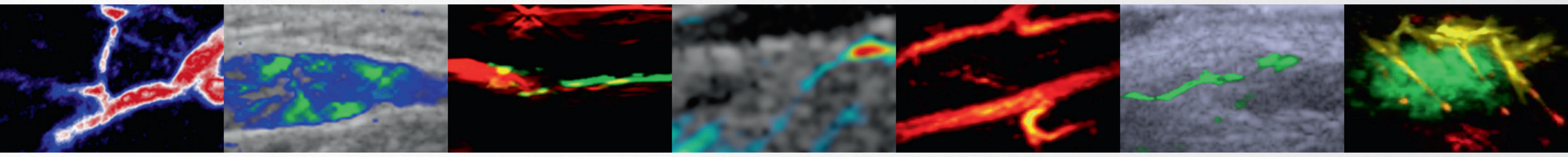


MSOT MULTISPECTRAL OPTOACOUSTIC TOMOGRAPHY ACUITY

MSOT Acuity* | Acuity Echo

- Imaging system for clinical research
- Tomographic handheld real-time imaging
- Anatomical, functional and molecular contrast

*CE marked as a medical device

www.ithera-medical.com

iTheraMedical
Listening to Molecules

MSOT TECHNOLOGY

Imaging sequence:

- Illumination of tissue with laser pulses at multiple wavelengths
- Detection of induced ultrasound pressure waves
- Image reconstruction to show optical absorption in tissue
- Spectral unmixing to analyze individual absorbers

Technology benefits:

Combines the molecular specificity of optical imaging with the depth and spatiotemporal resolution of ultrasound

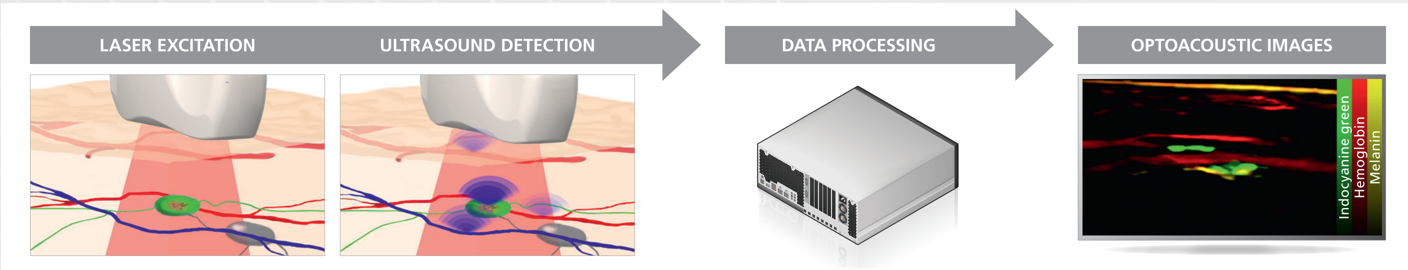
Molecular specificity:

Identify and quantify disease-related biomarkers, revealing endogenous absorbers and injected contrast agents

Depth & spatiotemporal resolution:

Acquire soft tissue images with spatial resolution down to 80 µm* *in vivo* and in real time

*Spatial resolution down to 400 µm for the CE marked detector



OPUS:
hybrid **OP**toacoustic & **U**ltra**S**ound imaging

Ultrasound imaging integrated in the MSOT Acuity *Echo* enables the visualization of both tomographic optoacoustic and ultrasound information at the same time, thus providing additional and complementary information on tissue morphology.

MSOT VS. OTHER IMAGING MODALITIES

Imaging is an essential tool for medical diagnosis. Various technologies have evolved over time, each one providing specific benefits – but also limitations. Innovation in biomedical imaging facilitates new avenues for diagnosis and treatment of diseases.

