MSOT Acuity Echo

Translational imaging of Duchenne Muscular Dystrophy (DMD) using MSOT

DMD is a lethal muscular disease posing significant burden on patients, their families and health care systems. Currently, the assessment of disease status and therapeutic response relies on functional tests, typically involving a physical challenge (e.g. walking) which is highly variable and unsuitable for young infants and other non-ambulant patient groups. A clear clinical need exists to objectively and quantitatively monitor the status of DMD patients, particularly for treatment response. We propose MSOT imaging as an age-independent technology to assess disease status in muscles, non-invasively, with high sensitivity and without the need of patient sedation.

Preclinical monitoring of collagen with MSOT

In a translational study [1], the collagen content of the distal extremities was monitored non-invasively by MSOT imaging without the need for sedation, in both healthy wildtype (WT) and DMD piglets over 4 weeks. The results reveal an excellent sensitivity and specificity of MSOT-derived collagen signal detection to distinguish between healthy and diseased tissue from birth. Validation of the presence of fibrosis biomarkers was performed by immunohistochemistry. An increase of different types of collagens could be found in all DMD piglets present from week one of life which strongly correlated with the MSOT findings.

INNOVATIVE
MSOT-based collagen detection could potentially provide a quantitative biomarker for DMD disease progression.

NON-INVASIVE
Handheld transcutaneous imaging, without the need for contrast agents or sedation.

HIGH PERFORMANCE
Real-time visualization of tissue chromophores at high spatial resolution at a depth of up to 3 cm.

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

IMAGING PROTOCOL

Imaging System	MSOT Acuity Echo
Repetition Rate	25 Hz
Excitation Wavelength	680, 700, 730, 760, 800, 850, 920, 1000, 1030, 1064 and 1100 nm.
Processing Methods	Back-projection tomographic image reconstruction; spectral unmixing by linear regression.

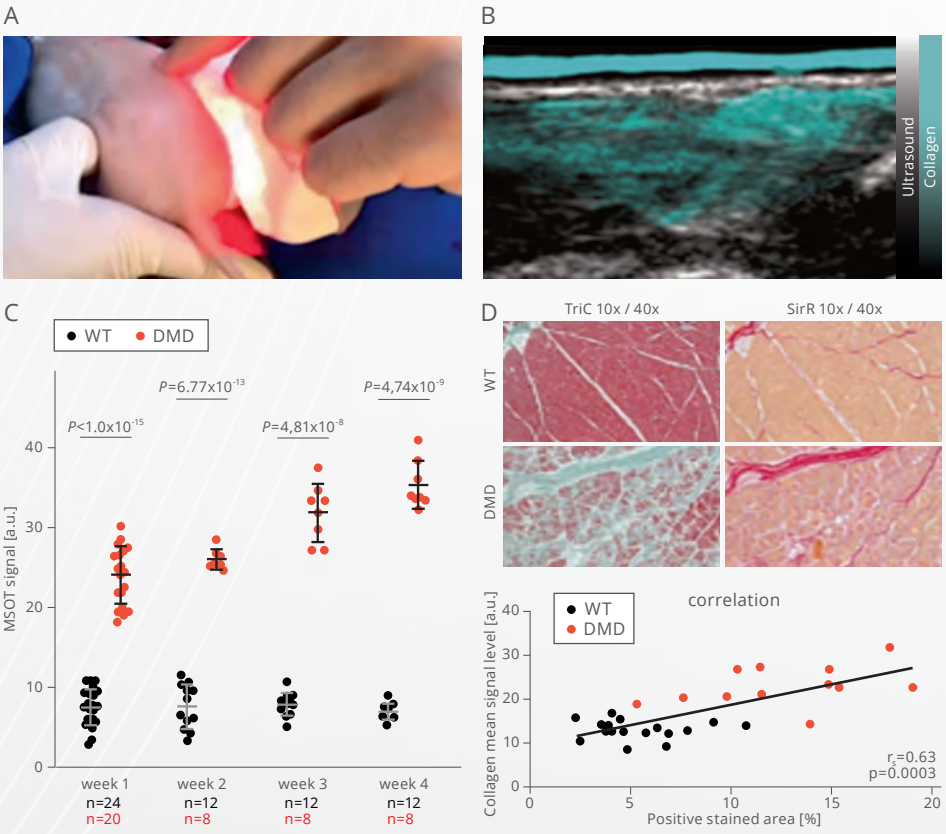

FIGURE 1: Longitudinal assessment of collagen content and *ex vivo* verification in DMD and WT piglets.

Panel A shows MSOT imaging of non-anesthetized piglets. Panel B shows the associated MSOT images with collagen signal overlaid onto ultrasound images. Panel C quantifies MSOT-derived collagen signal in WT and DMD piglets, showing an increase in signal over a period of 4 weeks that was not detectable in the WT group. Panel D shows that collagen content was verified by immunostaining of biopsy samples with Trichrome (TriC) and Sirius Red (SiR), with DMD animals exhibiting higher levels of collagen as compared to WT.

