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RAMAN SPECTROSCOPY IN CANCER DIAGNOSTICS AND BIO-IMAGING: BRIDGING PRECISION MEDICINE AND ARTIFICIAL INTELLIGENCE

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Abstract

Raman Spectroscopy (RS) has become a key diagnostic instrument for cancer detection along with bio-imaging as it offers non-contact sample analysis through label-less approaches which provides detailed chemical signatures in biological specimens. The fundamental aspects of RS and its versions like Surface-Enhanced Raman Spectroscopy (SERS), Raman imaging (RI) and Tip-Enhanced Raman Spectroscopy (TERS) are emphasized for their functions in enhancing detection accuracy and resolution performance. RS finds clinical implementation throughout cancer types including lung tissue and breast tissue as well as thyroid tissue, liver tissue and colorectal tissue where it helps identify early conditions while the surgeon operates under real-time and provide accurate margin assessments for tumor removal. Bridging RS with advanced Machine Learning (ML) approaches using convolutional neural networks (CNNs) along with Raman Net models delivers better spectral identification performance while overcoming noise issues. The field of RS progressed from examination of tissues to study of individual cells which permits the examination of tumor variations and metastatic properties. Raman-based optical probes and hybrid systems allow researchers to use the technology for in vivo imaging while monitoring therapy using these systems. Integration of Artificial Intelligence (AI) and ML with Raman has proven beneficial in terms of fast tracking the results and better accuracy. This review reveals that RS keeps expanding its role in precise cancer care while promising diagnostic advancements as well as individualized medical treatments leading to better result outcomes.

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INTRODUCTION

The World Health Organization documented more than 10 million cancer deaths across the globe during 2020 while keeping cancer as one of the primary mortality and disease factors across nations. Correct and fast disease diagnosis proves essential for better patient treatment results but standard testing systems which include histopathology alongside imaging methods demonstrate poor specific properties and sensitivity together with invasiveness issues (X. Liu, Jia, & Zheng, 2024). RS stands as a promising option because it provides non-destructive detection of biomolecules through label-free examination of their vibrational modes for highly specific molecular analysis (Canetta, 2021). Its ability to detect subtle biochemical changes enables the differentiation between malignant and healthy tissues, facilitating early cancer detection and precise surgical guidance (Esposito et al., 2024). Moreover, advancements in RS, including Surface-Enhanced Raman Spectroscopy (SERS) and RI, have significantly improved its sensitivity and spatial resolution, further enhancing its potential in cancer diagnosis and bio-imaging applications (X. Liu et al., 2024; Xu, Xie, Lin, Wu, & Jiang, 2024). Small molecules and biochemical signatures can now be identified using RS along with SERS which serve as innovative diagnostic tools for cancer research purposes. The detection methods use biomolecular vibrational modes to identify biochemical changes that occur in tissues and extracellular vesicles together with biofluids and provide early cancer detection capabilities with precise tumor characterization features and real-time intraoperative guidance. Scientific teams have implemented these diagnostic methods in various cancers, including liver (Esposito et al., 2024), breast (X. Liu et al., 2024), lung, colorectal, cervical (C. Liu et al., 2025), and prostate, demonstrating their versatility in detecting biomarkers, characterizing tumor margins, and enabling real-time intraoperative decisions (Yang, Dai, Chen, Li, & Yan, 2025).

