Perspectives Article

A review of early based cancer detection approaches for canine hemangiosarcoma*

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The leading cause of death in canines is cancer, with six million dogs diagnosed in the United States (U.S.) every year. Among these, hemangiosarcoma (HSA) – a common, aggressive, and malignant canine cancer is the particular focus of this review. Currently, there is a growing body of literature surrounding liquid biopsies, an emerging screening and diagnostic tool for cancers through the detection of DNA-based biomarkers (e.g., cfDNA, ctDNA). However, there is a gap linking liquid biopsy practices and specifically the detection of HSA. Therefore, this literature review aims to review the current methods for screening HSA and propose a biosensor system-based liquid biopsy approach to screening for HSA.

Keywords: Canine hemangiosarcoma, liquid biopsies, cancer detection, canine cancer

HSA is a malignant cancer that arises from endothelial cells in the bone marrow of the canine and travels throughout the body through blood vessels and to other organs where the tumor starts to grow (Borgatti et al., 2017). These cancerous cells divide rapidly and form in areas with high blood circulation, like the heart, the liver, and the spleen, but may also form on other organs; they are most commonly found in the right atrium of the heart. This cancer is most common in middle-aged and older thin-haired canines but may also occur in all breeds. (Ritt & Breen, 2007) If undiagnosed or untreated, it may cause the endothelial tissue to fill with blood, become thin, and rupture, leading to hemorrhage and ultimately death. Some clinical symptoms include skin discoloration and blood-filled tumors on organs that may unbiddenly bleed (NC State Veterinary Hospital, n.d). Treatment for this cancer is minimal; therefore, initial prevention is more effective (Cohen & Sylvester, 2024). Due to the cancer's fast-growing nature, by the time it is detected, it is usually too late, as canines typically pass away about a year after diagnosis (Jones, 2022).

Current Detection Methods for HSA

Early detection and treatment of cancerous cells can limit the spread of HSA tumors, as well as reduce the risk of death. Currently, diagnoses and screenings for HSA focus on the examination of tissue samples (i.e., tissue/ solid biopsies); moreover, the usage of liquid biopsies through biomarkers, such as cell-free DNA (cfDNA), is used as an additional screening (Hirahata et al., 2022).

Currently, the most well-understood and commonly used diagnostic procedure for

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canines with HSA is through tissue biopsies. In these biopsies, samples of tissue are extracted to be microscopically analyzed, followed by a pathologist, who will determine a diagnosis based on the collected analysis (Ko et al., 2025). As a result of its reliability, solid biopsies are the current gold standard in cancer diagnosis for dogs.

Additionally, liquid biopsies are becoming an increasingly more common detective method for screening HSA in canine patients. The relatively new emergence of this biopsy offers an exciting non-invasive approach (i.e., through a blood sample rather than a tissue sample) to screening and diagnosing cancer via biomarkers: notably, cfDNA - and other DNA-based biomarkers - are the most commonly analyzed due to their ease of accessibility (Hirahata et al., 2022). These biomarkers are extracellular fractions of double-stranded DNA that have a relatively short life span (Dao et al., 2023). cfDNA is collected and isolated from canine plasma via centrifugation, and the cfDNA is then analyzed, and a diagnosis is reached based on the conclusion (Ko et al., 2025). Liquid biopsies primarily analyze cfDNA through PCR and next-generation sequencing (NGS), the focus of this review, based on methods. Moreover, since the introduction of fragmentomics in 2015, it has emerged as a high-potential approach to cfDNA analysis for screening hemangiosarcoma (Qi et al., 2023).

The current analysis of cfDNA in clinical use for diagnosing, screening, and monitoring HSA is through NGS-based liquid biopsies. Next-generation sequencing technologies are becoming increasingly more adopted in clinical applications for screening cancers like HSA. NGS technologies have three primary levels of analysis: disease-targeted gene panels, exosome sequencing, and genomic sequencing (Rehm et al., 2013). However, this literature will only discuss disease-targeted gene panels.

Disease-targeted gene panels, as the name implies, target known disease-associated genes. This is a significantly different and cost-effective approach to a whole genomic sequence (WGS), in which the entire genome is sequenced. The focus on a set amount of genes rather than the whole genome allows for an increased sensitivity and specificity (Rehm et al., 2013). Having a high sensitivity and high specificity is a great combination for screening HSA; however, this approach is likely limited by pre-sequencing factors, such as collecting substantial amounts of cfDNA, especially in early-stage cancers.

