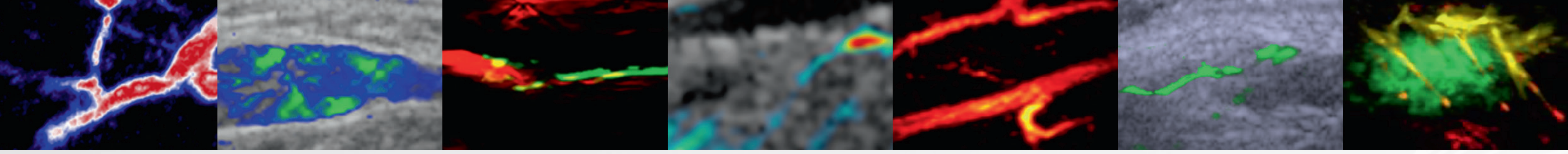
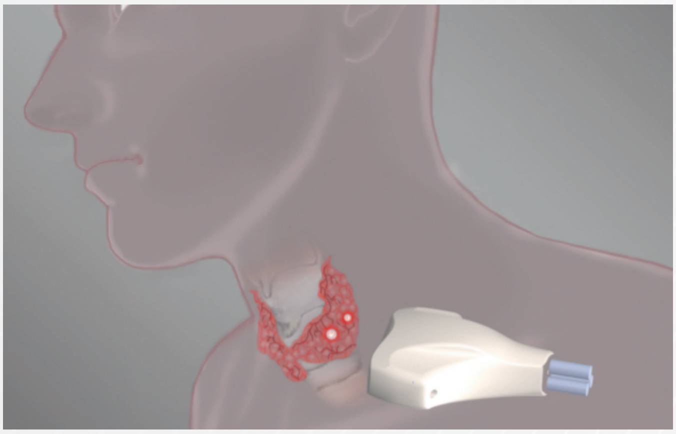


iTheraMedical
Listening to Molecules

Human thyroid imaging using Multispectral Optoacoustic Tomography (MSOT)

Thirty to fifty percent of the population in late adulthood have thyroid nodules, but only about 5 percent of those nodules are malignant. Today, malignancy risk is assessed through ultrasonography, blood tests and scintigraphy. However, the standard of care has its limitations. Scintigraphy exposes patients and staff to radioactivity, while the combination of the three tests can safely detect only a minority of benign nodules. Thus, most nodules proceed to a fine needle aspiration biopsy (FNAB). In addition to being unnecessarily invasive for diagnosing benign nodules, FNAB suffers from a false-negative rate of approximately 5 percent and is non-diagnostic in a further 10 percent of cases. Hence, better non-invasive diagnostic methods that do not give rise to radiation exposure are needed. In early proof-of-concept studies MSOT has been shown to be able to visualize the thyroid. Furthermore, initial results suggest that MSOT might be useful in thyroid nodule assessment.

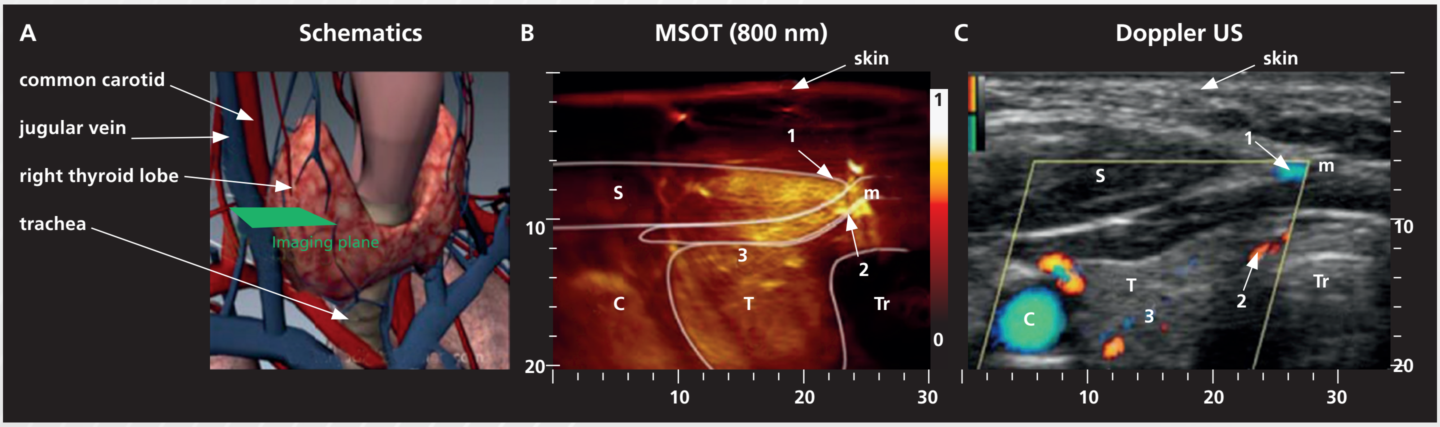
Figure 1: Schematic representation of handheld MSOT thyroid imaging



MSOT enables non-invasive, real-time imaging of vascular structures and oxygenation in the thyroid

Cancerous tissue requires an excess of nutrients and oxygen. Hence, cancers promote the growth of neovasculature, and are often characterized by a change in oxygenation of the tissue due to an imbalance between oxygen supply and consumption. MSOT can visualize vascularity, i.e. total hemoglobin content, and oxygenation status without the need for exogenous contrast agents. MSOT is therefore a useful tool to characterize malignant lesions. In a first *ex vivo* optoacoustic study conducted by Dogra et al. [1], benign and malignant thyroid lesions could be differentiated based on deoxyhemoglobin content. *In vivo*, MSOT has been used on healthy volunteers to visualize thyroid anatomy (Figure 2) [2].