FUNDAMENTALS OF RAMAN SPECTROSCOPY IN BIOMEDICAL SCIENCES

Basic Principle of Raman Scattering

Currently RS serves as an indispensable analytical technique between various fields of science because it detects vibrational changes which produce molecular fingerprints by analyzing light elastic scattering. Since its discovery by C.V. Raman (Choudhuri, 2024a) in 1928 (Choudhuri, 2024b), the technique has evolved into a versatile tool for probing vibrational, rotational, and low-frequency modes in diverse systems. The Raman effect, first observed in 1928 (Choudhuri, 2024b), revolutionized molecular spectroscopy by revealing energy shifts in scattered photons corresponding to molecular vibrations. Unlike elastic Rayleigh scattering, Raman scattering involves a minute fraction (~1 in 10^6 photons) undergoing energy exchange with molecular bonds, producing Stokes (energy loss) and anti-Stokes (energy gain) shifts (Chandra et al., 2024). These shifts, measured as wavelength differences, provide a unique spectral fingerprint reflective of molecular symmetry, bond polarizability, and chemical environment (Chandra et al., 2024; Chowdhry, Ryall, Dines, & Mendham, 2015). This is the way how RS works by providing unique spectra and differentiate between objects (Chandra et al., 2024).

Advantages of Raman in Medical Application

The medical field increasingly utilizes RS for different diagnostic purposes and drug development and tissue examination applications. RS helps scientists study API structures while observing how they interact with excipients (Jung & Windbergs, 2018). During surgical procedures surgeons utilize RS to separate diseased tissues from healthy tissues thereby enhancing surgical precision (Kouri & Spyratou, 2022). Coupled with AI and miniaturized devices, it enables real-time, in situ monitoring for personalized healthcare. Flexible SERS chips are emerging for point-of-care testing, allowing molecular-level health tracking and early intervention. These advancements promise to integrate New developments seek to merge Raman

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technology with wearable devices including systems that can manage health at home (G. Li et al., 2024).

Non-invasive and Label-free Detection

Real-time biological sample analysis becomes feasible with Raman spectroscopy because this method operates without damaging specimen integrity. RS offers valuable real-time diagnostic capabilities for in vivo assessments particularly when dermatological lesion evaluation or tumor diagnosis does not require biopsy testing (Y. Wang, Fang, Wang, & Xiong, 2024). Medical professionals use RS to evaluate cardiovascular disease through noninvasive blood tests which determine plaque makeup for disease analysis (Xie et al., 2025).

High Sensitivity to Molecular Composition

RS detects biological sample composition with high sensitivity which allows researchers to identify proteins together with lipids nucleic acids and metabolites (Eberhardt, Stiebing, Matthäus, Schmitt, & Popp, 2015). RS maintains high sensitivity that enables detection of disease biomarkers particularly for cancers requiring early diagnosis. The combination of SERS with RS leads to more sensitive detection through its ability to identify particular molecular indicators in intricate sample environments (Dos Santos et al., 2023).

High Spatial Resolution

Reliable spatial resolution of RS enables researchers to examine cellular structures together with tissue organization. Through Raman microscopy techniques researchers can observe tissue molecular structures thanks to their ability to show sample bimolecular interactions (Eberhardt et al., 2015). This capability is essential for understanding disease mechanisms at the cellular level.

Minimal Sample Preparation

The need for extensive sample preparation in RS decreases because of its simplified workflow design and reduced artifacts formation (Y. Wang et al., 2024). The system allows real-time analysis of cells with tissues and biological fluids that need minimal processing steps. RS analyzes fine-needle aspiration washouts for thyroid cancer diagnosis without requiring fixation or staining procedures (Schie, Stiebing, & Popp, 2021). The basic sample preparation settings of RS promote streamlined diagnostic operations and protect sample biological features to support rapid non-destructive medical examinations.

Ability to Monitor Dynamic Changes

RS can monitor biochemical changes in real-time, which is valuable for tracking disease progression or therapeutic effects. This valuable feature supports monitoring cellular responses to both drugs and environmental stressors (Eberhardt et al., 2015). Technical experts use RS to track metabolic changes in brain injuries and thus understand disease patterns and healing rates (Y. Wang et al., 2024). This real-time monitoring capability enhances our understanding of dynamic biological processes, supporting more informed and timely clinical decisions.