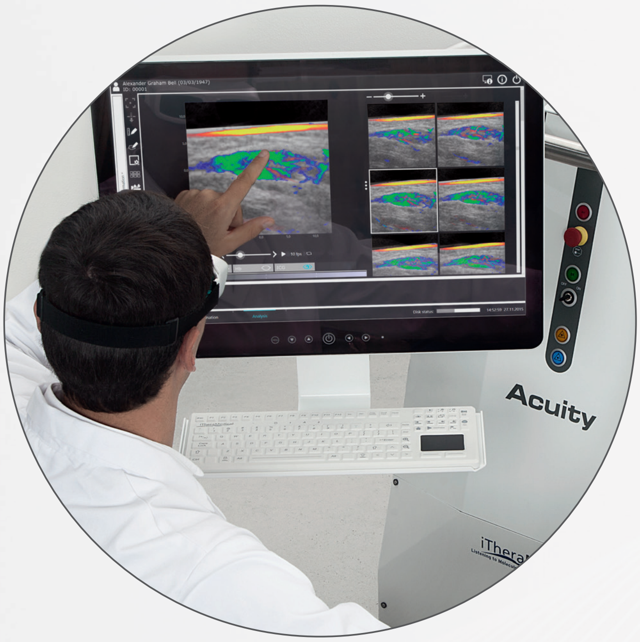
X-ray, ultrasound and magnetic resonance imaging (**MRI**) provide anatomical information at high spatial resolution but with limited molecular specificity and sensitivity. On the other hand, positron emission tomography (**PET**) is a molecular imaging modality with high sensitivity, but suffers from low spatial resolution.

MSOT – Multispectral Optoacoustic Tomography is a novel imaging technology. Besides its high spatiotemporal resolution and sensitivity for optical contrast, MSOT imaging comes at relatively low cost and low burden of use, especially no ionizing radiation.

Modality	Spatial resolution	Temporal resolution	Sensitivity	Cost and infrastructure	Burden of use
MSOT	+	+	O	+	+
X-ray	+	O	–	+	–
Ultrasound	+	+	–	+	+
MRI	+	O	–	–	O
PET/SPECT	–	–	+	–	–

+ = favorable O = medium – = unfavorable

Adapted from Ntziachristos V and Razansky D, Molecular Imaging by Means of MSOT, Chem Rev. 2010 May 12;110(5):2783-94.



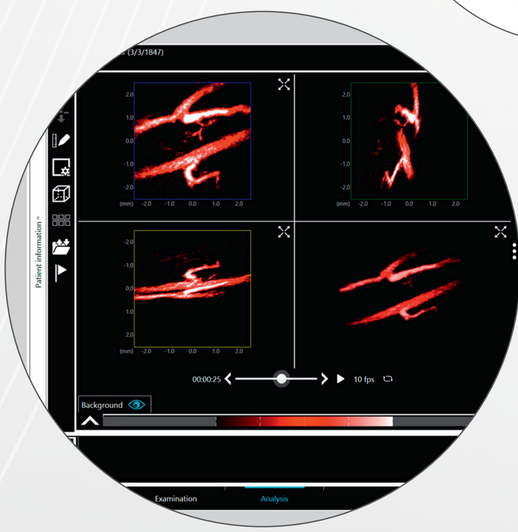
SYSTEM USE

- Workflow comparable to that of conventional ultrasound
- Handheld detectors for flexible use
- Foot pedal and laser safety goggles allow safe use of the system
- One click acquisition of single images and image sequences

SYSTEM COMPONENTS

MSOT scanner hardware

- Mobile imaging platform with integrated high-performance workstation and adjustable screen
- Graphical user interface controlled via touchscreen and customized keyboard
- Detectors for different applications with variable center frequency, geometry, and size



viewMSOT™ software

- Data management interface links scans to research subjects
- Application-specific presets enable change of acquisition settings
- Automated real-time spectral unmixing and signal quantification
- Wide range of tools for data analysis and export

ACCESSORIES AND OPTIONS

Accessories:

- Laser safety goggles
- Calibration phantom

Options:

