these cadavers using two techniques: the PMCT and conventional methods (the former were evaluated by veterinary radiologists). In a traditional necropsy, if necessary, organ sample collection was performed for laboratory analysis.

48 different necropsy and PMCT findings (RF) were detected. All of them assumed to be a potential *causa mortis*. The description of RF was defined according to both methods. The probability that an animal had died due to a specific relevant finding, that is, *P*(*RF*) was calculated

$$P(RF) = \frac{|necropsies\ RF^{+}|}{|necropsies|} \quad (4)$$

where $|necropsies\ RF^{+}|$ indicates the number of necropsies that had this RF, and $|necropsies|$ is the total number of necropsies.

3.2. Interviewing veterinarians

When an animal dies, some pathological changes (that may or may not be due to natural factors) occur in its organs. Biologically, the understanding of this process was simplified considering that a set of pathological changes is responsible for the animal's death. However, it is difficult to understand which of those relevant findings were decisive in its death. Given that a necropsied animal presented a specific RF, this type of conditional probability is the *a posteriori probability*,*P*(*dead*|*RF*) and has been previously introduced in (3). *P*(*dead*|*RF*) indicates the *a posteriori probability* of an animal´s death, considering that it has a specific *RF*. For example, suppose that there are one hundred necropsied animals registered in a veterinary hospital, and all these animals presented left ventricular hypertrophy (*LVH*). In other words, these 100 animals presented with LVH (therefore|*necropsies* $RF^{+}| = 100$). However, among these hundred cases, 65 animals were reported as having died due to *LVH*. The remaining 35 animals could have died due to different reasons (for example, a severe head injury).

Table 2
Summary of results obtained from necropsy data. PMCT: post-mortem computed tomography; CN: traditional necropsy; Sens: sensitivity of PMCT in respect to CN (gold-standard); RF: relevant finding; Und: undetermined.

Necroscopic relevant findings	Number of cadaver with this RF $\lvert necropsies\ RF^{+}\rvert$	PMCT	CN	Sens.	P(particular RF)[1]	P(dead | particular RF)[2]	P(particular RF | dead)[3]
Spleen inside the thoracic cavity	1	1	1	1.00	0.056	0.800	0.044
Bronchiectasis	1	1	0	Und.	0.056	0.700	0.039
Calcification of cardiac vessels	1	1	0	Und.	0.056	0.650	0.036
Stomach contents in the internal region of the abdominal wall with attached omentum	1	0	1	0.00	0.056	0.800	0.044
Hepatic Congestion	1	0	1	0.00	0.056	0.450	0.025
Pulmonary densification	1	1	0	Und.	0.056	0.500	0.028
Cardiac displacement to the caudal and dorsal region of the thorax	1	1	1	1.00	0.056	0.650	0.036
Stomach displacement into thoracic cavity	1	1	1	1.00	0.056	0.800	0.044
Dilation of cardiac chambers	1	0	1	0.00	0.056	0.600	0.033
Disjunction of the mental symphysis	1	1	1	1.00	0.056	0.400	0.022
Severe abdominal distension	1	1	1	1.00	0.056	0.700	0.039
Two perforations on right ventricle	1	0	1	0.00	0.056	1.000	0.056
Brain edema	2	2	2	1.00	0.111	0.850	0.094
Pulmonary edema	13	0	13	0.00	0.722	0.800	0.578
Pulmonary emphysema	6	0	6	0.00	0.333	0.700	0.233
Omentum adhered to the abdominal wall	1	0	1	0.00	0.056	0.450	0.025
Right-sided heart wall thickening	1	0	1	0.00	0.056	0.600	0.033
Eventration in the left inguinal region of the abdominal wall	1	1	1	0.00	0.056	0.600	0.033
Fracture of thyroid cartilage / hyoid bones	1	1	0	Und.	0.056	0.600	0.033
Fracture of scapulae	1	1	0	Und.	0.056	0.500	0.028
Palate fracture	1	1	1	1.00	0.056	0.500	0.028
Fracture of the right-sided zygomatic arch	1	1	1	1.00	0.056	0.450	0.025
Fracture of the left-sided zygomatic arch	1	1	1	1.00	0.056	0.500	0.028
Frontal bone fracture	1	1	1	1.00	0.056	0.750	0.042
Temporomandibular joint fracture (condyle)	2	2	0	Und.	0.111	0.650	0.072
Fracture in temporal region	1	1	0	Und.	0.056	0.700	0.039
Exposed fracture in tibio-tarsal joint region	1	1	1	1.00	0.056	0.400	0.022
Mediastinal herniated subcutaneous fat	1	1	0	Und.	0.056	0.400	0.022
Hemopericardium	1	0	1	0.00	0.056	0.800	0.044
Hemoperitonum	5	0	5	0.00	0.278	0.700	0.194
Bleeding between ribs	1	0	1	0.00	0.056	0.600	0.033
Hemothorax	10	0	10	0.00	0.556	0.800	0.444
Pulmonary laceration	3	2	3	0.67	0.167	0.900	0.150
Puncturing-lesion in the left-sided thoracic region	1	0	1	0.00	0.056	0.900	0.050
Abnormal lung location	1	1	0	Und.	0.056	0.700	0.039
Multiple rib fractures	4	4	3	1.00	0.222	0.800	0.178
Splenic neoplasia	2	1	2	0.50	0.111	0.600	0.067
Pulmonary parenchymal nodules	1	1	1	1.00	0.056	0.600	0.033
Loss of encephalic mass	1	1	1	1.00	0.056	0.900	0.050
Pneumothorax	2	2	0	Und.	0.111	0.800	0.089
Complete rupture of cardiac vessels	1	1	1	1.00	0.056	1.000	0.056
Rupture of the trachea in carina region	1	1	1	1.00	0.056	0.900	0.050
Aortic rupture	1	1	1	1.00	0.056	1.000	0.056
Abdominal wall rupture	1	0	1	0.00	0.056	0.800	0.044
Dorsal and ventral rupture of the diaphragm	1	1	1	1.00	0.056	0.900	0.050
Rupture of atria	1	1	1	1.00	0.056	1.000	0.056
Hepatic rupture	3	0	3	0.00	0.167	0.900	0.150
Increased left-sided ventricle	1	0	1	0.00	0.056	0.600	0.033

