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CANCER AS EVIDENCE: FORENSIC IMPLICATIONS IN DISEASE AND DEATH; A NARRATIVE REVIEW

Narrative Review

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ABSTRACT

Background: Cancer, while long considered a clinical concern, is increasingly recognized for its forensic relevance. Beyond its pathological manifestations, malignancy can complicate cause-of-death investigations and carry implications for legal accountability. Its ability to mimic trauma, induce fatal thrombotic events, or result from environmental and occupational exposures positions cancer as a critical but underexplored element in forensic science.

Objective: This narrative review aims to explore the intersection of oncology and forensic medicine, emphasizing the diagnostic, medico-legal, and evidentiary roles that cancer can play in death investigations. The review synthesizes recent advancements in molecular diagnostics and highlights their application in forensic pathology.

Main Discussion Points: The review discusses how cancer can be a primary, contributory, or incidental cause of death, and how its presentation may mimic trauma or natural diseases. It explores the forensic implications of cancer-associated thrombosis, toxicological exposures, and occupational carcinogens. Advanced molecular techniques such as next-generation sequencing (NGS), epigenetic profiling, liquid biopsy, digital pathology, and molecular autopsy are examined for their potential in clarifying cause and manner of death in complex cases. Ethical, legal, and genetic considerations, especially concerning hereditary cancer syndromes, are also addressed.

Conclusion: Cancer is both a pathological condition and a potential source of forensic evidence. Its integration into forensic investigations, supported by molecular and imaging technologies, enhances the accuracy of death certification and medico-legal accountability. Further research and standardized guidelines are needed to solidify forensic oncology as a core component of modern death investigation.

Keywords: Forensic Oncology, Molecular Autopsy, Cancer-Associated Thrombosis, Toxicogenomics, Postmortem Diagnostics, Digital Pathology.

INTRODUCTION

Cancer remains one of the leading causes of mortality globally, ranking among the top ten causes of death and accounting for millions of fatalities each year. Despite its profound health burden, the forensic implications of cancer remain under-explored in comparison to other common causes of death such as cardiovascular disease or infectious conditions (1,2). Traditionally viewed through the lens of clinical medicine—with emphasis on diagnosis, therapeutic management, and control—cancer is increasingly acknowledged within forensic science as a contributor to disease progression, sudden or unexpected death, and even legal inquiries spanning civil and criminal domains (3,4). The forensic dimension of cancer lies at the intersection of medicine and law, where malignancy not only represents a pathological entity but also an evidentiary object. Certain cancers can mimic traumatic injuries or accelerate processes like thrombosis or hemorrhage, thereby obscuring the actual cause of death or misleading forensic interpretation (5,6). In such scenarios, malignancy may mask a criminal act, be mistaken for natural death, or serve as a complicating factor in legal evaluations of liability or intent. The complexity of such cases necessitates multidisciplinary expertise involving pathology, oncology, toxicology, and legal analysis. Beyond postmortem diagnosis, the forensic relevance of cancer extends into occupational and environmental domains. Cancers induced by exposure to carcinogens like asbestos, benzene, or radiation often become focal points of workplace litigation and compensation claims, especially in contexts of negligence (7-9).

Similarly, instances of delayed cancer diagnosis or suboptimal management may lead to malpractice suits, particularly when they involve vulnerable populations or missed warning signs. In rare but significant cases, cancer or cancer-inducing substances have been weaponized to disguise homicide or administer slow-acting harm, blurring the boundaries between natural pathology and criminal intent. These scenarios demand the application of forensic toxicology and molecular biology to differentiate between naturally occurring malignancy and malignancy induced through external manipulation (10). Recent advances in molecular forensics—such as next-generation sequencing, digital pathology, molecular autopsy, and epigenetic profiling—have vastly improved the precision with which pathologists can classify malignancies by etiology, be it genetic, environmental, or iatrogenic (11,12). These tools not only support accurate cause-of-death determination but also aid in identifying population-level exposures and hereditary cancer syndromes, many of which carry profound legal and ethical implications. Given the rising incidence of cancer globally, particularly in aging populations, the need to integrate cancer-specific evaluations into routine forensic investigations has become increasingly urgent. The objective of this review is to critically examine the forensic dimensions of cancer, exploring its diagnostic complexities, legal implications, and the transformative role of modern molecular techniques in determining cause, intent, and liability.