Multiplexed Analysis

RS performs multi-component molecular assessments which allow its use in complex biomedical research fields. The multiplexing function serves as a critical requirement to detect various biomarkers in both cancer and diabetes medical situations (Y. Wang et al., 2024). SERS technology enhances molecular pattern detection in problematic biological solutions (Dos Santos et al., 2023). RS demonstrates enough reliability for clinical disease profiling through rapid multiplexed detection methods that enable the discovery of biomarkers.

Potential for Early Diagnosis

Researchers believe that RS provides an effective means for making early diagnoses through its capability to detect minor biochemical changes. RS serves as a method for cancer early detection by identifying molecular markers (Eberhardt et al., 2015). The early detection of diseases becomes essential because it allows health providers to intervene promptly which produces better clinical results (Y. Wang et al., 2024). RS plays an essential part in early diagnosis development which produces better patient survival results. **Table 1** shows the methods, practical implications and key findings in various cancer types.

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Table 1: Application of Raman across cancer type

Cancer type	Methods	Practical implications	Key findings	References
Lung	Integration of miR-155 with Surface-Enhanced Raman Spectroscopy.	Non-invasive, accurate lung cancer diagnostics using SERS	SERS detected miR-155 via silver nanoparticles for early NSCLC diagnosis	(Quin, McClelland, & Zeng, 2024)
	Integrated surface-enhanced Raman spectroscopy with catalytic hairpin assembly. Detected circRNA in human serum samples.	Early detection of lung cancer via blood circRNA. Potential liquid biopsy and prognostic tool.	Developed biosensor detects circRNA for early lung cancer detection. Higher circRNA concentrations found in lung cancer patients' serum.	(Luyun Xu et al., 2024)
	Surface-enhanced Raman spectroscopy for analysis. PCA-LDA diagnostic algorithms and machine learning techniques used.	Non-invasive lung cancer screening using serum SERS method. High classification accuracy with machine learning techniques.	SERS distinguishes lung cancer patients from healthy volunteers. Significant spectral differences due to bimolecular changes in serum.	(Tao et al., 2023)
	Electrochemical biosensors detect microRNA biomarkers in lung cancer. Nanomaterials enhance diagnostic sensitivity for early-stage detection.	Enhanced early-stage lung cancer detection using microRNA biosensors. Improved diagnostic sensitivity with advanced electrochemical biosensors.	MicroRNAs aid early-stage lung cancer detection. Enhanced biosensors improve diagnostic sensitivity for biomarkers.	(Shaterabadi et al., 2024)
Liver	Machine Learning assisted Raman Spectroscopy for diagnosis.	Combines Raman Spectroscopy and Machine Learning for liver cancer diagnosis.	AI-classified Raman spectra revealed elevated DNA in tumor nuclei	(Esposito et al., 2024)
	Raman micro-spectroscopy for cell analysis. Machine learning approaches for data analysis.	AI-assisted Raman spectroscopy effectively classifies liver cancer cells. Achieves nearly 90% accuracy in predictions.	AI-assisted Raman spectroscopy effectively classifies liver cancer cells. Achieved nearly 90% accuracy in predictions.	(Esposito et al., 2023)
	Raman spectroscopy for cell composition analysis. Machine learning classifiers for cancer detection.	Distinguishes cancerous cells from healthy ones effectively. Enhances cancer diagnosis using Raman	Raman spectroscopy effectively distinguishes cancerous from healthy cells. Extra Tree Classifier achieved 91% F-score	(Aversano et al., 2023)

