Fecal Immunochemical Test (FIT) for Color's Colorectal Cancer Screening Program

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Executive Summary

Colorectal cancer is the fourth most common cancer and one of the leading causes of cancer-related deaths in the US. While the overall incidence of colorectal cancer has been decreasing since the mid-1990s, rates have actually been increasing by 1% to 2% a year in individuals under 50 years of age.[1] Most colorectal cancers start out as small growths called polyps. With regular screening, most polyps can be found and removed before they have the chance to grow into colorectal cancer. Screening is necessary to detect and diagnose colorectal cancer early when it is easier to treat.

Colonoscopy, an imaging test that requires an in-person appointment and anesthesia, has long been a gold-standard screening methodology for colorectal cancer. However over the past few decades self-collected stool-based testing has proven to be an effective and less invasive way to screen for colorectal cancer in individuals who are at average risk. These tests are less invasive and can be self-collected, which also improves the uptake and compliance of individuals who are due for colorectal cancer screening.

A fecal immunochemical test (FIT) is a stool-based test used to screen for colorectal cancer. This technical document provides details about the FDA-cleared, iFOB immunochemical fecal occult blood (FIT) test offered through Color's Cancer Screening & Prevention Program.

Introduction

Fecal immunochemical testing (FIT) is one way to screen for colorectal cancer.

The American Cancer Society (ACS) recommends average-risk individuals begin colorectal cancer screening starting at age 45.[2] For those who are at increased risk, screening may begin earlier. There are several ways to screen for colorectal cancer – the primary ways to screen are with colonoscopies and stool-based tests. Depending on the test and the result, screening is recommended at different frequencies. FIT is recommended annually, while other methods are recommended every three to ten years.

When detected early, colorectal cancer is largely treatable. For those diagnosed with early stage colorectal cancer, the 5-year survival rate is 91%.[3] In contrast, for late stage colorectal cancer, the 5-year survival rate is 14%.[3]

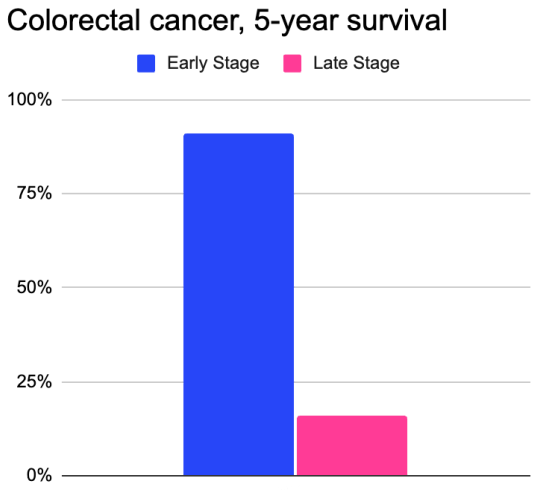

Figure 1. 5-year survival rate of early vs. late stage colorectal cancer

The fecal immunochemical test (FIT) analyzes a stool sample collected at home for the presence of blood, which may be an indicator of colorectal cancer. This convenient and non-invasive test increases adherence with guidelines for colorectal cancer screening, while also simplifying the end-to-end process of getting screening done. If the FIT result is abnormal, a colonoscopy is recommended as a follow up.

Utilization of colorectal cancer screening is low.

About 2 in 5 people who are eligible for screening are not up-to-date with recommended colorectal cancer screening.[4] In fact, over the past decade, there has been an increase in the incidence of early onset colorectal cancers.[5] In addition, individuals of lower socio-economic status, individuals in rural communities, and individuals who have lower access to healthcare have been disproportionately impacted by colorectal cancer due to low uptake of standard colorectal cancer screening and low follow-through with a diagnostic colonoscopy.

Alternative sample collection modalities can increase access to screening.

FIT testing using a self-collected stool sample has been proven to be an effective method to screen for colorectal cancer. As compared to a colonoscopy, self-collected FIT testing can help overcome several barriers of access for individuals who are due for screening.

The use of self-collected stool specimens for colorectal cancer screening has several advantages:

1. Self-collection requires less healthcare provider staffing to supervise the collection of specimens.
2. Self-collection is less invasive and can make for a better patient experience and decrease discomfort.
3. Self-collection can greatly increase access to testing – one of the major bottlenecks to sufficient testing in the United States.
4. Self-collection can decrease tester wait times for access to in-person testing and results where wait times for doctor appointments can be up to several months.

How it works

Step 1: At-home stool collection

Color's fecal immunochemical test (FIT) contains all of the materials needed to collect a stool sample at home and return it to the laboratory (Figure 1). Instructions for collecting a sample can be found here: https://support.color.com/en/articles/7996565-how-do-i-collect-my-stool-sample-for-my-at-home-fit-test

Figure 1. Color's Fecal Immunochemical Test (FIT) collection kit components.

Step 2: Stool-sample analysis

The FIT is performed at US Speciality Labs (USSL) with the OC-SENSOR io analyzer and processed with the iFOB immunochemical fecal occult blood test.