The emerging literature surrounding fragmentomics hints at it being a promising method for cfDNA analysis for screening HSA. Fragmentomics is the analysis of the physical characteristics of DNA biomarkers; however, cfDNA is the current focus in the growing literature. The fragmentation of cfDNA carries genetic information about the epigenome, which can be utilized to reflect the origin of the tissue; this allows for a greater comprehension of HSA diagnosis (Qi et al., 2023). There exist five key fragment characteristics with promise for sensitively detecting cancer: fragment length, fragment size distribution, end motifs, preferred endpoint motifs, and break point motifs (Qi et al., 2023). This review focuses on the comparative analysis of the fragment length between healthy and cancerous canine patients. The growing literature reveals that there is an association between fragment length and the diagnosis of patients, whether they have cancer or not. Particularly, the study conducted by Ko et al. (2023) finds that a reduced fragment size is associated with canines with cancer. Moreover, in regards to the difference in average base pair (bp) length (i.e., fragment length), the study revealed that healthy dogs exhibited a peak of 165 bp, whereas dogs with HSA exhibited a peak of 160 bp (Ko et al., 2023). This study aligns with previous studies surrounding human or canine patients, showing a promising approach to diagnosing cancer. However, the fragment analysis of cfDNA is not yet viable for clinical use as these fragments are susceptible to chemical damage in low concentrations (Qi et al., 2023).

Old liquid biopsies

Tissue biopsies, the predecessors of the emerging liquid biopsy, serve the purpose of cancer diagnostics through histological evaluations and analysis of tissue samples. However, these biopsies are expensive,

invasive, and specific to a certain area of the body (Hirahata et al., 2022). Moreover, studies find that tissue biopsies are significantly less cost-effective than liquid biopsies in patient testing, with one study finding an approximate difference in cost between the two biopsies being at $3,000 per patient (Zheng et al., 2022). In regard to the invasiveness of solid biopsies,

Current techniques

Conversely, liquid biopsies, on the superficial and molecular level, function by drawing bodily fluids ─ typically blood, but others may include urine, cerebrospinal fluid, saliva, etc. ─ then isolating, quantifying, and analyzing specific cancer-related biomarkers found circulating in the bloodstream (Hirahata et al., 2022). Nowadays, the current method of cfDNA - and similar DNA-based markers - quantification is through sequencing programs: NGS and WGS are two increasingly common techniques (Ko et al., 2025). These tools identify and quantify the size of DNA strands (i.e., regarding their base pair length) in hemangiosarcoma samples (Ko et al., 2025). Conversely, before the emergence of NGS technologies, Sanger sequencing - the gold standard of medical sequencing - was the more expensive and specific alternative to NGS technologies (Rehm et al., 2013). In regard to the analysis of the base pair lengths or the biomarkers, machine learning algorithms models (e.g., Python scikit-learn library) analyze and identify epigenetic changes found by performing fragment-size distributions (i.e., assessing the biomarkers based on their base-pair fragment lengths) (Ko et al., 2025). Current analysis techniques generally identify epigenetic changes, such as DNA fragment size, and genomic changes like chromosomal alterations and mutations (Dao et al, 2023; Ko et al., 2025).

Current biomarkers

Currently, numerous studies discuss various biomarkers used in liquid biopsies: common biomarker analytes include cfDNA, circulating tumor DNA (ctDNA), and potentially circulating tumor cells (CTCs)(Hirahata et al., 2022; Zheng et al., 2022).