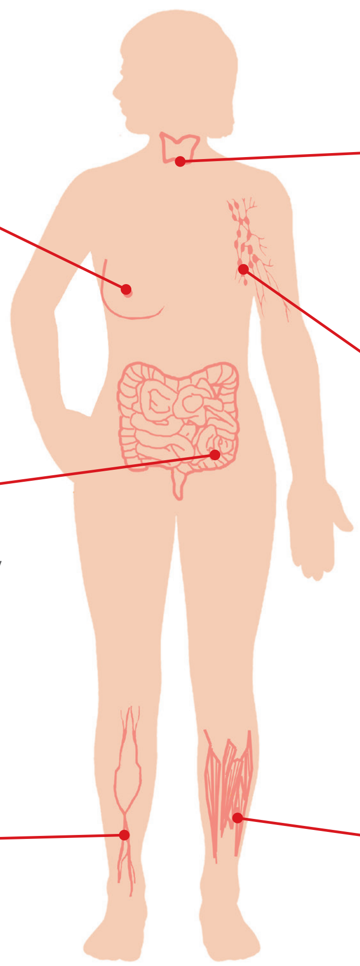
- 2D and 3D detectors customized for particular application needs (2.5-10 MHz, 128-512 elements)
- Advanced software tools for image analysis
- Scan station for imaging of tissue specimens

VISUALIZED CHROMOPHORES

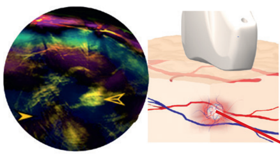
MSOT detects and visualizes signals that represent the spectrally distinct absorbance of chromophores in tissue. Research studies have proven the effective detection of endogenous chromophores such as hemoglobin, melanin and lipids as well as that of commonly used and clinically approved optical contrast agents such as indocyanine green (ICG) and methylene blue.

MSOT TRANSLATIONAL RESEARCH HIGHLIGHTS

MSOT has been applied in a variety of clinical research studies and has shown the potential to improve medical care in the future. Particular application areas include the following:

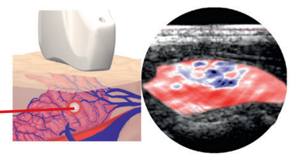


BREAST CANCER



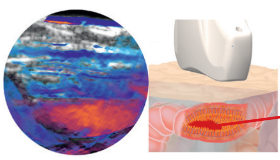
Assessment of suspicious lesions, potentially increasing sensitivity and specificity of diagnosis [1]

THYROID NODULES



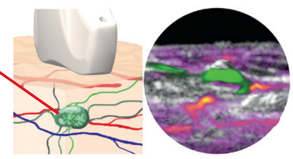
Assessment of thyroid nodules as well as autoimmune thyroid conditions [4]

INFLAMMATORY BOWEL DISEASE



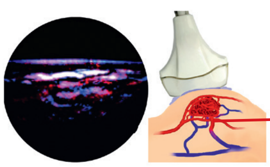
Non-invasive assessment of inflammatory activity in the bowel wall, correlating with endoscopic disease activity [2]

SENTINEL LYMPH NODES



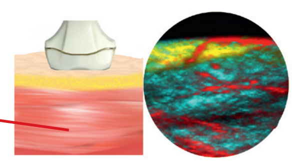
Non-radioactive identification of sentinel lymph nodes (SLN) using ICG, as well as non-invasive assessment of melanoma SLN metastases [5]

VASCULAR MALFORMATIONS



Differentiation of arterial and venous malformations [3]

MUSCULAR DYSTROPHY



Quantification of collagen and hemo-globin in muscle tissue, correlating with the gold standard, physiological tests [6]

[1] Diot G et al., **Multispectral optoacoustic tomography (MSOT) of human breast cancer,** Clin Cancer Res. 2017 Nov 15;23(22):6912-6922.

[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.

[3] Masthoff M et al., **Use of Multispectral Optoacoustic Tomography to Diagnose Vascular Malformations,** JAMA Dermatol. 2018 Dec 1;154(12):1457-1462.

[4] Roll W et al., **Multispectral optoacoustic tomography of benign and malignant thyroid disorders - a pilot study,** J Nucl Med. 2019 Mar 8.

[5] Stoffels I et al., **Metastatic status of sentinel lymph nodes in melanoma determined noninvasively with multispectral optoacoustic imaging,** Sci Transl Med. 2015 Dec 9;7(317):317ra199.

[6] Regensburger A et al., **Multispectral Optoacoustic Tomography in the Extended Near Infrared Range for Non-invasive *in vivo* Detection of Collagens in Duchenne Muscular Dystrophy,** (submitted).