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		spectroscopy and AI.	accuracy.	
	Raman spectroscopy for tissue analysis and diagnosis. Deep learning for data interpretation and classification.	Enables rapid, label-free liver cancer diagnosis during surgery. Reduces reliance on traditional biopsy methods and pathologists.	Rapid, label-free diagnosis of liver cancer using Raman spectroscopy. Deep learning distinguishes carcinoma from non-tumour tissues effectively	(Huang et al., 2023)
Thyroid	Surface-enhanced Raman spectroscopy on MXene-coated nanoparticle substrate. Deep learning for feature extraction from Raman spectra.	Efficient thyroid cancer diagnosis using exosome profiling. High diagnostic accuracy with deep learning integration.	Efficient exosome profiling using SERS and deep learning. 96.0% accuracy in thyroid cancer diagnosis.	(Sun et al., 2024)
	Surface-enhanced Raman scattering for biomarker detection. Sandwich assay with Tg Capture and Detection antibodies.	Enables rapid, sensitive detection of thyroid cancer biomarkers. Applicable in point-of-care and intraoperative settings.	Developed SERS platform for ultrasensitive Tg detection. Achieved detection limit of 7 pg/ml in biopsies.	(Spaziani et al., 2024)
	Nanopipette dielectrophoresis for sEV extraction. Surface-enhanced Raman scattering for exosome characterization.	Integrates sEV extraction with SERS for cancer diagnostics. Uses explainable AI for interpretable diagnostic analysis.	Integrated nanopipette dielectrophoresis with SERS for sEV analysis. Used SHAP for explainable AI in cancer diagnostics.	(Vang et al., 2024)
	Machine Learning procedure for nodule classification. eXplainable. Artificial Intelligence for result interpretability.	Non-invasive thyroid cancer diagnosis using Raman spectroscopy. Reduces unnecessary surgeries through effective discrimination of nodules	Raman spectroscopy effectively discriminates malignant from benign nodules. Machine Learning models achieve performance exceeding 0.9 ROC curve.	(Bellantuono et al., 2023)
Endometrial	Analyzed plasma samples using surface-enhanced Raman spectroscopy. Recorded three spectra for each sample analyzed.	Raman spectroscopy aids in diagnosing endometrial pathologies. High accuracy in differentiating between conditions.	83% accuracy in differentiating endometrial polyps from control group. Raman spectroscopy shows potential for diagnosing endometrial pathologies.	(Artemyev et al., 2024)
	Surface-enhanced Raman spectroscopy	High sensitivity for detecting EMT-related	SERS detects microRNA-200a-3p and ZEB1 in	(Artemyev et al., 2024)

	for target detection. Silver nanoparticles modified with iodine and calcium ions.	targets in endometrial cancer. Potential for diagnosing and predicting prognosis in malignancy.	endometrial cancer. High sensitivity and stability for EMT target detection.	
	Surface-enhanced Raman spectroscopy of blood plasma samples. Discriminant analysis by projection onto latent structures (PLS-DA).	Early diagnosis of endometrial cancer improved using SERS. Differentiates cancer from benign conditions effectively.	SERS accurately differentiates endometrial cancer from benign conditions. Diagnostic accuracy: 87% for adenocarcinoma vs. control group.	(Artemyev et al., 2024)
	Analyzed blood plasma from 95 female patients aged 22–79 years. Used surface-enhanced Raman scattering for spectral analysis	Enhances early detection of endometrial cancer. Distinguishes benign conditions from malignant diseases effectively	SERS distinguishes endometrial cancer from benign conditions effectively. Accuracy rates for adenocarcinoma diagnosis reached 93%.	(Zuev et al., 2023)
	Robotic Raman device with high-efficiency Raman probe developed. Algorithms compared: PCA-DA, SVM, CNN with/without data augmentation.	Portable Raman device enables rapid cancer screening. High sensitivity for detecting endometrial cancer stages.	High F1-scores for cancer classification: 91%, 94%, 97%. CNN with data augmentation is the most reliable classifier.	(Nambudiri et al., 2023)
Colorectal	Raman spectroscopy analysis on dried plasma samples. Longitudinal studies of CRC patients post-surgery.	Raman spectroscopy can noninvasively diagnose colorectal cancer. It monitors disease progression post-surgery effectively.	Identified six spectral features distinguishing CRC from non-CRC patients. Achieved 87.5% accuracy in classifying CRC patients.	(Morasso et al., 2024)
	Raman spectroscopy and Raman optical activity used for analysis. Linear discriminant analysis and principal component analysis applied for classification.	Potential disease-specific diagnostic tool for gastrointestinal cancers. High accuracy in differentiating cancer types from healthy controls.	87% accuracy in distinguishing cancer from healthy samples. 87% accuracy in classifying three cancer types.	(Kralova et al., 2024)
	In vivo analyses using fiber-optic microprobe and portable Raman	Enables real-time diagnostics during colonoscopy	Achieved over 91% accuracy in colorectal lesion detection.	(Fousková et al., 2023)

