Long-Wavelength Near Infrared Light Source Exploration For Hypoxia Assessment Using Sample-Free pH Sensing

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Abstract: Tissue acidity measured in pH is the clinical gold standard to assess hypoxia. Currently available photonics sources are explored to develop sample-free, non-invasive devices for continuous tissue pH monitoring using long-wavelength near infrared (LWNIR) spectroscopy.

1. Introduction

Hypoxia is a physiological stress response triggered by a reduction in oxygen available to human tissue. For critical patients such as neonates or those undergoing dialysis, a delay in reversing hypoxia can result in long-term tissue damage or even death [1]. In current clinical practice, blood samples are extracted invasively, and pH levels are measured using a bench-top instrument. However, this method is not suitable for continuous monitoring.

To develop a device for continuous, sample-free pH monitoring, we explore spectroscopic methods in the long-wavelength near infrared region of 1350-2500 nm (LWNIR) [2,3,4]. The moderate water absorption allows light at this wavelength range to penetrate to about 1 mm depth into water-rich human tissue [5]. At this depth physiologically relevant parameters can be accessed from the capillary bed under the skin [6]. Wearable pH sensors now use biochemical reactions with small amounts of body fluids like sweat or interstitial fluid, collected through microneedles or nanosensors [7]. However, these devices breach the skin barrier to access samples and cannot be used for long periods. Hence, the need for the development of sample-free, continuous spectroscopic pH sensors using spectroscopic techniques in LWNIR region.

In the LWNIR region, the pH sensor would rely on the spectral shift with change in pH in the two water absorption peaks around 1480 and 1900 nm with 30 and 100 cm^{-1} absorption coefficients, respectively. pH change of 7 units has shown to shift 3500 nm water absorption peak by 300 nm in gases [8]. The optical source selection is an important choice in developing the pH sensor depending on clinical need. The choice of source is dictated by the limited penetration depth at these water absorption bands [9]. To access tissue depth larger than that allowed by the penetration depth a large source-detector separation with higher source power can be used while balancing the local heating of the tissue with either pulsed source or other mechanism.

In this work, we are exploring the available photonics light sources in the LWNIR region as a potential candidate for continuous clinical pH monitoring device. We look at six different sources that span the conventional tungsten halogen lamps, light emitting diodes, multi-spectral lasers, novel tunable lasers and Thulium-doped fiber-based amplifiers (TDFA) used as spontaneous emission broadband sources [9]. We look at their effectiveness in either bands as potential pH sensor optical source.

2. Materials and methods

Six optical sources were used the conventional tungsten halogen lamp (ILT L8008), light emitting diodes in 1480 nm (Thorlabs M1450F1), TDFA was used with either commonly used 1900 nm band or a dual - 1480 and 1900 nm band – profile (custom built [10]), multi-spectral combination of five slotted waveguide lasers in 1900 nm band (Eblana photonics) or a commercial tunable laser in 1480 nm band. A fiber based optical setup was used to measure absorption through the sample in a 0.5 mm quartz thick cuvette with a collimated beam in transmission, the collimated beam width was 0.38 mm with single mode fibers for lasers and TDFA based sources and 2 mm beam with 550 µm fiber for LED source. The lamp had a lensed end and was used to illuminate the sample directly, the light was collected using an 8 mm collimator into a 550 µm fiber and measured using the optical spectrum analyzer (OSA). Samples were prepared with deionized water and hydrochloric acid and sodium hydroxide to have pH ranges of 4-10 units with increment of 1 pH unit. Detection was done using an OSA (Yokogawa AQ6375 B) with 0.1 nm resolution and average 100 for each spectrum collected for each pH sample. Water absorption measured by normalizing to source then smoothed for plotting. All pH data was normalized to the base and smoothed. For analysis only the wavelengths with spectral power > -70 dBm and falling within the water absorption bands were considered.

The data was fitted to a linear regression line at each wavelength. The goodness of the fit, R^2, was considered as accuracy parameters for the measurements. The estimated slope at each of the wavelengths was considered to be sensitivity to pH measurement.

3. Results and discussions

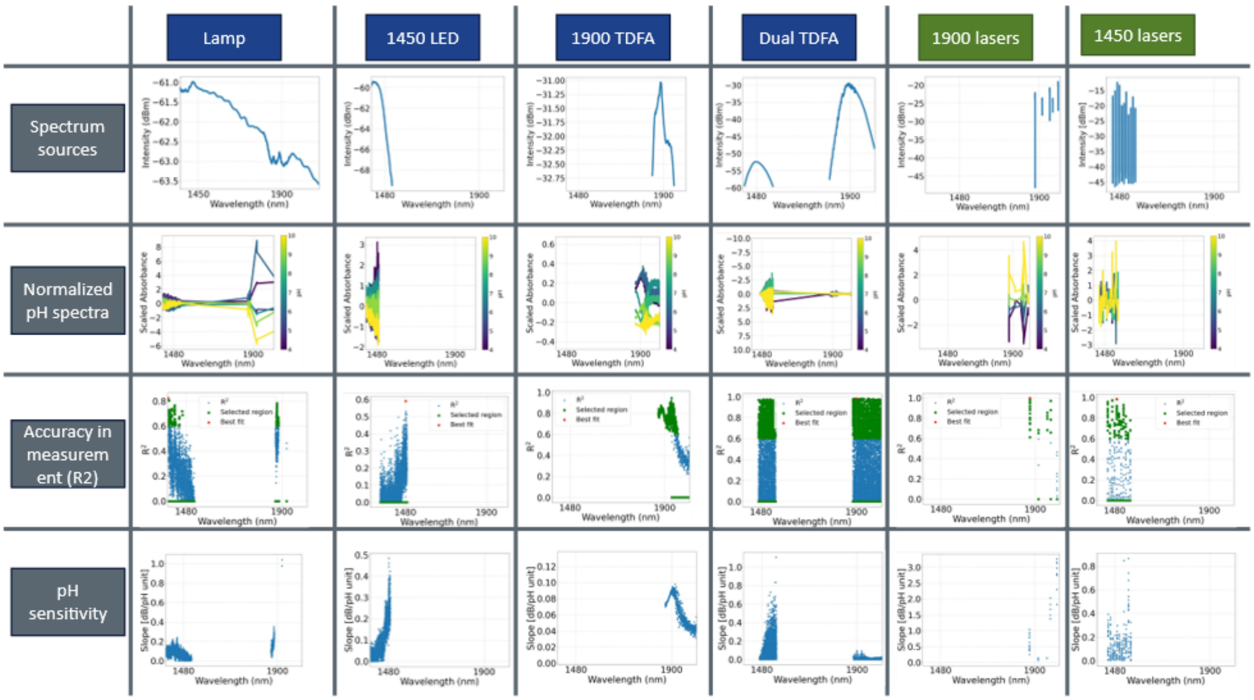

Figure 1: Comparison of different sources in a potential pH sensing device. Source spectra, their pH response, accuracy in pH sensing and sensitivity are shown in the panel.

Different sources vary in terms of their efficacy in pH sensing at different wavelength regions depending on the nature of the source emission and spectral power as shown in ***Figure 1***. The choice of broadband or narrowband lasers, continuous or pulsed, higher power or multiple wavelengths can be made based on the clinical application's limitations. Wearables have a limited size and electrical power consumption while requiring a high integration into photonics chips with a compromise in clinical accuracy. Bedside monitors can have large footprints and power consumption; however, the accuracy of the measurement has stringent limits to be clinically relevant.

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