

# Recent advances in surface-enhanced Raman spectroscopy based liquid biopsy for colorectal cancer (Review)

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**Abstract.** As colorectal cancer (CRC) is one of the forms of cancer with the highest prevalence globally and with a high mortality, screening and early detection remains a major issue. Colonoscopy is still the gold standard for detecting premalignant lesions, but it is burdened by some complications. For instance, it is laborious, with some difficulties of acceptance for some patients, and is ultimately an imperfect standard, given that some premalignant lesions or incipient malignancies can be missed by colonoscopic evaluation. In this context, new non-invasive approaches such as surface-enhanced Raman spectroscopy (SERS) based liquid biopsy have gained ground in recent years, showing promising results in oncological pathology diagnosis. These new methods have enabled the detection of subtle molecular profile alterations prior to any macroscopic morphological changes, thus providing a useful tool for early CRC detection. In the present review, we provide a summary of published studies applying SERS in CRC detection, along with our personal experience in using SERS in the diagnosis of different oncological pathologies, including CRC.

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## 1. Introduction

Colorectal cancer (CRC) is one of the most common types of cancer, ranking third in terms of prevalence among other primary sites, accounting for 11% of all cancer diagnoses and ranking second in cancer-related mortality (1). Its high prevalence has prompted large population scale screening programs, aiming at identifying patients with incipient forms of CRC in which curative therapeutic interventions are effective. For the moment, screening for CRC is recommended in asymptomatic adults aged 45-75 years. Patients with a high risk for developing CRC benefit from a specific screening protocol (family history of CRC, inflammatory bowel disease, known or suspected high risk genetic profiles). The standard target population for CRC screening consists in average risk patients, with none of the aforementioned characteristics (2). Screening in CRC is essential, as it detects the pre-cancerous structures that can develop in the colon, namely adenomatous polyps, but also early cancers. The gold standard for screening in CRC is colonoscopy, which was shown to decrease incidence by 64% [95% confidence interval (CI) 50 to 74%] and mortality by 66% (CI 38-81%) in a meta-analysis of observational studies (3).

On the contrary, performing colonoscopy brings with it an important economic burden on healthcare systems, but also discomfort for patients and sometimes complications such as bleeding or perforation. Another drawback that comes frequently in the attention of gastroenterologists is that some premalignant lesions can be missed by standard endoscopy. For instance, in a study including 463 patients with 1294 neoplastic

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