Oxygen Imaging For Non-Invasive Metastasis Detection

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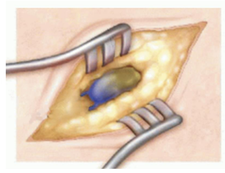
Background

- 66% of solid tumor deaths are due to metastasis.[1]
- Identifying degree of metastasis is vital to ensure proper treatment

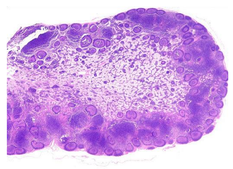
Gold Standard for Metastasis Detection: Sentinel Lymph Node Biopsy (SLNB)

Lymph Node Identification

Lymph Node Excision



Histological Analysis for Cancer Cells



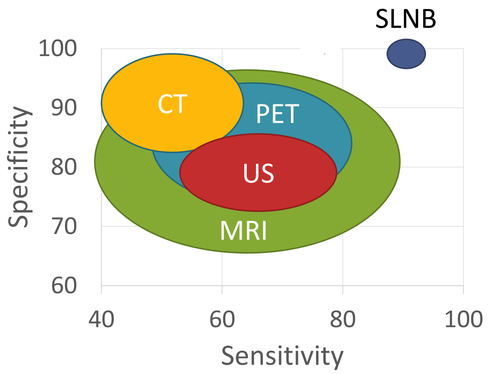
Disadvantages:

Post-procedural complications including lymphedema and shoulder pain.

Misses micro-metastatic deposits causing surgeons to continue removing lymph nodes even after a negative biopsy

There is a need for a non-invasive method to sensitively and specifically detect metastatic deposits to prevent over-treatment and reduce patient morbidity.

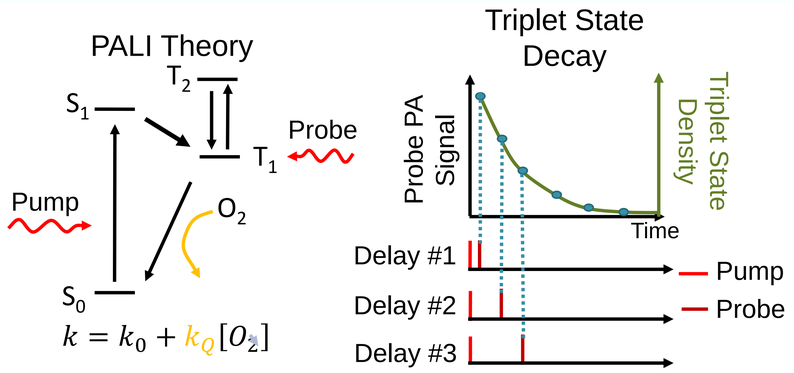
Current Technology



Current imaging methods are not comparable to SLNB's sensitivity and specificity.[2]

Due to the hyper-metabolism of cancer cells, we hypothesize that oxygen imaging can improve the sensitivity and specificity to levels comparable with SLNB.

Oxygen Imaging using Photoacoustic (PA) Lifetime Imaging (PALI)



PALI "pumps" molecules to the T_1 state and "probes" the number of molecules in this state by measuring the photoacoustic (PA) signal generated when T_1 molecules absorb the probe light. By measuring the decay over time, the decay rate of molecules from T_1 to S_0 can be calculated and used to calculate oxygen concentration once k_0 and k_Q are calculated using a calibration.

Experiment Design

Goal: Demonstrate PALI's feasibility as a useful metastasis detection technique by evaluating its imaging depth

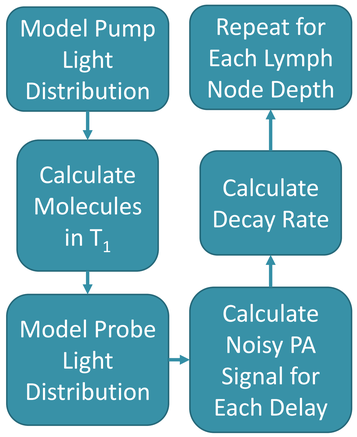
Simulation

The simulated phantom consists of a tissue-embedded, spherical lymph node filled with 200 µM methylene blue at either 100% or 0% oxygenation. Lymph node depth was varied between 4 and 25 mm. 5 PALI measurements were collected at each depth.