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	spectrometer. Laser excitation at 785 nm, integration time 23 s.	procedures. Requires skilled endoscopists for challenging lesion access.	Raman spectroscopy distinguishes cancerous from benign polyps effectively.	
	Chiroptical spectroscopy combined with Raman and FT-IR. Linear discriminant analysis for spectral data evaluation.	Non-invasive early detection of colorectal cancer through blood analysis. Potential to improve survival rates and reduce incidence.	Chiroptical spectroscopy shows potential for early CRC detection. 90% sensitivity and 75% specificity achieved in blood analysis.	(Miskovicova et al., 2020)
	High-throughput serum Raman spectroscopy platform developed for diagnostics. Comparison of dry and liquid data acquisition methodologies.	Early and effective colorectal cancer diagnosis for patients. Validation of Raman spectroscopy for liquid serum biopsies.	High-throughput Raman platform shows potential for colorectal cancer detection. Achieved 83% sensitivity and specificity in pilot study.	(Jenkins et al., 2018)

RAMAN SPECTROSCOPY TECHNIQUES FOR CANCER DETECTION

Surface Enhanced Raman Spectroscopy (SERS)

The detection of cancer biomarkers with high sensitivity becomes possible through SERS since metal nanoparticles enhance Raman signals. The combination of SERS with PCR helped identify BRAF, KRAS and PIK3CA gene mutations in colorectal cancer patient plasma samples down to 10^{-11} M detection sensitivity. The analysis through this technique confirmed that genetic mutations occurred in direct relation to where tumors developed in the body (tumor lateralization) (X. Li et al., 2018). Ratiometric SERS nanoprobes that focus on both urokinase plasminogen activator receptor (uPAR) and epidermal growth factor receptor (EGFR) achieved background-free subtype separation of MDA-MB-231 and MCF-7 breast cancer cells through ratio measurements of nanoprobes intensities (L. Li, Liao, Chen, Shan, & Li, 2019). SERS technology combined with ML now enables prediction of antibiotic responses as well as immunotherapy effects on cells using 94% lung cancer detection accuracy (Y. Zhang et al., 2024). Collectively, these advancements highlight the significant potential of SERS-based approaches in enhancing the sensitivity, specificity, and clinical applicability of cancer diagnostics and personalized treatment strategies.

Raman Imaging

Through Raman Imaging (RI) scientists can create spatial charts which identify tumor edges precisely. The sensitivity of Raman spectroscopy for border inspections in head and neck cancers ranges between 71 and 100 percent yet its tissue penetration reaches only 6mm (Y. Zhang et al., 2024). Fingerprint Raman analysis (800-1700 cm^{-1}) helped identify malignant tissues apart from benign conditions (emphysema/bronchiolitis) in lung cancer samples with 94% sensitiveness and 80% specificness (Leblond et al., 2023). The identification of biochemical protein changes (amide I/III) and nucleic acids during real-time surgical guidance becomes possible due to clinical studies according to research outcomes (Y. Zhang et al., 2024).

Confocal Raman Spectroscopy

Confocal Raman Microscopy allows scientists to perform non-invasive diagnostic testing at specific skin layers. By analyzing collagen structure at 1245 cm^{-1} and lipid/protein ratios the technology separates malignant skin lesions (Narayanamurthy et al., 2018). Single-cell investigations show that

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senescent breast cancer cells manifest alterations in their nuclear membrane lipid isomers (-cis/-trans) which indicates that higher fluidity relates to cycle arrest (Mariani et al., 2010). RI has proven its increasing clinical value for real-time non-invasive tumor margin assessment needed for operative choices.

