Section G: Sample Size/Data Analysis

G1. Sample Size

How many subjects (or specimens, or charts) will be used in this study?

Local: 47 Worldwide: 100

Please indicate why you chose the sample size proposed:

Approximately 100 subjects with 50 in the WL-arm and 50 in the HRME-arm. We anticipate that 15-20% of subjects may be not complete their endoscopy for various reasons (lack of biopsies, loss of Barrett's mucosa, visualization of a lesion > 2 cm, inability to complete endoscopy, etc.) which would allow 40 in each arm. Since each patient only requires one visit for enrollment into the study, we expect that 80 patients will be enrolled and randomized and complete the study.

G2. Data Analysis

Provide a description of your plan for data analysis. State the types of comparisons you plan (e.g. comparison of means, comparison of proportions, regressions, analysis of variance). Which is the PRIMARY comparison/analysis? How will the analyses proposed relate to the primary purposes of your study?

In this trial, the randomization will be stratified by risk group: high risk and average risk. All analyses described below will be stratified as well.

The primary outcome of the randomized trial is Diagnostic Yield, defined as the proportion of all biopsies that are truly neoplasia after histopathological review. A generalized linear model for logistic regression with multiple correlated binary outcomes within each patient will be used for data analysis (McCullagh and Nelder, 1989). In this model the binary outcome for each biopsy specimen is whether the specimen is classified as neoplasia or non-neoplasia, and the explanatory variable is the biopsy protocol group (Group A is standard of care, the control group; Group B is the optical biopsy protocol with HRME). PROC GLIMMIX in SAS will be used because of the correlations among samples from the same patient. The model will allow for testing whether the proportion of samples classified as neoplasia differs between the two biopsy protocols. The analysis will be stratified by risk group --- High Risk and Average Risk. A secondary outcome will be the estimation of the accuracy of each biopsy protocol. Because of the small numbers of true neoplasia patients that are expected to be present among patients enrolled in the trial, sensitivity on a patient-basis will not be estimated. However, specificity will be estimated, stratified by risk group, for each of the two biopsy protocols, along with a one-sided 95% confidence interval

Section H: Potential Risks/Discomforts

H1. Potential Risks/Discomforts

Describe and assess any potential risks/discomforts; (physical, psychological, social, legal, or other) and assess the likelihood and seriousness of such risks:

Possible risks associated with the study procedures are listed below. There may also be risks that are not known. Many side effects go away soon after the procedure, but in some cases, side effects may be serious, long-lasting or permanent, and may even cause death. It is important that the participant tell the study staff about any side effects that he/she may have had even if he/she does not think it is related to the procedure.

Proflavine: There is the possibility of a severe allergic reaction (anaphylaxis) to the Proflavine contrast dye in which the participant may have difficulty breathing and their blood pressure may drop.Proflavine may also cause irritation of gastric mucosa resulting in nausea and vomiting. Jaundice and serious toxic hepatitis may also occur. There are procedures in place to treat the participant in the endoscopy room in the event that this happens. Proflavine enhances visualization of the cell nuclei, because of the very low doses used, we have not noted any clinical sequelae or side effects related to the drug.

Specimen Imaging Probe: There are no known risks from the use of the imaging probe.

Anesthesia: There may be additional risks from the added time of additional sedation, such as decreased blood pressure.

Aspiration (inhaling) of fluid into the lungs during endoscopy: This might cause inflammation in the lungs. Safeguards to prevent this from happening while the participant is under anesthesia will be in place during and after the procedure, and participant's breathing and other vital signs will be carefully monitored.

Biopsies: There is the possibility of some hoarseness, sore throat, difficulty and/or pain in swallowing, bleeding or infection, as well as discomfort at the surgical site.

If the participant experiences any symptoms other than those that the study doctor has informed the participant are associated with the procedure, please let the study doctor know.

There always exists the potential for loss of private information; however, there are procedures in place to minimize this risk.