- **cfDNA**
- As mentioned, cfDNA are double stranded DNA that exists outside of the normal and cancerous tumor cells (Dao et al., 2023). Since cancer is caused by an alteration in the genome, resulting in the uncontrollable proliferation of cells.. Therefore, current cfDNA analysis (i.e., after the biomarker is isolated and quantified) is based on the number or length of mutations found in the collected sample of cfDNA (Dao et al., 2023).

ctDNA

Furthermore, in current applications of liquid biopsies, the use of ctDNA is common. Dao et al. (2023) classify ctDNA as shorter fragmented parts of cfDNA originating from tumor cells. Due to the similar nature of the two DNA biomarkers, ctDNA and cfDNA are analyzed in a similar process. Advantageously, ctDNA is more specific to certain tumors (Dao et al., 2023) and is easy to isolate from cfDNA (Hirahata et al., 2022). However, Hirahata et al. (2022) claim that ctDNA is lacking in the area of analyzing DNA-related irregularities, meaning there is a lack in comprehensive analysis of the genetic change (e.g., mutation) for the ctDNA strand.

- **CTCs**

CTC analysis involves the profiling of the entire intact tumor cell, which is released into the bloodstream via primary and secondary tumors (Hirahata et al., 2022). As a result, information on cellular components like DNA and RNA can be gathered, which is advantageous in early diagnosis. However, Hirahata et al. (2022) find that the concentration of CTCs in the earliest stage of cancers is a pressing issue; while there are techniques and devices that can make use of minuscule concentrations, they may be inexpensive. Therefore, the issue of low concentration in the early stage can be problematic for diagnosing fast-acting cancers like HSA.

Gaps in research

While liquid biopsies have emerged as valuable tools with an ability to screen for aggressive cancers such as lymphoma, their

effectiveness in detecting early-stage canine hemangiosarcoma remains limited. Hemangiosarcoma often progresses rapidly and aggressively, decreasing the likelihood of early detection and intervention. Moreover, in human oncology, the analytical and clinical validity of ctDNA assays follows a standardized framework set by the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP) (Merker et al., 2018). In contrast, although veterinary oncology does have the Veterinary Cancer Guidelines and Protocols, these guidelines primarily focus on histopathology and do not offer guidelines for liquid biopsy functions, such as cfDNA assay validation (The Veterinary Cancer Guidelines and Protocols, 2021). This is problematic due to the lack of consensus on assay sensitivity, specificity, and appropriate thresholds for circulating biomarkers in canines. As a result, diagnostic interpretations can vary significantly across laboratories, reducing reliability and contributing to false negatives. To address these shortcomings, using more sensitive and specific biomarkers presents a promising solution. Unlike more generalized markers used in multi-cancer liquid biopsies, specific biomarkers (e.g., circulating microRNAs) may offer greater tumor type specificity, which may enhance early detection for HSA (Naranbat et al., 2025).

New age liquid biopsies

While “Old Age” liquid biopsies have been utilized in the detection of canine HSA for several years, synthetic applications can provide a new and innovative perspective to bridge the limitations of traditional liquid biopsies, such as cost and access to specific equipment. This review proposes an alternative perspective to current liquid biopsies by introducing potential and viable biomarkers, notably miR-214 and miR-126, alongside a synthetic biology-based analysis. A few studies show the potential of these two biomarkers as possible analytes due to their association with HSA tumors. Through these biomarkers, fluorescent proteins, and engineered bacteria, this synthetic approach may allow for a more effective screening of canine HSA.

Synthetic applications

Biomarker

The research **on** biomarkers is evolving to shift into more tumor-associated biomarkers other than DNA-based markers. In fact, Little (2023) highlights the potential for alternative nucleic acids like RNA (e.g., cell-free RNA (cfRNA), **microRNA** (miRNA), and circulating RNA (circRNA) miR214.

In the context of a “New Age” liquid biopsy biosensor approach for canine HSA, the miR-214 and miR-126 biomarkers stand out for their consistent expression in HSA patients, making them promising biomarkers for early HSA screening. In a study conducted by Heishima et al. (2015), it is revealed that there is a direct association between the concentration of both biomarkers and HSA in canines - and likely angiosarcoma, the human counterpart to HSA. This increase in concentration is explained by the increased secretion of microvesicles - vesicles containing specific microRNAs (e.g., miR-214) in canine patients with HSA (Heishima et al., 2015). Moreover, studies find that the excretion of microvesicles has a secretion profile reflecting different biological changes, such as metastases; this further hints at miR-214 and miR-126 increasing in concentration as the cancer progresses (Heishima et al., 2015). As for the biosensor aspect, within a synthetic gene circuit, the presence of miR-214 in a simple blood sample can activate a “switch”, such as a toehold switch, which is a programmable RNA sequence that unlocks translation only when bound to a specific RNA target (Wyss Institute, 2024). This embedded switch would allow for the production of a reporter fluorescent protein when detected. MiR-214 plays a particularly important role in HSA (Heishima et al., 2025), hinting at the possibility of higher specificity in this approach. Moreover, since the secretion profile of the biomarker reflects the progression of HSA, this suggests the possibility for a higher sensitivity through the use of this model. This model may offer a higher sensitivity and specificity in comparison to current detection methods for the screening of HSA.