CANCER IN FORENSIC PATHOLOGY

Determining Cause of Death

Forensic pathology plays a pivotal role in discerning whether malignancy was the direct cause of death, a contributing factor, or an incidental finding. Advanced cancers can precipitate fatal events such as hemorrhage from hepatic tumor rupture, respiratory failure due to lung carcinoma, or herniation resulting from intracranial tumors (1). Accurate determination requires comprehensive autopsy analysis, including histopathology and immunohistological studies, to elucidate the mechanism of death (2). This process is critical for medico-legal documentation and to address queries raised by next-of-kin regarding the role of cancer in death (3). However, complexities arise when cancer coexists with other fatal conditions like pneumonia, malnutrition, or sepsis—either as sequelae of the disease itself or as adverse effects of treatment modalities such as chemotherapy or radiotherapy (2). In these instances, forensic experts must distinguish between natural death, iatrogenic effects, or indirect cancer-related complications. This causal chain holds particular weight in legal claims involving negligence, insurance disputes, or occupational exposure, demanding a robust scientific rationale that aligns with legal frameworks (3).

Mimicking Trauma and Natural Disease

Malignancies frequently masquerade as trauma or other natural disease processes, complicating forensic assessments. For example, metastatic bone lesions may lead to pathological fractures that mimic blunt force trauma (4). Similarly, spontaneous tumor ruptures, such as those seen in hepatic carcinomas, can cause internal hemorrhage that might be misconstrued as an inflicted injury without careful histological scrutiny (5). The differentiation of injury origin is essential to avoid misinterpretation of cause or manner of death (6).

Cardiac tumors, including atrial myxomas or metastases, can induce sudden arrhythmias and may be erroneously diagnosed as ischemic events during autopsy (7). Brain tumors can mimic cerebrovascular accidents or present as isolated seizures, which could lead to misattribution of cause of death if malignancy is not thoroughly investigated (8). This underscores the necessity for forensic oncological perspectives, even in cases where cancer is not initially suspected, particularly in sudden or unexplained deaths (9).

Tumor-induced Thrombosis

Cancer-associated thrombosis remains a significant yet under-recognized cause of death. Tumor cells often secrete pro-coagulant substances such as tissue factor, leading to a hypercoagulable state and increased risk of venous thromboembolism (VTE), particularly pulmonary embolism (10). Malignancies of the pancreas, lung, gastrointestinal tract, and ovaries are particularly prone to induce such events. Determining whether death resulted from tumor-induced thrombosis or therapy-related immobility or toxicity requires histological, radiological, and clinical record correlation (11,12). In legal contexts, this information becomes critical, particularly in malpractice litigation or workers' compensation claims involving delayed or inappropriate management (13,14).

TOXICOLOGICAL AND ENVIRONMENTAL IMPLICATIONS

Carcinogen Exposure

Forensic toxicology contributes significantly to identifying occupational and environmental exposures to known carcinogens such as benzene, arsenic, vinyl chloride, and polycyclic aromatic hydrocarbons (15). Through biological sampling and environmental testing, forensic experts can provide scientific backing for claims involving industrial negligence, regulatory failure, or unsafe occupational environments (16). These exposures, when linked with specific malignancies, serve as powerful evidence in civil suits and regulatory enforcement.

Chemical and Radiation-induced Malignancies

The causal relationship between chemical or radiation exposure and tumor development is well-documented. Classic examples include mesothelioma due to asbestos, bladder cancer from aromatic amines, and thyroid cancer from ionizing radiation (17). In scenarios involving nuclear accidents, medical radiation mishaps, or intentional radioactive poisoning, forensic analysis must determine whether malignancy arose spontaneously or from identifiable exposure. Techniques like mutational sequencing and cytogenetics aid in establishing causality (18).

Poisoning Cases with Cancer Outcomes

Some carcinogens operate on a delayed timeline, making them harder to link definitively to malignancy. Chronic exposure to aflatoxins or arsenic may only manifest as liver or skin cancer decades later (19). Such latency complicates legal attribution, requiring integration of epidemiological data, toxicogenomic biomarkers, and exposure histories to support causation in court (20). These scenarios challenge forensic experts to bridge medical science with legal standards of evidence in the pursuit of justice.

MOLECULAR FORENSIC ONCOLOGY

DNA Profiling from Tumor Tissues

Tumor tissues, although genetically unstable, can still be used in forensic DNA profiling when other biological materials are unavailable. Innovations such as single-cell DNA sequencing and next-generation sequencing (NGS) allow for differentiation between somatic and germline mutations, aiding in victim identification and offering ancillary insights into cancer biology (3,6). This has proven particularly useful in mass disasters or cases involving decomposed remains (13).

