CORRESPONDENCE

Multispectral Optoacoustic Tomography for Assessment of Crohn's Disease Activity

TO THE EDITOR: In chronic inflammatory diseases, uncontrolled inflammation is associated with increased rates of hospitalization, complications, and death. Because of the potential severity of these conditions, there is an increased demand for new diagnostic approaches.[1,2] Multispectral optoacoustic tomography (MSOT) is a new imaging technique that permits the noninvasive quantification of hemoglobin-dependent tissue perfusion and oxygenation as surrogates of inflammation.[3] This approach uses the excitation of short-pulsed laser light with near-infrared wavelengths to induce the photoacoustic effect in targeted tissues, which results in detectable sound waves induced by thermoelastic expansion.

In this single-center, cross-sectional diagnostic study (ClinicalTrials.gov number, NCT02622139), MSOT Acuity Echo (iThera Medical) was used to perform transabdominal evaluation of intestinal inflammation in 108 patients with Crohn's dis-

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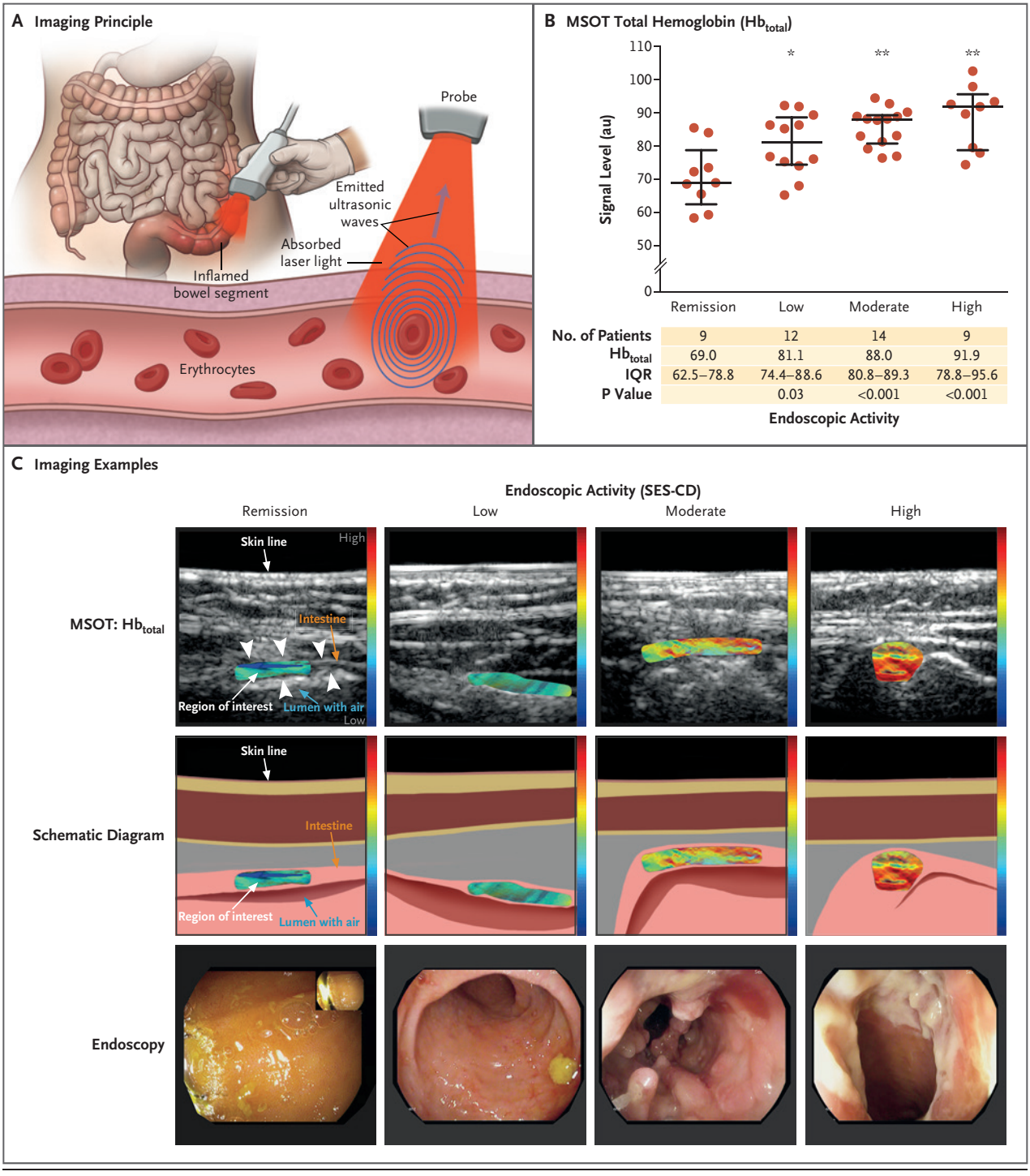
Figure 1 (facing page). MSOT Imaging for the Assessment of Crohn's Disease Activity.