Limitations

This proposed biosensor model has clearly not been tested and is bound by current limitations on whether it is a viable approach in comparison to cfDNA-based liquid biopsies. When comparing the concentration of cfDNA and miR-214 in patients with HSA, it is hard to determine which is secreted more in earlier stages for two particular reasons: 1) this review did not find any comparative studies about cfDNA and miR-214, and 2) there is a lack of literature on the miR-214 biomarkers. Both biomarkers - particularly the overall concentration of cfDNA - have elevated concentrations in cancer patients and an increase in concentration in later stages (Dao et al., 2023; Heishima et al., 2015). Furthermore, due to a lack of studies regarding miR-214, there is not enough information to extrapolate that the concentration is substantial enough to be collected for testing in early-stage HSA. Likewise, the low concentration of cfDNA is also bound to this limitation (Hirahata et al., 2022). While the utilization of miR-214 has the potential for moderate to high specificity for HSA, it is also present in other cancers (e.g., lung cancer, ovarian cancer), highlighting a limitation in discriminating between cancers.

Comparing analytical techniques

As mentioned previously, traditional liquid biopsy techniques commonly target biomarker analytes such as cfDNA, ctDNA, and CTCs.. Similarly, molecular biomarkers such as miR-214 offer a viable diagnostic in synthetic applications for "New Age" liquid biopsies. While traditional approaches are effective, these processes typically involve labor-intensive protocols such as RNA extraction, amplification, and sequencing, all of which require costly laboratory equipment (Toiyama et al., 2018). In contrast, molecular biomarkers utilized in synthetic applications introduce a fundamentally different alternative. Utilizing a toehold switch allows for direct and sequence-specific detection without the need for amplification or complex equipment. Therefore, considering a switching perspective from an NGS-based liquid biopsy in which epigenetic and genomic changes are analyzed to the proposed biosensor-based liquid biopsies may be an innovative approach to targeting HSA specifically.

Fluorescent protein (GFP)

Fluorescent proteins, such as green fluorescent protein (GFP), are well-known in the synthetic biology field for revolutionizing the methods that researchers use to detect and visualize molecular processes (Kremers et al., 2010). In the context of "New Age" synthetic liquid biopsies for the detection of canine HSA, these proteins offer interpretable and accessible results that indicate the presence of specific molecular biomarkers, such as miR-214, which can be attributed to the detection of canine HSA.

Specifically, when incorporated into a gene circuit, a fluorescent protein can be expressed in response to the activation of a toehold switch. In this context, the specific RNA target would be miR-214, a microRNA commonly associated with hemangiosarcoma. Upon detection, this synthetic gene circuit translates the fluorescent gene, producing a visible signal, such as a color output. The fluorescence intensity can be directly linked to the concentration of miR-214, indicating the progression of the cancer. For instance, Naranbat et al. (2025) mention that once the correlation between specific miRNAs and disease is established, the abundance of the target miRNA in affected individuals can be measured and compared to controls, serving as a diagnostic marker.

Bacteria

Engineering bacteria, also known as genetic engineering, is a common method used in synthetic biology that involves modifying a bacterium's genomic sequence to introduce new traits or enhance existing ones (Patil et al., 2022). In the context of a "New Age" liquid biopsy synthetic approach for canine HSA, bacteria can be engineered to act as biological biosensors. By introducing synthetic gene circuits into bacterial hosts, such as *Escherichia coli* (E. coli), these bacterial chassis can recognize specific sequences such as miR-214 and, through a toehold switch, will remain inactive until the detection of target RNA (i.e., miR-214), which will trigger a gene

response mechanism.

