



## Assessment of inflammatory disease activity in IBD patients with Multispectral Optoacoustic Tomography (MSOT)

*Patients affected by inflammatory bowel disease (IBD) go through cycles of active disease and remission caused by chronic relapsing of inflammatory processes within the colon wall. Knowing the current status of inflammation is of great importance in choosing the appropriate treatment. To save patients from discomfort while increasing the monitoring frequency, non-invasive alternatives to the contemporary diagnostic gold standard – endoscopy and biopsy – are needed. MSOT has shown that it might provide a solution to these issues.*

### Use of MSOT technology in IBD patients

Inflammatory processes are linked to perfusion of tissue. Inflammation within the intestinal wall leads to an increased blood supply which gives rise to MSOT signals. Without the need for contrast agents, MSOT can visualize hemoglobin content and oxygenation status as surrogate markers for inflammation activity, determined invasively by endoscopy as a gold standard. In a feasibility study from Waldner et al. (2016), MSOT has shown potential to assess the disease activity in the intestinal wall of IBD patients non-invasively [1].

#### INNOVATIVE

High sensitivity to detect low levels of inflammation, showing the best correlation with colonoscopy as compared to patient questionnaire (HBI), blood tests (CRP), and ultrasound examination.

#### NON-INVASIVE

Acquires transabdominal images of the colon wall without the need for contrast agents.

#### HIGH PERFORMANCE

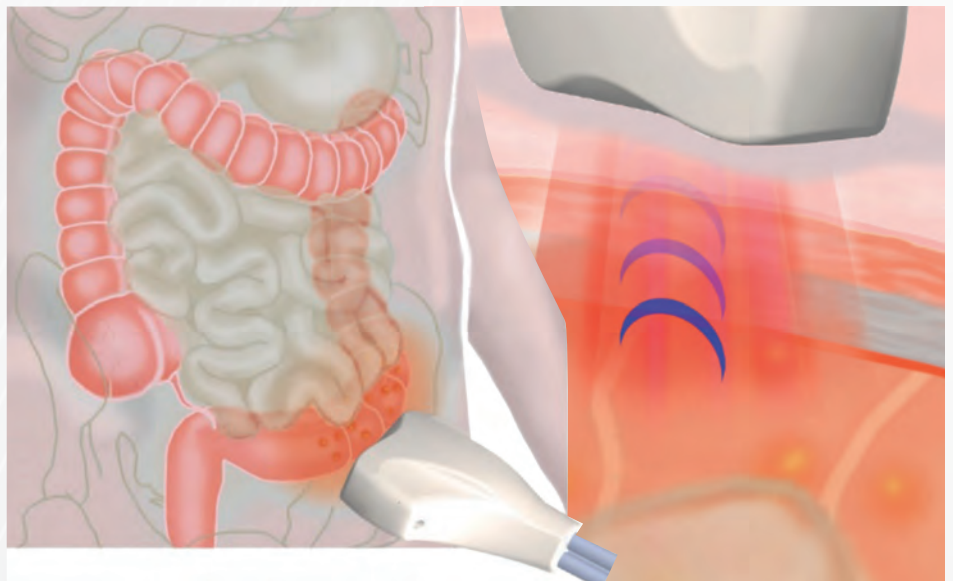
Combines the high molecular specificity of optical imaging with the high spatiotemporal resolution of ultrasound.

#### EASY TO USE

Similar workflow as in ultrasound examinations; examination carried out in less than 5 minutes.

#### IMAGING PROTOCOL

|                              |   |
|------------------------------|---|
| <b>Imaging System</b>        | MSOT Acuity Echo  |
| <b>Repetition Rate</b>       | 25 Hz   |
| <b>Excitation Wavelength</b> | 700, 730, 760, 800, 850 and 900 nm.   |
| <b>Processing Methods</b>    | Back-projection tomographic image reconstruction; spectral unmixing by linear regression. |



**Figure 1: Principle of MSOT measurements in IBD patients**

MSOT enables transabdominal, real-time imaging of disease activity in the colon wall in IBD patients. Tissue is illuminated by near-infrared light. Chromophores such as oxy- and deoxy-hemoglobin become excited when the light is absorbed. When these molecules relax, a small amount of heat is generated, which creates a pressure wave and a subsequent ultrasound signal. A tomographic array of ultrasound transducers is used to detect these signals. The illumination and detection occur with a single, integrated handheld device.



## MSOT imaging versus endoscopy

In a larger study of 109 Crohn's patients, disease activity determined by MSOT was compared to several clinical parameters, including endoscopy [2]. It was established that MSOT can provide substantial clinical value in discriminating patients in remission

from patients with different levels of disease activity. MSOT therefore shows promise to replace or complement invasive endoscopic procedures. This would allow for more frequent follow-ups and better treatment monitoring.

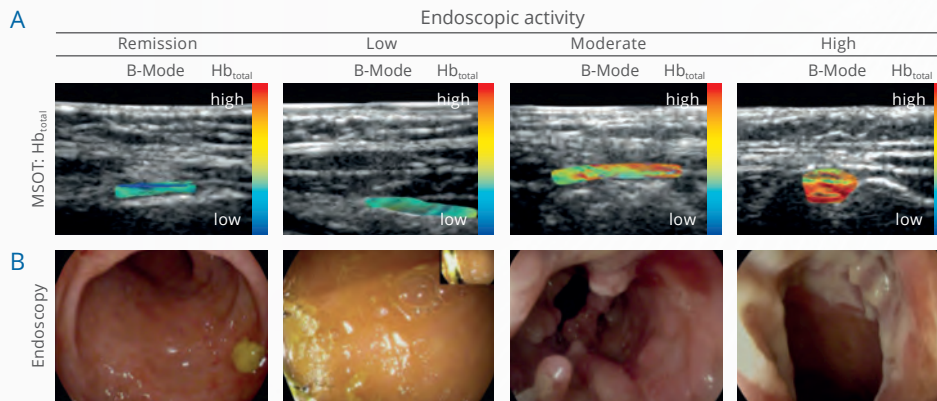


Figure 2: MSOT results were compared with colonoscopy as the gold standard.