Molecular Autopsy

Molecular autopsy has extended beyond cardiometabolic disorders to include oncological investigations. In unexplained sudden deaths, genomic screening may reveal hidden malignancies or predisposing mutations (12). Cancers like cardiac sarcomas or certain hematological malignancies may be clinically silent yet identifiable postmortem through molecular tools (13). The discovery of hereditary cancer syndromes, such as BRCA or TP53 mutations, holds implications for both public health and family genetic counseling (14,15).

Epigenetic Biomarkers

Epigenetic modifications, such as DNA methylation patterns, reflect cumulative environmental and lifestyle exposures. These biomarkers are becoming valuable in forensic oncology to establish causation and context in cancer cases (16). For instance, gene-

specific hypermethylation may implicate tobacco or arsenic exposure, while global hypomethylation might suggest radiation-induced transformation. Their application strengthens forensic arguments in occupational claims or suspected poisonings (17).

MEDICO-LEGAL AND ETHICAL CONSIDERATION

Medical Negligence

Cancer-related deaths frequently raise concerns of delayed diagnosis or substandard care. Forensic specialists examine histology, autopsy findings, and clinical documentation to assess whether timely interventions could have altered the disease trajectory (18). Malpractice litigation often hinges on proving that earlier detection or alternative treatment might have extended survival or mitigated suffering (19).

Criminal Cases

While rare, malignancy has been implicated in criminal acts involving deliberate exposure to carcinogens. Notable cases include poisoning with radioactive isotopes or chronic arsenic ingestion intended to induce terminal illness (10,12). Here, forensic toxicology, molecular diagnostics, and histopathology are essential in establishing causation and intent.

Genetic and Ethical Issues

With increasing use of genetic profiling, ethical dilemmas arise concerning privacy, consent, and familial implications. Discovery of hereditary cancer syndromes postmortem can affect living relatives' insurability and psychological well-being (11,15). Forensic professionals must carefully navigate these sensitive disclosures, balancing the legal imperative of truth with ethical responsibility to safeguard genetic information.

EMERGING TECHNOLOGIES IN FORENSIC ONCOLOGY

Digital Pathology and AI

The integration of AI into digital pathology is revolutionizing cancer evaluation in forensic practice. Automated pattern recognition enhances diagnostic accuracy, reduces inter-observer variability, and provides enduring digital records that are admissible in legal contexts (14,17). These technologies improve reproducibility and minimize diagnostic errors in complex cancer cases.

Forensic Radiology (Virtopsy)

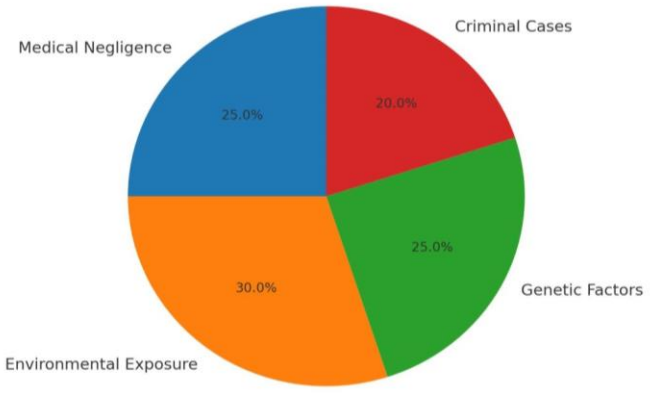
Virtopsy, or postmortem imaging through CT and MRI, offers a non-invasive means of identifying tumors, metastases, and related complications (13,18). It is particularly useful when traditional autopsies are culturally or legally restricted. Radiologic findings can be preserved as digital evidence, offering clarity in contentious forensic investigations.

Liquid Biopsy in Postmortem Samples

Circulating tumor DNA (ctDNA), exosomes, and other tumor-derived biomarkers can be retrieved from postmortem fluids, even in partial decomposition. These minimally invasive tools complement molecular autopsy findings, offering a snapshot of malignancy burden and subtype (14). Liquid biopsy enhances the diagnostic yield where tissue sampling is limited.