Incorporating bacteria offers multiple advantages that address the limitations of current "Old Age" liquid biopsies. Bacteria are cost-effective, easy to cultivate, and adaptable to a variety of environments. Additionally, bacteria are easily able to be embedded in paper-based diagnostics (e.g, test strips or diagnostic kits), allowing for easy distribution and handling for potential commercial use that is outside a traditional laboratory setting.

Next steps

Additional research can be conducted on a local and global scale to expand the detection of canine HSA through synthetic approaches for researchers, veterinarian organizations, and pet owners. For example, research can be conducted to make the "New Age" liquid biopsies safer and more effective for canines, eliminating any possible danger or risks. Research can also be conducted to examine the ability of fluorescence intensity to determine specific cancer progression. Our next step may be contacting a veterinary oncologist (a veterinarian with specialized training and expertise in animal cancers) for extra assistance and background on canine hemangiosarcoma to learn more about canine cancer detection and diagnostics.

Author contributions

This research idea began with the main idea of improving canine cancer detection. This research paper was completed with the joint efforts of the team. A.E., E.F., A.G., C.M., Z.J., K.P., A.S.C., and B.W. all contributed to the development of this research paper, including the manuscript writing and editing process.

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References

Antonella B, Andrea M. F, and Jaime F. M (2017). *Hemangiosarcoma detailed article*. College of Veterinary Medicine. https://vetmed.umn.edu/modiano-lab/cancer-center/hemangiosarcoma-detailed-article

Borgatti, A., Fahrenkrug, A.M., & Modiano, J.F. (2017). *Studying cancer in dogs as a path towards a world where we no longer fear cancer – a contemporary update on canine hemangiosarcoma.* College of Veterinary Medicine. https://vetmed.umn.edu/modiano-lab/cancer-center/hemangiosarcoma-detailed-article

Cohen, A. & Sylvester, S. (2024, Oct). *Hemangiosarcoma in dogs.* College of Veterinary Medicine. https://www.vet.cornell.edu/departments-centers-and-institutes/riney-canine-health-center/canine-health-information/hemangiosarcoma-dogs

Dao, J., Conway, P. J., Subramani, B., Meyyappan, D., Russell, S., & Mahadevan, D. (2023). Using cfDNA and ctDNA as oncologic markers: A path to clinical validation. *International Journal of Molecular Sciences*, *24*(17), 13219. https://doi.org/10.3390/ijms241713219

Heishima, K., Mori, T., Ichikawa, Y., Sakai, H., Kuranaga, Y., Nakagawa, T., Tanaka, Y., Okamura, Y., Masuzawa, M., Sugito, N., Murakami, M., Yamada, N., Akao, Y., & Maruo, K. (2015). MicroRNA-214 and MicroRNA-126 are potential biomarkers for malignant endothelial proliferative diseases. *International Journal of Molecular Sciences*, *16*(10), 25377–25391. https://doi.org/10.3390/ijms161025377

Hemangiosarcoma in dogs. PetMD. (2022). https://www.petmd.com/dog/conditions/cancer/hemangiosarcoma-dogs

Hirahata, T., ul Quraish, R., Quraish, A. ul, ul Quraish, S., Naz, M., & Razzaq, M.

A. (2022). *Liquid biopsy: A distinctive approach to the diagnosis and prognosis of cancer. Cancer Informatics, 21*, 1–7. https://doi.org/10.1177/11769351221076062

Ko, S., Jang, J., Yi, S. S., & Kwon, C. (2025). *Early detection of canine hemangiosarcoma via cfDNA fragmentation and copy number alterations in liquid biopsies using machine learning. Frontiers in Veterinary Science, 11*, 1489402. https://doi.org/10.3389/fvets.2024.1489402

Kremers, G., Gilbert, S. G., Cranfill, P. J., Davidson, M. W., & Piston, D. W. (2010). *Fluorescent proteins at a glance. Journal of Cell Science, 124*(2), 157–160. https://doi.org/10.1242/jcs.072744

Little, L. (2023, January). *An overview of alternative biomarkers in liquid biopsies. Front Line Genomics*. https://frontlinegenomics.com/an-overview-of-alternative-biomarkers-in-liquid-biopsy/