Raman Spectroscopic Fingerprinting

Raman Spectroscopic Fingerprinting leverages unique molecular signatures for cancer screening. Demarcating cancer stages using serum-based SERS technology with silver nanowires along with AI processing yielded 95.8% correct results for pan-cancer identifications among 1,964 patients including first-stage cancer patients (Dong et al., 2023). Raman spectroscopy with enhanced gold nanoparticles served to detect squamous cell carcinoma in oral tissues by monitoring phenylalanine (1003 cm^{-1}) intensification and phospholipid (1449 cm^{-1}) reduction rates (Hamdy et al., 2024). The combination of Raman spectroscopic fingerprinting with nanotechnology and AI systems proves to be robust for early non-invasive cancer screening of various cancer types.

Single Cell Raman Analysis

The technological method Single-Cell Raman Analysis reveals tumor heterogeneity patterns. The combination of micro droplet SERS platforms with immunomagnetic beads allowed the analysis of multiple proteins (HER2/EGFR/CD44) in breast cancer subtypes at single-cell sensitivity through effects of interface aggregation (J. Wang, Cong, Shi, Xu, & Xu, 2023). The EV-protein profiles became predictive for metastatic potential by using ML algorithms (Y. Zhang et al., 2024). The advancements described in this field make single-cell Raman analysis an effective method to measure tumor diversity while achieving accurate metastatic predictions.

Tip-enhanced Raman Spectroscopy

TERS detects DNA lesions with resolution so precise that it reaches the nanometric scale. Early versions of the technique proved DNA modifications can be detected for cancer purposes yet technical obstacles remain for identifying single DNA bases (Kolodziejski, Gurjar, & Wolf, 2011). Recent research studies implement TERS to study membrane protein clusters (including EGFR) at sub-50 nm scales which shows morphological changes in metastasis processes (Y. Zhang et al., 2024). TERS proves its potential as an advanced nanotechnology for measuring cancer-related molecular changes through precise spatial analysis.

Raman-Fluorescence

TERS establishes itself as a promising nanoscopic analytical method which enables the discovery of molecular changes in cancer with high-resolution capabilities (Hamdy et al., 2024). The integration of SERS tags together with fluorescent antibodies delivers systems that perform both molecular detection and assessment of their local environment (L. Li et al., 2019). The hybrid systems demonstrate the partnership advantages of performing Raman and fluorescence analysis to provide enhanced cancer diagnosis capabilities and sensitive tumor environment monitoring.

RAMAN SPECTROSCOPY IN CANCER BIO-IMAGING

Tissue and Cell Bio Imaging

The ability of RS for distinguishing normal from malignant tissues through their unique biochemical compositions has been shown to be remarkable. The metabolic changes and protein expression modifications and lipid profile alterations brought about by cancer development result in distinguishable Raman spectral signatures (Canetta, 2021; Watanabe, Sasaki, & Fujita, 2022). Spectral variations form an objective basis for cancer diagnosis that does not require sample staining or time-consuming preparation.

Brain Tumors

The introduction of SRS microscopy creates an instrument that surgeons can use during operations to guide their surgery for brain tumor removal. Stimulated Raman histology allowed surgeons to examine tissue during surgery in order to identify tumor margins therefore preserving healthy tissue structures (Luther, Matus, Eichberg, Shah, & Ivan,

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2019). This application demonstrates the potential of RI for real-time surgical guidance.

Multiple Cancer Types

RS now enables exact identification of different cancers through their individual light patterns to become a substitute for standard diagnostic instruments including endoscopes (S. Zhang, Qi, Tan, Bi, & Olivo, 2023). This detection method can identify precancerous lesions early which create substantial possibilities for diagnosing diseases at an earlier stage with better patient results.