Step 3: FIT results
Clinical samples that produce a valid result will be reported as shown in Table 1.

Result	Meaning
Detected	A 'Detected' result means that the stool sample contained >20µg hHb/g stool. A 'Detected' result does not mean that colorectal cancer is definitely present; follow-up testing is needed.
Not Detected	A 'Not Detected' result means that the stool sample contained < less than 20µg hHb/g stool. A negative result does not mean that colorectal cancer or colon polyps are not present. Unless otherwise indicated, this test should be repeated in one year.
Indeterminate	Testing has yielded inconclusive results. This could be due to inadequate specimen collection. A result of "Indeterminate" does not imply a Detected or Not Detected result. Retesting is recommended with a new specimen.

Table 1. Clinical result types of the Color FIT test. This test is an immunoassay and intended for the qualitative detection of human hemoglobin (hHb) in the stool. The cutoff of a positive ('detected') result is >20µg hHb/g stool. Positivity rates with immunochemical fecal occult blood tests have been shown to vary in each patient population depending on the test used, age and ethnicity of the patient and the predisposition to colorectal disease and other factors that may be associated with gastrointestinal bleeding.

Technical Details

The fecal immunochemical test (FIT) used in Color's Cancer Screening and Prevention Program is an FDA-cleared immunoassay intended for the qualitative detection of fecal occult blood (hHb) in feces by professional laboratories. The full details of the FDA 510(k) clearance can be found here, and are summarized below.

Analytical Sensitivity
The sensitivity of OC-Auto Sensor io iFOB test to hemoglobin S (HbS), hemoglobin C (HbC), and hemoglobin F (HbF) was determined using one reagent lot with 21 replicates. Spiked stool samples containing seven concentrations of each variant were prepared: 0, 50, 80, 100, 120, 450, and 700 ng/mL. Agreement of positive or negative results for each concentration level was ≥ 90%. Such results showed that the OC-Auto Sensor io iFOB test is sensitive to HbS, HbC, and HbF.

Precision

A method comparison of the OC-Auto SENSOR io iFOB Test with the predicate device at 3 clinical sites on a total of 405 samples demonstrated the substantial equivalence to the predicate device. Table 2 shows the overall percent agreement, positive percent agreement, negative percent agreement, and the 95% confidence interval for the 3 sites.

		Predicate			OPA (95% CI)	PPA (95% CI)	NPA (95% CI)
		Positive	Negative	Total			
OC-Auto SENSOR io	Positive	105	0	105	100% (99.1% - 100%)	100% (96.5% - 100%)	100% (98.7% - 100%)
	Negative	0	300	300			
	Total	105	300	405			

Table 2. The overall percent agreement (OPA), positive percent agreement (PPA), negative percent agreement (NPA) and 95 % confidence intervals for 3 sites.

Repeatability and between site reproducibility tests were performed on the OC-Auto SENSORio iFOB Test. For reproducibility study, twenty-one replicates of fecal samples were performed over twenty days at seven levels of hemoglobin concentrations (ranging from 0-700 ng/mL) at 3 clinical sites. For a total of 5,880 samples in the repeatability study, the PPA was 100% and the NPA was 100%.

For a total of 17,640 tests in the reproducibility study, OPA was 100%; NPA of 0, 50, and 80 ng/mL was 100%; PPA of 120 ng/mL was 99.9% and of 450 and 700 ng/mL was 100%.

Analytical Specificity

The analytical specificity study tested suspected potentially interfering substances in fecal samples using one reagent lot with 21 replicates. Test samples were prepared by spiking Hb-free stool specimens with known levels of human hemoglobin to obtain fecal samples with the following seven hemoglobin concentrations: 0, 50, 80, 100, 120, 450, and 700 ng/mL. Fecal samples were spiked to the final concentration of 2.0% of following animal meat extracts: beef, pork, chicken, lamb, and fish. Fecal samples were spiked to the final concentration of 2.5% of rabbit meat extract. Agreement of positive or negative results for each concentration level was ≥ 90%. No significant interference to the OC-Auto Sensor io iFOB test was observed for these animal meat extracts listed above.

References

1. Cancer Facts & Figures 2023. Atlanta: American Cancer Society, Inc. 2022
2. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281.
3. SEER*Explorer: An interactive website for SEER cancer statistics [Internet]. Surveillance Research Program, National Cancer Institute; 2023 Apr 19. [updated: 2023 Jun 8; cited 2023 Nov 7]. Available from: https://seer.cancer.gov/statistics-network/explorer/. Data source(s): SEER Incidence Data, November 2022 Submission (1975-2020), SEER 22 registries (excluding Illinois and Massachusetts). Expected Survival Life Tables by Socio-Economic Standards.
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5. Koh B, Tan DJH, Ng CH, et al. Patterns in Cancer Incidence Among People Younger Than 50 Years in the US, 2010 to 2019. *JAMA Netw Open*. 2023;6(8):e2328171.