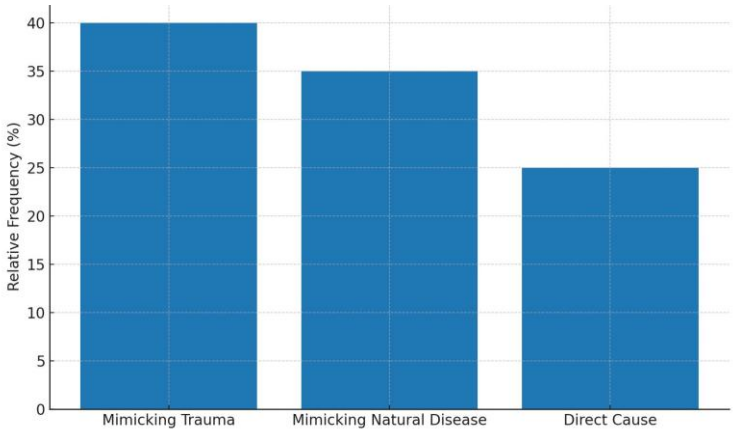
Omics Approaches

Omics technologies—including genomics, transcriptomics, proteomics, and metabolomics—are providing unprecedented detail in understanding cancer's origin and evolution (15). These methods help differentiate spontaneous from exposure-related malignancies and identify molecular fingerprints of iatrogenic or natural cancer pathways. As bioinformatics and databases expand, their utility in forensic settings will only grow, integrating seamlessly into multidisciplinary cancer investigations (16).



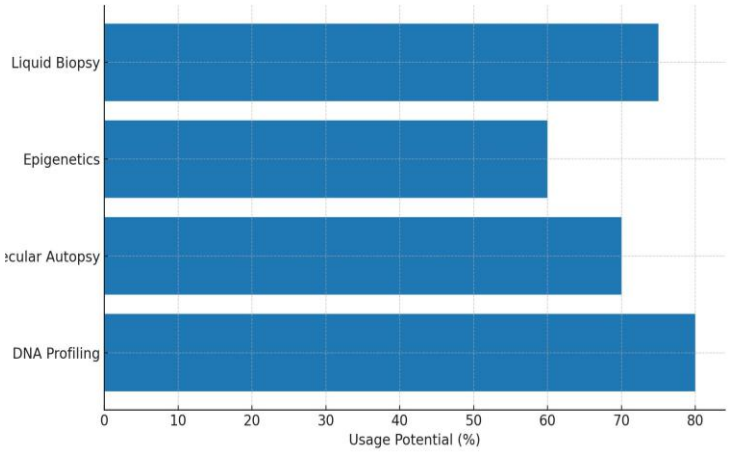
Forensic Contexts of Cancer

Figure 1 Forensic Context of Cancer



Cancer Presentation in Forensic Pathology

Figure 2 Cancer Presentation in Forensic Pathology



Emerging Molecular Tools in Forensic Oncology

Figure 3 Emerging Molecular Tools in Forensic Oncology

CRITICAL ANALYSIS AND LIMITATIONS

The existing literature on the forensic implications of cancer, though expanding in recent years, demonstrates several limitations that restrict the robustness and applicability of findings across diverse medico-legal contexts. A critical analysis reveals that much of the current evidence is derived from observational case reports, retrospective chart reviews, or descriptive studies lacking the methodological rigor typically associated with randomized controlled trials. The scarcity of prospective studies with large, representative cohorts hinders the ability to draw causal inferences or generalize findings across varied forensic populations. For instance, studies exploring tumor-induced thrombosis or carcinogen-related malignancies often rely on single-center autopsy reviews or case series without sufficient statistical power to establish broader forensic significance (20-23). Methodological biases also pervade this body of research. Selection bias is notable in literature that focuses on high-profile forensic cases or autopsy-confirmed malignancies, inadvertently excluding cases that may have remained clinically undiagnosed or were subject to cultural objections against autopsy. Performance bias, such as lack of blinding among evaluators interpreting histopathological or toxicological findings, further limits

objectivity in determining cause of death or the role of occupational exposure. Moreover, the retrospective nature of many studies limits the ability to control for confounding variables like comorbidities, treatment history, or genetic predispositions, which are crucial in forensic interpretations involving cancer. Another considerable issue is the presence of publication bias. Literature tends to disproportionately highlight rare or dramatic cases—such as criminal poisonings or radiation-induced malignancies—while negative or inconclusive findings are underreported. This creates a skewed perception of the forensic relevance of cancer, potentially overstating its frequency or diagnostic clarity in routine practice. There is limited evidence on cancer cases that were initially suspected to be of forensic interest but were later confirmed as clinically natural deaths, thus neglecting the full spectrum of diagnostic ambiguity faced by forensic pathologists.

