## High-Contrast Lymph Node Detection with the Infrared Tissue Imaging System (ITIS)

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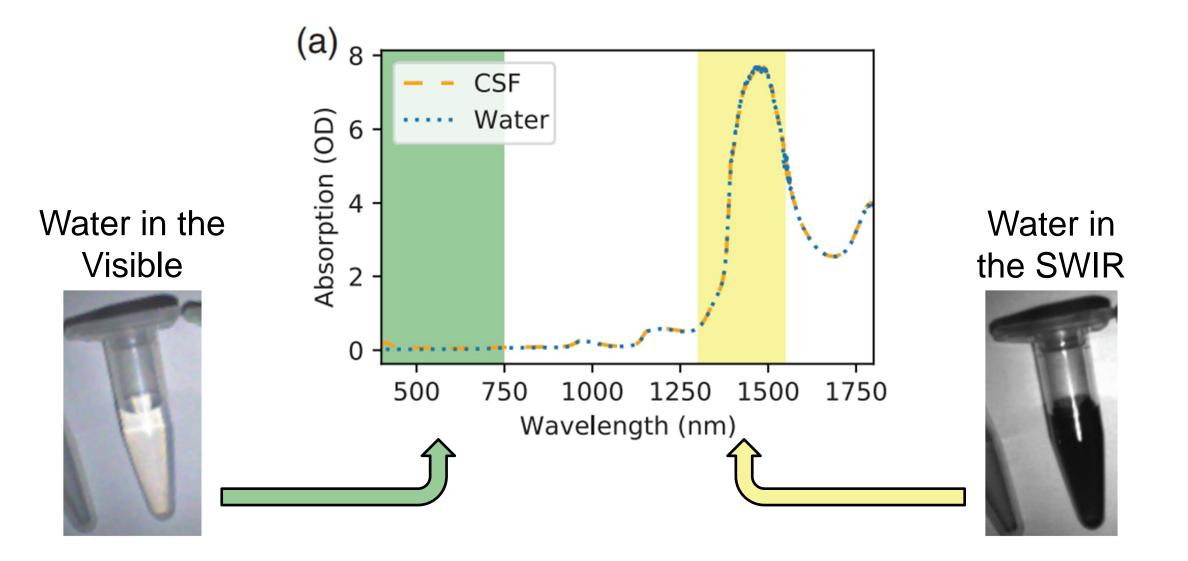
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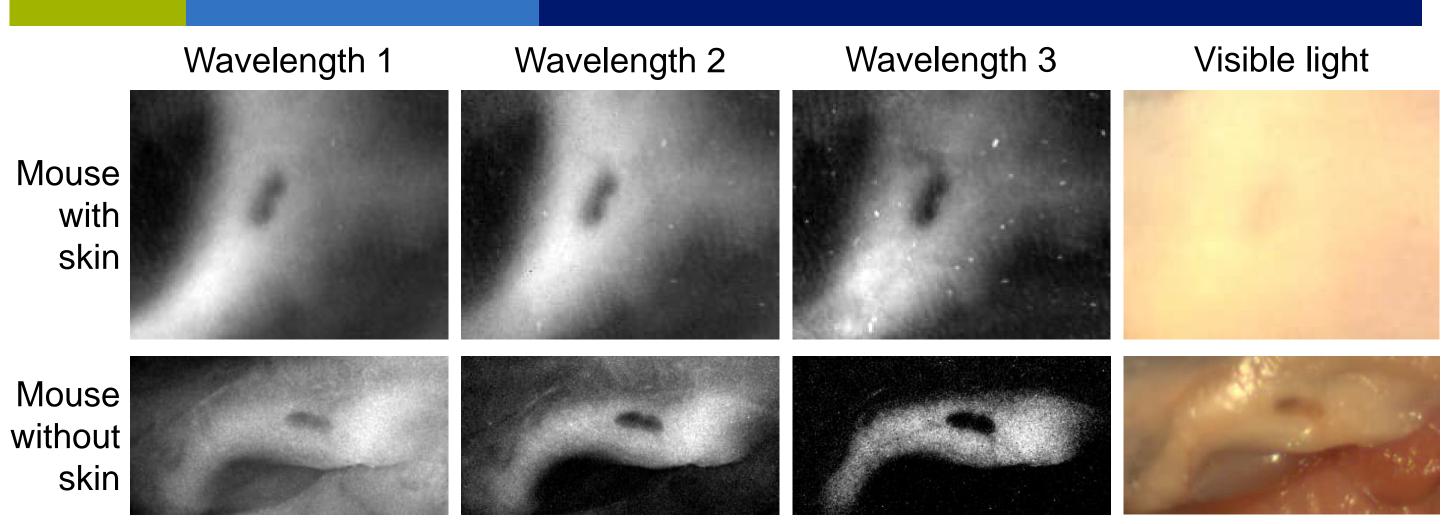
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#### Introduction