Megquier, K., Turner-Maier, J., Swofford, R., Kim, J.-H., Sarver, A. L., Wang, C., Sakthikumar, S., Johnson, J., Koltookian, M., Lewellen, M., Scott, M. C., Schulte, A. J., Borst, L., Tonomura, N., Alfoldi, J., Painter, C., Thomas, R., Karlsson, E. K., Breen, M., & Modiano, J. F. (2019). Comparative Genomics Reveals Shared Mutational Landscape in Canine Hemangiosarcoma and Human Angiosarcoma. *Molecular Cancer Research*, *17*(12), 2410–2421. https://doi.org/10.1158/1541-7786.mcr-19-0221

Merker, J. D., Oxnard, G. R., Compton, C., Diehn, M., Hurley, P., Lazar, A. J., Lindeman, N., Lockwood, C. M., Rai, A. J., Schilsky, R. L., Tsimberidou, A. M., Vasalos, P., Billman, B. L., Oliver, T. K., Bruinooge, S. S., Hayes, D. F., & Turner, N. C. (2018). Circulating tumor DNA analysis in patients with cancer: American Society of Clinical Oncology and College of American Pathologists joint review. *Archives of Pathology & Laboratory Medicine*, *142*(10), 1242–1253. https://doi.org/10.5858/arpa.2018-0901-sa

Naranbat, D., Herdes, E., Tapinos, N., & Tripathi, A. (2025). Review of microRNA detection workflows from liquid biopsy for disease diagnostics. *Expert Reviews in Molecular Medicine*, *27*. https://doi.org/10.1017/erm.2025.2

NC State Veterinary Hospital (n.d.) *Medical oncology: Hemangiosarcoma* https://hospital.cvm.ncsu.edu/services/small-animals/cancer-oncology/oncology/hemangiosarcoma/

Patil, P. L., Gharat, S. K., Jadhav, K. R., & Kadam, V. J. (2022). Engineered bacteria: general overview as a therapeutic agent and a novel drug delivery system. *Current Pharmaceutical Biotechnology*, *24*(11), 1351–1364. https://doi.org/10.2174/1389201024666221220113517}

Qi, T., Pan, M., Shi, H., Wang, L., Bai, Y., & Ge, Q. (2023). Cell-free DNA fragmentomics: the novel, promising biomarker. *International Journal of Molecular Sciences*, *24*(2), 1503. https://doi.org/10.3390/ijms24021503

Rehm, H. L., Bale, S. J., Bayrak-Toydemir, P., Berg, J. S., Brown, K. K., Deignan, J. L., Friez, M. J., Funke, B. H., Hegde, M. R., Lyon, E., & Working Group of the American College of Medical Genetics and Genomics Laboratory Quality Assurance Committee (2013). ACMG clinical laboratory standards for next-generation sequencing. *Genetics In Medicine: Official Journal Of The American College Of Medical Genetics, 15*(9), 733–747. https://doi.org/10.1038/gim.2013.92

Ritt, M. G., & Breen, T. (2007, August). *Canine hemangiosarcoma - the road from despair to hope*. *AKC Canine Health Foundation.* https://www.akcchf.org/canine-health/your-dogs-health/canine-hemangiosarcoma.html

Takizawa, S., Matsuzaki, J., & Ochiya, T. (2022). *Circulating microRNAs: Challenges with their use as liquid biopsy biomarkers. Cancer Biomarkers, 35*(1), 1–9. https://doi.org/10.3233/cbm-210223

Toiyama, Y., Okugawa, Y., Fleshman, J., Richard Boland, C., & Goel, A. (2018). *MicroRNAs as potential liquid biopsy biomarkers in colorectal cancer: A systematic review. Biochimica et Biophysica Acta (BBA) - Reviews on Cancer, 1870*(2), 274–282. https://doi.org/10.1016/j.bbcan.2018.05.006

Weiss Institute. (2018, August). *Toehold switches for synthetic biology. Wyss Institute.* https://wyss.harvard.edu/technology/toehold-switches-for-synthetic-biology/

Zheng Y., Viox, H., Liu, F.X., Singh, B., Sharma, S., & Sharda, D. (2022). Diagnostic and economic value of biomarker testing for targetable mutations in non-small-cell lung cancer: a literature review. *Future Oncology, 18*(4), 505-518. https://doi.org/10.2217/fon-2021-1040