MSOT measurements for patients in remission, and low, moderate and high inflammatory activity state as determined by endoscopy. (A) Representative MSOT measurements of Hb<sub>total</sub> shown as color-coded maps overlaid on B-mode ultrasound images. (B) Corresponding endoscopy images.

## Diagnostic performance of MSOT

The investigators further explored the correlation of MSOT signal intensity with the clinical gold standard, endoscopy, as compared to other standard clinical tests, i.e. clinical symptom-based activity scoring (HBI), Doppler sonography (Limberg score) and laboratory assessment of C-reactive protein, a commonly used

inflammatory marker. Notably, MSOT outperformed the current non-invasive clinical approaches to assess disease status. Furthermore, these study results suggest that MSOT may be translated to inflammatory processes of the skin, thyroid, muscle, joints, vasculature and other superficial organs.

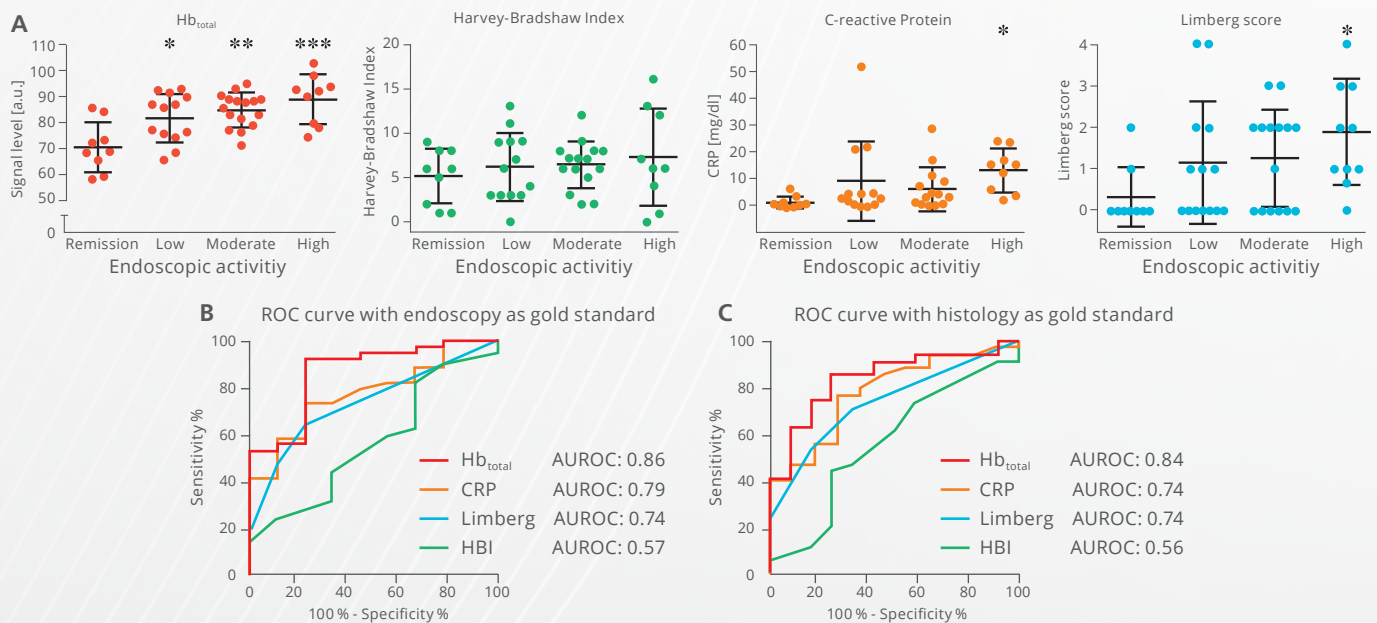


Figure 3: Performance of MSOT (Hb<sub>total</sub>) vs. standard clinical tests.

(A) Dot plots of measurements in patients grouped by endoscopic activity. From left to right: MSOT (Hb<sub>total</sub>), clinical disease activity score (Harvey-Bradshaw Index), C-reactive Protein and Doppler Ultrasound (measured according to Limberg score). Stars indicate levels of statistical significance (\*=p<0.05, \*\*=p<0.01, \*\*\*=p<0.001, \*\*\*\*=p<0.0001). (B) and (C) Receiver operator characteristics (ROC) for the tested non-invasive diagnostics against endoscopy (B) and histology (C) as reference. Corresponding area under the receiver operator curve values (AUROC) are shown.

1. Waldner, M. J., et al., Multispectral optoacoustic tomography in Crohn's disease: Non-invasive imaging of disease activity, *Gastroenterology*. 2016 Aug;151(2):238-40.  
2. Knieling, F., et al., Multispectral Optoacoustic Tomography for Assessment of Crohn's Disease Activity, *N Engl J Med*. 2017 Mar 30;376(13):1292-1294.