Panel A shows the transabdominal imaging approach, which uses the same detector for laser light emission and ultrasonic detection of signal levels by means of multispectral optoacoustic tomography (MSOT). Erythrocytes are the target for laser-light absorption and ultrasonic emission. Six different wavelengths (700, 730, 760, 800, 850, and 900 nm) were used for MSOT data acquisition; MSOT measurements, such as total hemoglobin (Hb), oxygenated Hb, deoxygenated Hb, and oxygen saturation, are calculated from these measurements. These hemoglobin-based measurements permit the evaluation of tissue perfusion and oxygenation as surrogates of inflammation with MSOT. Panel B shows MSOT-derived total Hb signal levels in the intestinal wall (in both the large bowel and the small intestine) in 44 patients with Crohn's disease with different degrees of endoscopic inflammation. Such evaluation was performed by means of the Simplified Endoscopic Score for Crohn's Disease (SES-CD), which ranges from 0 to 56, with higher scores indicating a greater severity of intestinal inflammation; remission is defined as a score of less than 3, low disease activity as a score of 3 to 6, moderate disease activity as a score of 7 to 15, and high disease activity as a score of 16 or more. The signal levels are expressed as normalized z scores and transformed into a linear scale of arbitrary units (au). The red dots represent single measurements for each patient; the horizontal lines indicate medians, and I bars the interquartile range. A single asterisk denotes $P<0.05$ and a double asterisk $P<0.001$ for the comparison with remission. Panel C shows representative images of MSOT measurements of total Hb in the large bowel and small intestine in patients with different grades of endoscopic disease activity (as evaluated by means of SES-CD). The top row shows representative MSOT measurements of total Hb as color-coded maps with an overlay of B-mode ultrasonographic images. The middle row shows schematic representations of the images shown in the top row. The bottom row shows the corresponding endoscopic evaluation.



ease (Fig. 1A; also see Table S1 and Fig. S1 in the Supplementary Appendix and the protocol, available with the full text of this letter at NEJM.org). We compared the distribution of MSOT measurements between patients with active Crohn's disease and those with nonactive disease, which was determined on the basis of clinical scoring (Harvey–Bradshaw index), endoscopic scoring

(Simplified Endoscopic Score for Crohn's Disease), and histologic scoring (modified Riley score) as reference tests. Furthermore, we compared the diagnostic performance of MSOT with clinical and laboratory assessments and conventional ultrasonography (Section 1 in the Supplementary Appendix). Clinical and laboratory assessments and ultrasonography (including the calculation of Limberg scores, which measure intestinal-wall thickness and perfusion) were conducted immediately before MSOT imaging, and endoscopy was performed within 6 months (median interval, 8.7 weeks; interquartile range, 1.4 to 13.8) after MSOT imaging.

A total of 17 patients were excluded from the study, because MSOT imaging could not be evaluated. In the remaining patients, we explored MSOT values, including single-wavelength measurements (700, 730, 760, 800, 850, and 900 nm) and spectrally unmixed measurements, including total hemoglobin, oxygenated hemoglobin, deoxygenated hemoglobin, and oxygen saturation (Section 1 and Fig. S2 in the Supplementary Appendix). Using endoscopy as a reference standard to distinguish active Crohn's disease from nonactive disease in 44 patients, we found that there were significant differences between active disease and nonactive disease for all the MSOT values except for oxygen saturation ($P \leq 0.001$) (Table S3 in the Supplementary Appendix). We had similar results when we used histologic characteristics as the reference standard in 42 patients but not when we used clinical scoring in 86 patients (Section 2 and Tables S2 and S4 in the Supplementary Appendix). Our findings suggest that there was a significant difference in single-wavelength measurements at 760 nm and spectrally unmixed total hemoglobin between patients with endoscopic remission and those with low-grade active disease ($P=0.02$ and $P=0.03$, respectively) (Fig. 1B and 1C, and Table S5 in the Supplementary Appendix). In addition, we compared the diagnostic accuracy of MSOT to detect active disease with the accuracy of standard ultrasonography and clinical and laboratory assessments (Table S6 and Figs. S4 and S6 in the Supplementary Appendix), but given the small sample size and the lack of validations of our findings in an independent population, we consider these estimates and comparisons to be preliminary and exploratory.

In conclusion, this preliminary study suggests that MSOT-based assessment of hemoglobin levels in the intestinal wall has the potential to be used to distinguish active disease from remission in patients with Crohn's disease without the need for more invasive procedures; further study is needed.

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