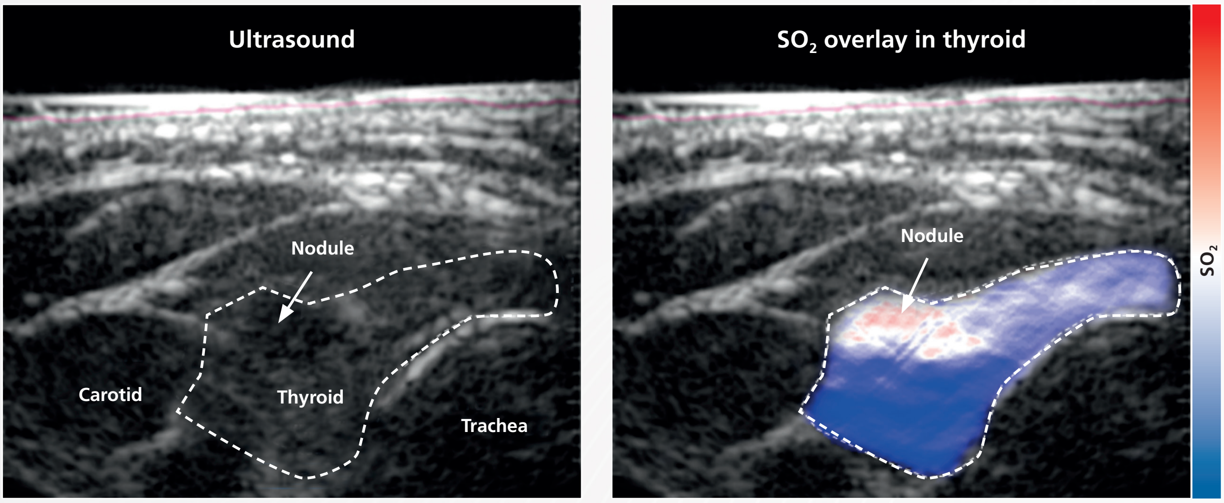
Figure 2: MSOT imaging of a healthy thyroid



(A) Schematic representation of the thyroid anatomy and imaging plane. (B) Single-wavelength MSOT imaging reveals anatomic features of the thyroid: sternocleidomastoid and infrahyoid muscles, respectively (s, m), thyroid (T), trachea (Tr), the carotid artery (C) as well as smaller vascular features (1,2,3). (C) Doppler sonography of the same field of view shows the same vascular structures. MSOT can provide tissue perfusion information on bulk tissue, whereas Doppler ultrasound cannot.

In Figure 3, an MSOT scan of a patient with a small nodule in the upper left corner of the thyroid is shown. The nodule is clearly visible on the MSOT scan; it shows a higher degree of oxygenation than the surrounding healthy tissue parenchyma.

Figure 3: MSOT oxygenation measurement of a thyroid nodule



In vivo multispectral imaging of the thyroid of a patient with a small thyroid nodule. MSOT oxygenation measurement is shown as overlay on an ultrasound image, cropped to the thyroid area. The nodule shows higher oxygen saturation than the surrounding healthy thyroid parenchyma.

In the future, correlations of MSOT *in vivo* measures with *ex vivo* nodule histology will clarify the diagnostic utility of MSOT in thyroid nodule diagnosis. MSOT could also be used to assess autoimmune thyroid conditions that alter the tissue oxygenation and vascularity.

Conclusions

MSOT can assess total hemoglobin, oxygenation and vascular structures in the thyroid. It shows promise to complement current diagnostic methods as a non-invasive, real-time tool to assess thyroid conditions such as nodules or autoimmune disease. Potentially, MSOT could be used to replace radioactive methods such as scintigraphy in some patients, or rule out the need for invasive procedures such as FNAB or core biopsy. Furthermore, there might be a role of MSOT in guiding FNABs to avoid false-negative or inconclusive results and maybe monitor newer treatment modalities such as ablation therapy.

MSOT Imaging Protocol

Acquisition System	Single-Wavelength Image Acquisition/ Display Rate	Multispectral Acquisition Wavelengths used	Analysis Method
MSOT EIP	10 Hz	700/730/760/800/850/900/920 and 950 nm	Model-based and back-projection tomographic image reconstruction; Spectral unmixing by linear regression
MSOT Acuity Echo	25 Hz		

References

[1] Dogra V. S., Chinni B. K., Valluru K. S., Moalem J., Giampoli E. J., Evans K., & Rao N. A., **Preliminary results of *ex vivo* multispectral photoacoustic imaging in the management of thyroid cancer.** American Journal of Roentgenology, 2014, 202(6), W552-W558.

[2] Dima, A., & Ntziachristos, V., ***In vivo* handheld optoacoustic tomography of the human thyroid.** Photoacoustics., 2016.