In certain regions of the shortwave infrared (SWIR; 1000 to 2000 nm) light is highly absorbed by water



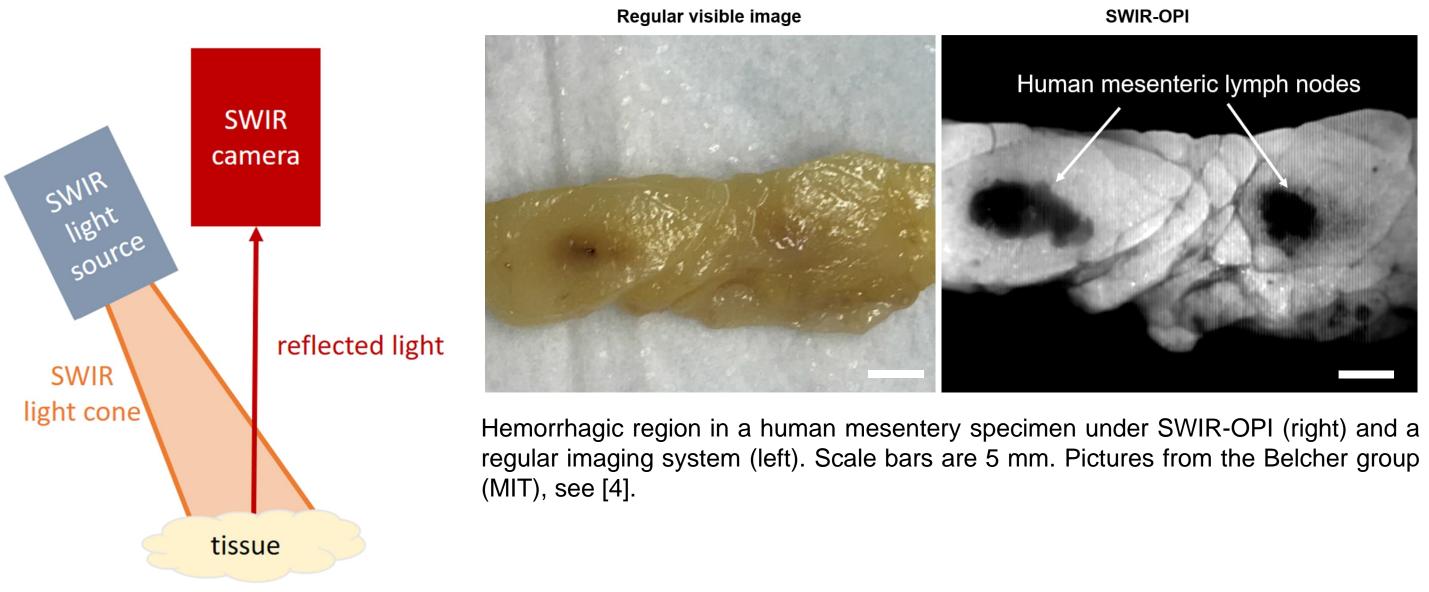
#### **Contrast of tissue is dependent on the SWIR wavelength**



The colored bands in the spectra show the wavelength range for the illumination of the images. The green (left) wavelength range is located in the visible where water appears translucent. The yellow (right) wavelength range is located in the SWIR at a point where most of the light is absorbed by the water making it appear dark. Source: [1].