MSOT performance in patients and healthy volunteers

For studying MSOT performance in humans, 10 ambulatory DMD patients, aged 3 to 10 years and 10 age-matched healthy volunteers (HV) were enrolled. The results demonstrate the excellent diagnostic performance of MSOT imaging to distinguish healthy from diseased muscular tissue. Moreover, MSOT signals were significantly correlated to standard physiological and functional tests like the 6-minute walk test (6MWT). These results suggest that MSOT imaging might fill the urgent need for an easy and objective assessment of DMD disease progression and could be evaluated for treatment monitoring in future clinical studies.

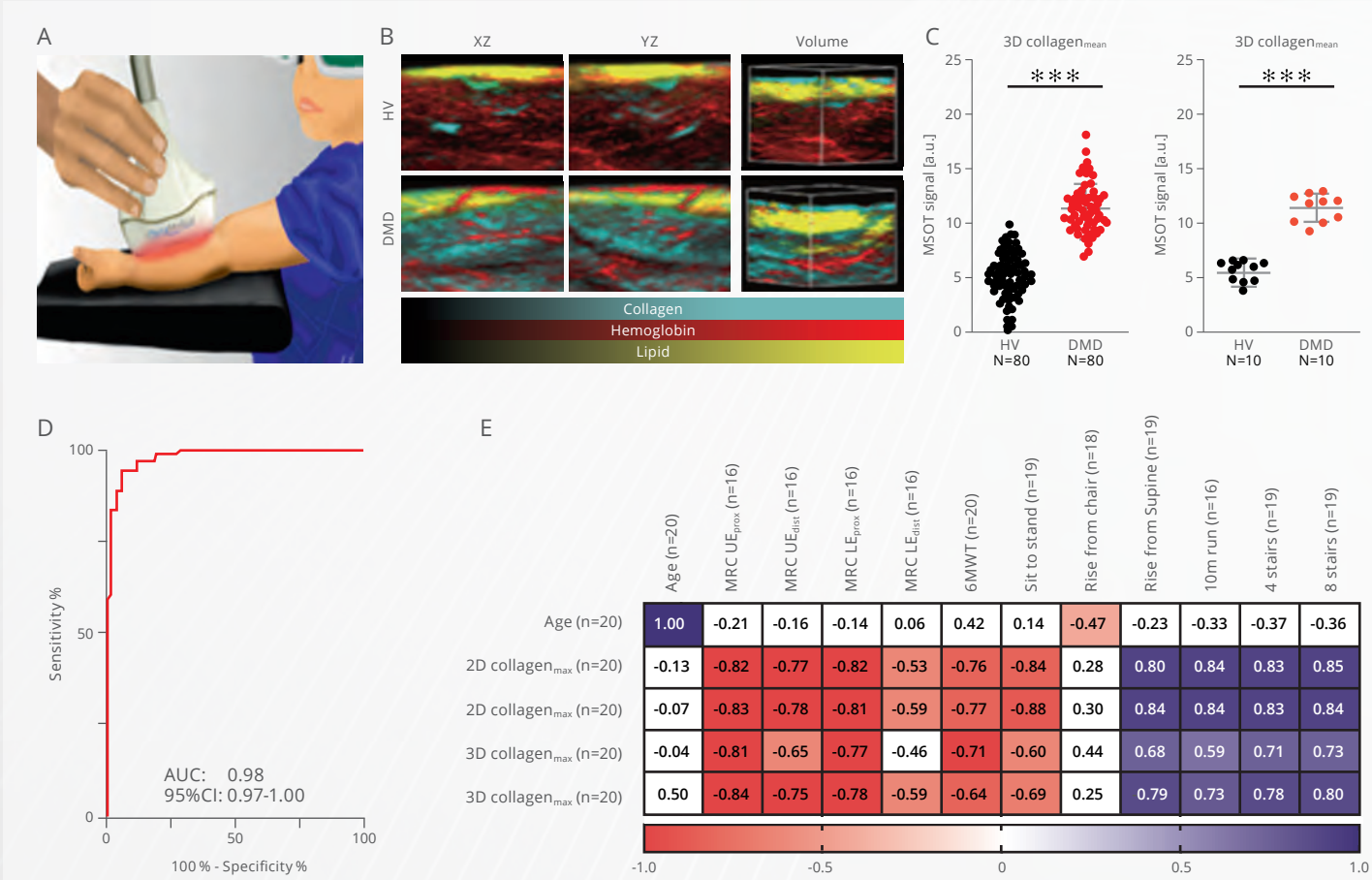

FIGURE 2: Performance of MSOT (collagen) detection and comparison to physical examinations.

Panel A shows schematically the MSOT detector being used on a patient. Panel B shows a representative MSOT image in a HV vs. DMD patient. Panel C shows quantification of collagen, revealing significant differences in signal strengths between independent muscle regions (n=80 HV, 80 DMD; p<<<0.05) and mean values for each subject (n=10 HV, 10 DMD; p<<<0.05). Panel D shows a ROC curve which illustrates the high sensitivity and specificity of MSOT (independent muscle regions, n=80 HV, 80 DMD; p<<<0.05). Panel E shows correlations to physical examinations, with significant correlations to timed function tests and muscle strength tests (red: negative; blue: positive).

1. Regensburger AP et al., **Detection of collagens by multispectral optoacoustic tomography as an imaging biomarker for Duchenne muscular dystrophy**, Nature Medicine (in print).