Measurement variability across studies also complicates comparison. Different research articles employ inconsistent criteria for diagnosing cancer-associated thromboembolism, exposure-induced malignancy, or molecular autopsy findings. This lack of standardization makes it difficult to assess the accuracy or reproducibility of forensic tools such as DNA profiling, epigenetic assays, or postmortem imaging in identifying cancer-related causes of death. Without validated benchmarks for interpreting these technologies, findings remain context-dependent and prone to misclassification. Generalizability of current findings remains constrained. Most forensic oncology studies are conducted in specialized centers or developed countries, where access to advanced molecular diagnostics, virtopsy, and omics technologies is available. This limits the applicability of their conclusions to low- and middle-income regions where cancer burden is equally high but forensic infrastructure is often lacking. Moreover, sociocultural, religious, and legal differences regarding postmortem examination further affect the integration of cancer-related evidence in forensic practice globally. Hence, while molecular autopsy and digital pathology show promise, their translation into diverse forensic settings remains aspirational without equitable access and contextual adaptation. To advance the field of forensic oncology, there is a pressing need for multicenter, prospective studies with standardized protocols, transparency in reporting negative findings, and improved methodological controls. A greater emphasis on interdisciplinary collaboration—bridging oncology, toxicology, pathology, molecular genetics, and law—will be instrumental in ensuring that forensic interpretations of cancer are not only scientifically sound but legally defensible and ethically grounded.

IMPLICATIONS AND FUTURE DIRECTIONS

The forensic investigation of cancer has emerged as a critical interdisciplinary domain with significant implications for clinical practice, medico-legal policy, and scientific inquiry. The integration of molecular autopsy, digital pathology, forensic radiology, and advanced toxicological assessments into routine postmortem protocols enhances the precision and scope of determining cancer-related causes of death. For clinicians, these advancements underscore the importance of maintaining detailed medical records, including treatment history, genetic testing outcomes, and exposure documentation, as such data may later inform forensic judgments in malpractice claims or insurance disputes. Additionally, awareness of tumor-induced complications such as thromboembolism or organ compression necessitates more vigilant clinical monitoring in high-risk cancer patients, potentially reducing mortality and improving prognostic accuracy (24,25). From a policy and guideline perspective, the review advocates for the standardization of forensic oncology procedures across institutions. Uniform guidelines are needed to determine when molecular tools such as epigenetic profiling or liquid biopsy should be deployed in postmortem evaluations. Regulatory bodies and professional organizations must also clarify ethical frameworks for the disclosure of genetic findings, especially when they bear implications for surviving family members. The implementation of these guidelines can help ensure both legal accountability and public health benefit, especially in regions where hereditary cancer syndromes remain under-recognized (23,24).

Despite growing literature, numerous unanswered questions persist. There remains limited data on the diagnostic accuracy of omics technologies in forensic oncology, particularly in resource-constrained settings. The specificity and sensitivity of postmortem ctDNA detection in differentiating spontaneous from induced malignancies are still poorly characterized. Additionally, long-term effects of low-dose carcinogen exposure and their latency in causing cancer are not well quantified, especially in forensic timelines requiring legal attribution (26). These gaps demand targeted research to validate and optimize emerging tools for their utility and admissibility in court. Future research should prioritize multicenter, prospective studies with standardized protocols to evaluate diagnostic accuracy and interobserver reliability of molecular techniques in forensic practice. Studies incorporating control groups, blinded assessments, and stratification based on cancer type, exposure source, and treatment history would offer more robust insights. There is also a need for longitudinal research on families affected by hereditary cancers discovered through forensic investigation, which can elucidate downstream health outcomes and psychosocial impacts. Ultimately, the field would benefit from interdisciplinary collaborations

between forensic pathologists, oncologists, geneticists, and legal experts to build a comprehensive evidence base that informs both practice and policy while upholding ethical responsibilities in the investigation of cancer-associated deaths (27).

CONCLUSION

Cancer is increasingly recognized within forensic science not only as a natural cause of death but also as a vital indicator of environmental exposure, delayed medical care, or, in rare instances, covert criminal intent. This review highlights that, malignancies can mimic traumatic injuries, induce fatal thrombotic events, and complicate toxicological interpretations, making their accurate forensic evaluation both challenging and essential. The application of emerging molecular technologies—such as digital pathology, virtopsy, liquid biopsy, and multi-omics profiling—has significantly enhanced the ability to determine cause of death with greater precision and medico-legal relevance. Although current evidence is promising, much of it is derived from limited or context-specific studies, warranting cautious interpretation. Clinicians, forensic specialists, and policymakers are urged to adopt multidisciplinary frameworks and ethical protocols when investigating cancer-related deaths. Future research should aim to strengthen the evidence base through large-scale, standardized, and ethically guided studies that integrate clinical data, molecular diagnostics, and forensic evaluation to ensure justice and scientific integrity in death investigations involving malignancy.

AUTHOR CONTRIBUTION

Author	Contribution
Raza Ullah*	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Muskan	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sania Baloch	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Farwah Siddiqi	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Dolat Ram	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Salman Ahmed	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published
Iqra Solangi	Contributed to study concept and Data collection Has given Final Approval of the version to be published
Ishrat Bibi	Writing - Review & Editing, Assistance with Data Curation

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