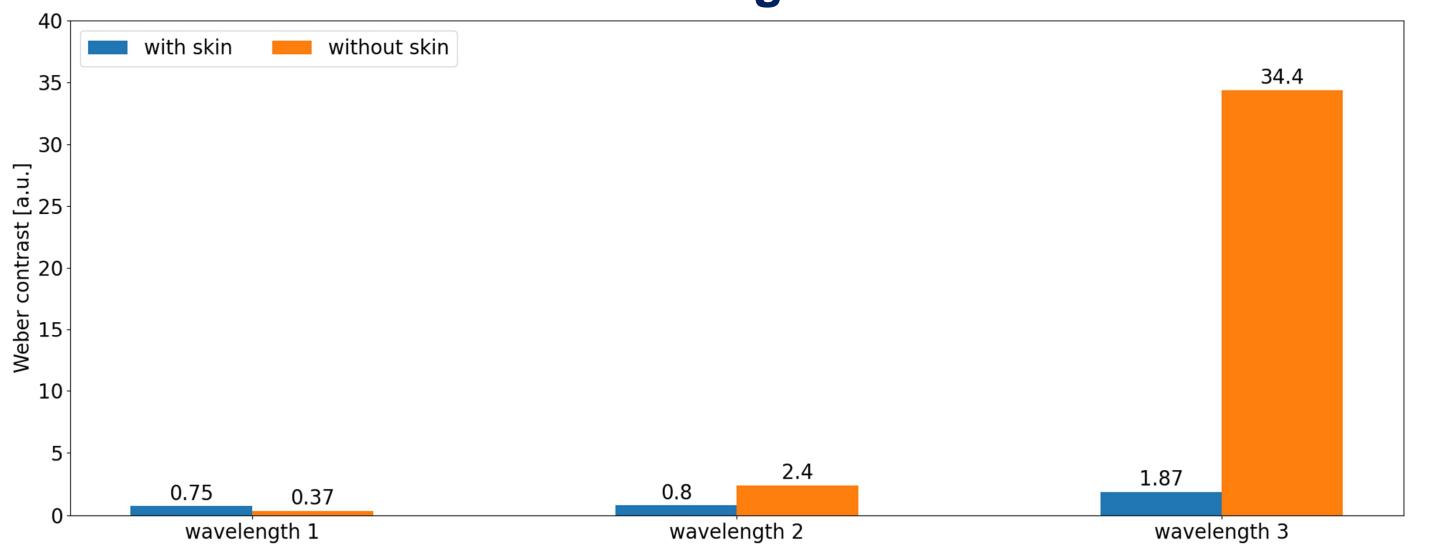
# Lymph node detection is currently challenging and can be improved with SWIR reflectance imaging

Lymph nodes are important for staging cancer [2,3], but they show low contrast in the visible [4,5].



The panel shows the inguinal lymph node of a mouse when illuminated with different wavelengths in the SWIR and with visible light. In the top row, the skin of the mouse was intact. In the bottom row, the skin of the mouse was removed. The position of the sample changed but the same lymph node was imaged in both situations.

## Skin reduces the contrast by a magnitude at certain wavelengths



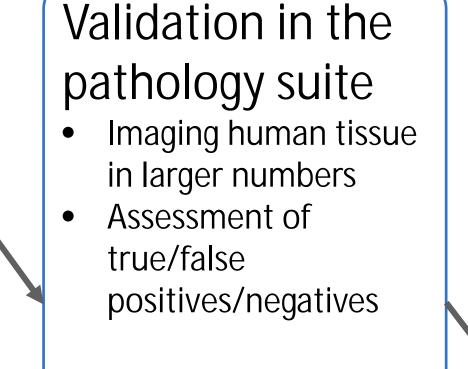
The Weber contrast between mouse lymph node and surrounding tissue is plotted. The blue bars show the achieved contrast with skin while the orange bars depict the contrast without the skin.

Illumination and detection of the system. No contrast agents are required.

