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## Emergence of a New Optical Marker for Colorectal Neoplasms: To What Extent Should We Accept It?

To the Editor:

Colorectal cancer (CRC) is among the most common cancers worldwide whose incidence and prevalence have been increasing, especially among subjects younger than 50 years of age.<sup>1</sup> Colonoscopy is considered the most sensitive and effective CRC screening method as well as an essential prevention strategy because it can be used to detect and remove premalignant adenomas. Furthermore, the introduction of high-definition and magnifying endoscopy has increased adenoma detection rates and made it possible to predict CRC histological results and invasion depth.<sup>2</sup> The Japan NBI Expert Team (JNET) classification, which is accepted as the NBI magnifying classification standard, classifies tumors into four types according to surface and vessel patterns: 1, 2A, 2B, and 3.<sup>3</sup> Type 2B ranges from high-grade dysplasias to superficial submucosal invasive (SM-s) carcinomas. However, the actual diagnostic performance of type 2B is so weak that 37% and 12% of type 2B lesions were identified as low-grade dysplasia and deep submucosal invasive (SM-d) carcinoma, respectively.<sup>4</sup> The accurate prediction of histological findings through endoscopic examinations can enable the selection of the correct endoscopic resection method and reduce non-curative resection rates, thereby reducing unnecessary subsequent management efforts and the risk of poor outcomes such as recurrence.<sup>5,6</sup>

I received inspiration from an article on the usefulness of white opaque substances (WOS) in colorectal epithelial neoplasms observed during magnifying endoscopy. Yamasaki

et al. reported that irregular WOS are useful predictors of early colorectal carcinoma with an accuracy, sensitivity, and specificity of 87%, 91%, and 86%, respectively.<sup>7</sup> Notably, the presence of WOS is a relatively objective indicator with a 96% negative predictive value for carcinoma. However, endoscopists must consider several points before using WOS as a new optical marker. First, a significant number of colorectal epithelial neoplasms do not feature WOS. More than half of the 511 initially recruited lesions were WOS-negative, and 72 of the remaining 197 neoplastic lesions included WOS in less than half of the area under maximal magnification endoscopy, making them unsuitable for analysis. This phenomenon may be due to the characteristics of a retrospective study evaluating recorded endoscopic images only because it is unknown how many WOS-positive cases will emerge in a prospective study. Second, WOS showed poor performance for discriminating between SM-d carcinoma and superficial carcinoma ( $p=0.727$ ) cases, making it a less suitable option because the most important objective of magnifying endoscopy is predicting SM-d carcinoma. Therefore, to distinguish between SM-d carcinoma and superficial carcinoma cases, it is necessary to observe the pit pattern using traditional chromoendoscopy. In conclusion, WOS can currently play only an auxiliary role in the observation of surface patterns, and the accumulation of more data is required to determine the clinical significance of the presence of WOS.

### Conflicts of Interest

The author has no potential conflicts of interests.

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## RESPONSE

We thank Dr. Han Hee Lee for their interest in our recent manuscript.<sup>1</sup>

First, since this was our first investigation of white opaque substances (WOS) morphology, it was unclear whether the morphology of WOS was useful for qualitative diagnosis. Therefore, in this study, we focused on cases where the morphology of WOS could be clearly determined and we included WOS-positive lesions in which WOS was present in more than half the area at maximum magnification. Currently, we are able to evaluate the morphology of WOS that are present in less than half the area.

Second, as Dr. Lee pointed out, WOS did not show good performance in discriminating between deep submucosal invasive (SM-d) carcinoma and superficial carcinoma. If the surface pattern and vessel pattern cannot be seen by narrow band imaging with magnifying endoscopy due to the presence of WOS, it cannot be applied to the Japan NBI Expert Team (JNET) classification. We believe that the morphology of WOS is very useful for the differential diagnosis between adenoma and carcinoma when the surface pattern and vessel pattern are

not visible. Although WOS has not been adopted as a marker in the current JNET classification, we reported it as a reproducible marker for surface pattern.

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