For more information on the research, please see the original publications or:

https://www.ithera-medical.com/applications/clinical-research

TECHNICAL SPECIFICATIONS

Specifications	MSOT Acuity*	MSOT Acuity Echo **
Image acquisition		
Image rate (live display)/ single wavelength	up to 25 images per second	
Image rate (multispectral)	up to 12 images per second	
Key system components		
SpectraPULSE™ illumination system		
Laser wavelength spectrum	Standard*: 680-980 nm | Optional**: 660-1300 nm	
Pulse repetition rate	≤ 25 Hz (adjustable)	
Maximum pulse energy @ 750 nm	25 mJ	
Laser performance monitoring	Yes	
Wavelength tuning	Tuning time: < 10 ms | Minimum step size: 1 nm	
RapidSCAN™ data acquisition electronics		
Channels for simultaneous acquisition	up to 512	
Sampling rate	up to 40 MS/s	
OPUS™ hybrid ultrasound mode		
Transmit frequency	n/a	2-8 MHz**
Image formation method	n/a	Synthetic aperture beamforming, spatial compounding**
viewMSOT™		
Data management	Study data administration, creation of reports, data export	
Data acquisition	2D/3D**, single images, image sequences, multispectral data sets	
Data processing	Image reconstruction, spectral unmixing, signal quantification	
Data analysis	Measurements, spectral analysis, color maps, image filters	
General technical specifications		
Hardware scanner console	Intel Core i7/Xeon, 32 GByte RAM, 4 TByte HDD data storage, 24'' TFT touchscreen	
Operating system	Windows 10 embedded	
External interfaces	1 GBit Ethernet, remote interlock connector	
Dimensions (width x depth x height | weight)	73 x 91 x 152 cm | 290 kg	
Power	16A/230VAC, 50/60 Hz	
Laser classification	Class 4	

TomoARC™ detectors	Standard 2D*	Standard 3D**	Optional detectors**
Angular coverage	125°	98°	90-180°
Center frequency	4 MHz	8 MHz	2.5-10 MHz | > 50%
Number of elements	256	256-384	128-512
Field of view	25 mm	15 x 15 mm	up to 30 | 20 x 20 mm

VISIBLE AND INVISIBLE LASER RADIATION

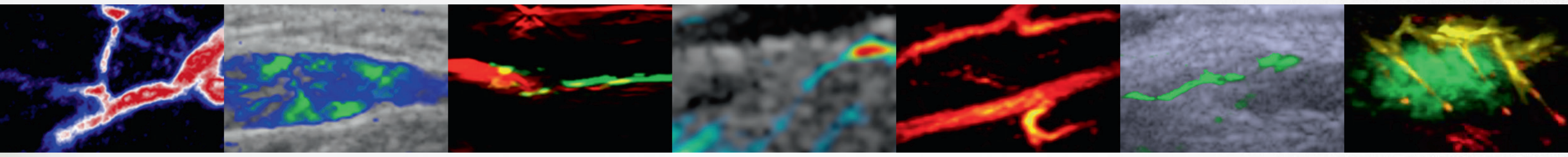
DANGER
CLASS 4
LASER PRODUCT
IEC60825-1:2014

Maximum Output: 25 mJ
Pulse duration: 4-7 ns
Wavelengths: 660-1300 nm

AVOID EYE OR SKIN EXPOSURE
TO DIRECT OR SCATTERED RADIATION

*CE marked in Europe ** For investigational use only

MKT-2-BR-01 v2.0



SELECTION OF RELATED PUBLICATIONS

- Regensburger A et al.,
  Multispectral Optoacoustic Tomography in the Extended Near Infrared Range for Non-invasive *in vivo* Detection of Collagens in Duchenne Muscular Dystrophy,
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- Ntziachristos V and Razansky D,
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iTheraMedical
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iThera Medical GmbH
Zielstattstrasse 13
D-81379 Munich

Phone: +49 (0) 89 700 7449-0
Fax: +49 (0) 89 700 7449-90
Email: info@ithera-medical.com