### Aims and approach

### System prototype

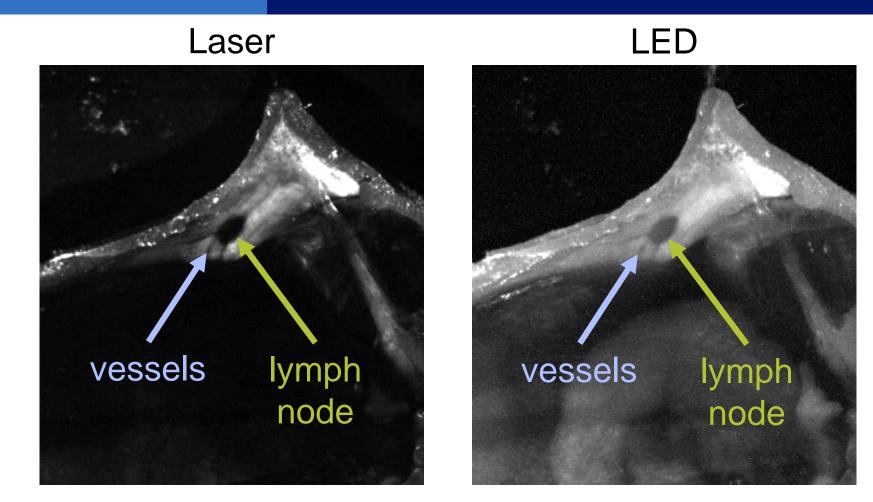
- Selection of wavelengths for optimal contrast
- Light source definition
- Software design for integration of hardware and userfriendly experience
- Validation in the lab with animal tissue
- Preparation for the



## Use in the operation room

- Back-table solution for fresh tissue
- Open surgeries (handheld device)

#### Lasers can yield a higher contrast compared to LEDs

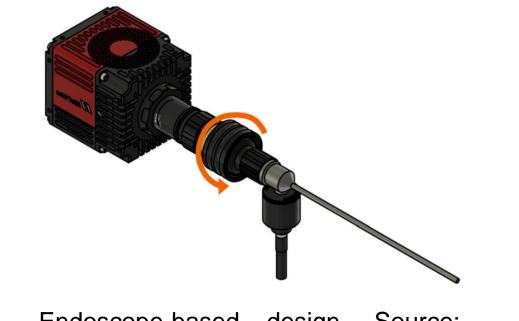


Mouse inguinal lymph node (green arrow) in surrounding white adipose tissue (skin removed) illuminated with two different light sources. Some vessels running to/from the lymph node can be seen (blue arrow). Laser and LED are at approximately the same wavelength.

#### **Determination of system performance in clinical samples**

Within a preclinical study, different types of tissue will be imaged in pathology and the system will be characterized based on its performance. The following step is to move the system into the operating room, first as a back-table solution and eventually as an endoscope.

### **Future perspectives**



Use intraoperatively with

clinic, e.g., hardware packaging  Minimally invasive surgeries (endoscopic device)

#### a handheld device

- an endoscope
- Identification of other target structures

Endoscope-based design. Source: [1].

#### References

[1] Klein TW, Yang S, Tusty MA, Nayak JV, Chang MT, Bruns OT, Bischof TS, Valdez TA. Development of a shortwave infrared sinuscope for the detection of cerebrospinal fluid leaks. J Biomed Opt. 2023 Sep;28(9):094803. doi: 10.1117/1.JBO.28.9.094803. Epub 2023 May 12. PMID: 37188003; PMCID: PMC10181794.
[2] Leong, S. P., M. Zuber, R. L. Ferris, Y. Kitagawa, R. Cabanas, C. Levenback, M. Faries and S. Saha (2011). "Impact of

nodal status and tumor burden in sentinel lymph nodes on the clinical outcomes of cancer patients." J Surg Oncol 103(6): 518-530.

[3] Pereira ER, Jones D, Jung K, Padera TP. The lymph node microenvironment and its role in the progression of metastatic cancer. Semin Cell Dev Biol. 2015;38:98-105.

[4] Li Z, Huang S, He Y, et al. A new label-free optical imaging method for the lymphatic system enhanced by deep learning.
Preprint. bioRxiv. 2023;2023.01.13.523938. Published 2023 Jan 15. doi:10.1101/2023.01.13.523938
[5] Marino MA, Avendano D, Zapata P, Riedl CC, Pinker K. Lymph Node Imaging in Patients with Primary Breast Cancer:

Concurrent Diagnostic Tools. Oncologist. 2020;25(2):e231-e42.

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