Detection of Tumor Cells

RS has revolutionized oncological research through novel cancer cell recognition techniques that trace bio-molecular indicators to specify diagnostic information about different tumors. The analysis through RS succeeds in recognizing different breast cancer subtypes Luminal A, A blood plasma test has proven effective for identifying (Luminal B, HER2+, Triple-Negative) at stage IA breast cancer with 90% sensitivity and 95% specificity (Tipatet, Hanna, Davison-Gates, Kerst, & Downes, 2025). After neoadjuvant treatment it accurately separates remaining tumors from nearby tissues for surgical margin evaluation in breast preservation surgery (Wu et al., 2025). The diagnostic power of serum analysis using ML reaches 98% success rates across breast cancer examinations and benign lesion identification and healthy control assessment (R. Lin et al., 2023). When combining Visible resonance Raman (VRR) spectroscopy with deep learning a near-perfect glioma tumor to healthy tissue discrimination occurs and cancer grade detection uses raw spectral data (Llanos et al., 2024). When atomic force microscopy operates with RS the technique detects cancer cell intrusion within brain tumor extracellular matrixes. FLIM enables combined with Raman to analyze cellular metabolism in individual cells which reveals both drug response patterns and side effects (Y. Zhang et al., 2024). Ensembl learning methods resolve spectral overlaps in complex biological samples, enabling real-time intraoperative guidance (Llanos et al., 2024). New innovations consist of Raman devices with portability for diagnostic testing at care points together with self-driven automated laboratories and genomic relationship mapping software (Y. Zhang et al., 2024). RS transforms medical practice in oncology by combining recent technological development which accelerates both early detection ability and treatment measurement capacities while fostering present-day individualized therapeutic models.

Optical Probe in Vivo Imaging

The technique of optical probe-based in vivo imaging using RS provides researchers with an emerging approach to conduct high-resolution molecular analysis of living tissues without doing harm to the samples (Austin, Osseiran, & Evans, 2016; Barik et al., 2022). Our method features a combined setup of Raman equipment with fiber-optic probes that enables real-time tissue testing right at its location without requiring additional colorants (Barik et al., 2022; Remmelink et al., 2024). This technology shows particular promise for early cancer detection (Remmelink et al., 2024), metabolic phenotyping (L. L. Lin et al., 2025), and intraoperative surgical guidance (Gaba et al., 2022) . Clinical translation efforts focus on liquid biopsy applications (extracellular vesicle analysis) (L. L. Lin et al., 2025) and real-time surgical margin assessment, with Raman systems achieving >90% diagnostic accuracy in prostate and breast cancer trials (Gaba et al., 2022). The work requires additional research to standardize probe designs as well as to validate these probes in extensive multicenter studies (L. L. Lin et al., 2025). Altogether, optical probe-based RI represents a transformative step toward real-time, non-invasive cancer diagnostics with ongoing innovations aimed at overcoming technical challenges and enabling widespread clinical adoption.

Integration of RS with AI for Cancer Detection

Machine learning in medical diagnosis enhances precision and decision-making by supporting clinical expertise (Ahmad et al., 2025). The integration of RS with ML has unlocked transformative capabilities in analytical science, enabling rapid, non-destructive diagnostics and material characterization with unprecedented accuracy. A label-free SERS-CNN framework achieved 88.1% accuracy in distinguishing malignant from benign thyroid fine-needle aspiration (FNA) samples by analyzing

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spectral features of proteins, lipids, and nucleic acids. This approach reduces reliance on time-consuming cytology (Gao et al., 2024). Key spectral differences included altered phenylalanine (1,004 cm^{-1}) and collagen (1,665 cm^{-1}) peaks in malignant samples. CNNs outperformed traditional ML models (RF, SVM) in classifying murine mammary tumors via Raman spectra, achieving 97.58% accuracy (Ya Zhang et al., 2024). SERS-CNN analysis of vaginal fluids achieved 99% accuracy by identifying spectral changes linked to *Gardnerella vaginalis* overgrowth (Wen et al., 2025). These advancements demonstrate the significant potential of label-free SERS-CNN frameworks in enhancing diagnostic accuracy and efficiency across various medical applications, paving the way for more rapid and reliable clinical decision-making. **Table 2** includes recent applications of RS combined with AI for cancer diagnosis, highlighting methods used, practical benefits, and existing limitations.