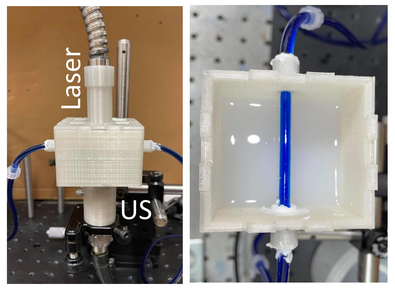
Benchtop Testing

Methylene blue filled tubing was used to represent a lymph node and was fixed at the single element transducer's and laser's focal point. Oxygenation in the tubing was set to either 100% or 0%. Phantom fluid mimicking the optical properties of tissue was prepared and depth of the "lymph node" was varied by varying the height of phantom fluid above the tubing. PALI measurements collected when the box was filled with water were used as the reference decay rate for each oxygenation level. 7 PALI measurements were collected at each depth.

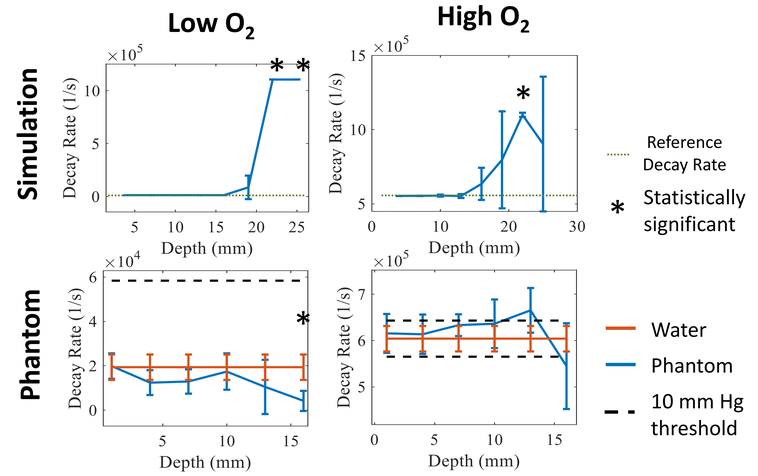
Workflow



Phantom



Results



- Average PALI measurements with one standard deviation error bars are shown for simulation and bench top experiments.
- Maximum imaging depth was determined as the depth where difference between reference and measured values were statistically significant.
- Maximum imaging depth according to simulation was 19 and 22 mm for low and high oxygen solutions, respectively.
- For bench top testing, the imaging depth was 16 mm and beyond 16 mm for low and high oxygen solutions, respectively.
- According to data collected by Becker et al.[3], 10 mm Hg provides 95% confidence in differentiating metastatic from normal lymph nodes.
- The depth where PALI has a mean error of less than 10 mm Hg is beyond 16 mm and 10 mm for low and high oxygenations, respectively.

Conclusions and Future Work

- PALI can measure low oxygen concentrations up to a depth of 13 mm but up to 16 mm for high oxygen concentrations. As the maximum imaging depth for simulation was 19 and 22 mm for low and high oxygenations, more work must be done to identify how to further maximize imaging depth.
- The distribution of PALI measurements was less than 10 mm Hg for the low oxygenation level for all depths measured. As 10 mm Hg provides a 95% confidence in differentiating metastatic and normal lymph nodes, PALI may be a promising modality for metastasis detection.
- As even head and neck cancers, which are known for having shallow lymph nodes, have an average depth of 2.5 cm, research must be done on methods to directly deliver light to the lymph node, such as using optical fibers.

Acknowledgements and References:

1. H. Dillekås, M. S. Rogers, and O. Straume, "Are 90% of deaths from cancer caused by metastases?," *Cancer Med*, vol. 8, no. 12, pp. 5574–5576, Aug. 2019, doi: 10.1002/cam4.2474.
2. L.-J. Liao, W.-C. Lo, W.-L. Hsu, C.-T. Wang, and M.-S. Lai, "Detection of cervical lymph node metastasis in head and neck cancer patients with clinically N0 neck—a meta-analysis comparing different imaging modalities," *BMC Cancer*, vol. 12, p. 236, Jun. 2012, doi: 10.1186/1471-2407-12-236.
3. [3]A. Becker, G. H¨ansgenh¨ansgen, M. Bloching, C. Weigel, C. L. Lautenschl¨ager, and J. Dunst, "PII S0360-3016(98)00182-5 • Clinical Investigation OXYGENATION OF SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK: COMPARISON OF PRIMARY TUMORS, NECK NODE METASTASES, AND NORMAL TISSUE," 1998.