[1] $P(particular\ RF)$ was calculated according to Eq. (4)
[2] $P(dead|particular\ RF)$ was indicated according to the median grade of veterinarians
[3] $P(particular\ RF|dead)$ was calculated according to Eq. (3) based on the results of $P(particular\ RF)$ and $P(dead|particular\ RF)$

Therefore, the *a posteriori probability* of death of an animal who presented *LVH* is:

$$P(dead|LVH) = 65/100 = 0.65 \quad (5)$$

Observe from this example, that the total of necropsies ($|necropsies|$) is not informed.

To estimate all $P(dead|RF)$ of the 48 *RF*, a simple survey based on the Delphi method was elaborated [9–11]. In this survey, veterinarians were invited to evaluate these 48 *RF* and to assign a grade in a Likert scale [12] from 0 to 10 for each RF. In this scale, 0 (zero) indicates that the *RF* does not contribute to the animal's death, and 10 (ten) indicates that this *RF* contributes to the animal's death.

3.3. Estimation of general sensitivity

For this study, 57 veterinarians participated in our survey. Therefore, each of the 48 *RF* presented a grade sample of 57 grades. To summarize all these grades in a unique value, the median of each set of the grades was calculated. Thus, 48 median values were obtained.

Each of these median values was normalized to fit in a range of values from 0 to 1. Finally, these normalized values are the $P(dead|RF)$ for each *RF*. Therefore, for each of the 48 values of $P(dead|RF)$ and P

(*RF*), the respective $P(RF|dead)$ was estimated (3).

4. Results

A summary of all results of the veterinary interview is presented in Table 2 with values of sensitivity, values of the probabilities that a RF is observed, the probabilities of an animal is dead, given that the RF is true and the probabilities of a RF is observed given that the animal is truly dead. The table illustrates the possibility of using this statistical method to compare two distinct techniques.

5. Discussion

In this study, we present a novel and successful approach to estimate the combined sensitivity of PMCT and traditional necropsy in a set of animal cadavers. This approach combined Bayesian theory with the Delphi method to estimate the desired sensitivity values. The method proposed assumes that the opinions of the interviewed veterinarians represent the equivalent of the Bayesian *a posteriori* probability that each relevant finding contributed to each animal's cause of death. The Bayesian equivalent of the *a priori*, that is, the probability of the event, in this case death, is equal to 1. Therefore, we simply inverted the Bayesian equation to obtain the combined sensitivity of the traditional necropsy with the PMCT of the 18 animals in our sample.

When confronted with situations in which no reliable gold standard is available in diagnostic studies, researchers try to construct, modify or assume an *ad hoc* reference to obtain the necessary statistics related to accuracy. However, in many cases, these approaches cannot be applied because a reliable reference standard simply does not exist [7]. This justifies the applicability of the method in the comparison between traditional necropsy and PMCT. For example, gas accumulations are more clearly depicted on PMCT than assessable at traditional necropsy, which was considered until then a gold standard for all post-mortem findings. In addition, PMCT revealed multiple rip fractures in 4 and CN only in 3 of all necropsies.

To the best of our knowledge, this is the first study that addresses the problem of estimating the sensitivity of diagnostic methods in the absence of a gold standard using the Bayesian theory. It circumvents the classical problem of the absence of a standard reference by assuming the opinion of experts and by simply inverting the Bayesian equation to obtain the combined sensitivity of both necroscopic methods.

The positive side of this approach is its simplicity, in the sense that an easy calculation of the inverted Bayesian equation can provide the desired sensitivity. However, its limitations consist of the necessity of a reliable source of pathology knowledge to provide the correspondent *a posteriori probability* related to the causes of deaths. The set of voluntary veterinarians interviewed in this study are general practitioners that only had basic pathology training and was included in this study to illustrate the method proposed. Therefore, our results should not be assessed with any diagnostic value but rather provide an illustration of the methods proposed in this work. For that reason, it is not necessary, in this specific situation, to discuss individual values of necropsy and PMCT findings listed in the descried table. The aim of this study was to introduce a new method for comparison between two post-mortem diagnostic techniques.

Finally, we believe that this work represents a relevant contribution to the evaluation of diagnostic performances of complementary methods in forensic pathology. Future studies could provide more relevant cases that could confirm the validity of this new approach.

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