Table 2: AI integration in RS for Cancer Diagnosis

References	Cancer type	Methods	Practical implications	Limitations
(Esposito et al., 2024)	Liver Cancer	Raman spectroscopy for cell characterization and differentiation. Machine learning approaches for spectrum classification and recognition.	Rapid classification of liver cancer cells using AI. Improved diagnostic techniques for hepatocellular carcinoma.	Limitations of current diagnostic techniques for HCC. Complexity of hepatocellular carcinoma diagnosis.
(Kalatzis et al., 2023)	Colorectal cancerous growths	Baseline correction, L2 normalization, filtering, and PCA. Machine learning and deep learning algorithms for classification.	Enhanced classification of colorectal abnormalities using AI and Raman spectroscopy. Improved accuracy in medical diagnostics for real-time analyses.	-
(Soong et al., 2024)	Gastric Neoplasia	Raman spectroscopy-based AI (SPECTRA IMDx™) for assessment. High-definition white light endoscopy (HD-WLE) by expert endoscopists.	SPECTRA AI can assist less experienced endoscopists. Real-time diagnosis of gastric lesions is achievable.	Interoperator variability in endoscopic assessment. Lack of real-time capability in traditional methods.
(Bellantuono et al., 2023)	Thyroid Cancer	Raman spectroscopy for detecting biochemical changes. Machine Learning for classifying nodules as healthy or malignant.	Non-invasive thyroid cancer diagnosis using Raman spectroscopy. Reduces unnecessary surgeries through effective discrimination of nodules.	Identification of significant patterns and peaks is challenging. Need for interpretable results in machine learning models.
(Qi, Liu, & Luo, 2023)	Tumor diagnosis	Conventional Raman spectroscopy and surface-enhanced Raman spectroscopy (SERS). Raman imaging and artificial intelligence applications.	Urgent need for intelligent tumor diagnosis technology. AI enhances accuracy in Raman spectroscopy applications.	SERS substrates affect sample characteristics, hindering nondestructive testing. Imaging speed and resolution issues in Raman imaging methods.
(Talari, Rehman, & Rehman, 2019)	Breast Cancer	Raman spectroscopy (RS) with principal component (PCA) and linear discriminate (LDA) analyses Chemometric methods applied on breast cancer tissues for	AI and ML combined with RS can improve cancer diagnosis accuracy. RS with chemometric methods can classify breast cancer subtypes.	Unwanted affects in spectra: noise, fluorescence, normalization Optimization of spectral data using chemometrics

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		classification.		

CONCLUSION

RS is set to change how diagnosis and treatment of cancer can be done by giving fast, detailed information about molecules without needing dyes or labels. When combined with surface-enhanced Raman scattering, it becomes even more sensitive, making it possible to detect cancer-related DNA early and track how well treatments are working, even at very low levels. Special SERS tools can now find small cancer spots and detect several cancer markers at once, helping doctors understand how different each tumor is. Machine learning tools like CNNs have made it easier to read the complex data from Raman scans, and new models like Raman Net are helping to reduce problems caused by noisy signals. Ultimately, RS holds the promise to transform cancer care by making diagnosis faster, treatment more precise, and outcomes significantly better for patients worldwide.

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AG, AA & MF: Developed the research design and objectives

KJ, AJ & AHS: Research write up and drafting

AG, MF & F: Collecting literature, analysing, and summarizing relevant studies

AG, F, & AR: Critical analysis, editing, proof reading and managing submission, all authors approved the final version.

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