In Vitro pO_2 Measurement of Islet Encapsulation Devices in Oxygen Measurement Core

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Statement of Purpose: The lack of oxygen supply to the highly metabolic pancreatic islet cells is one of the major factors contributing to the failure of islet transplantation devices targeting the cure of type I diabetes (T1D). The loss of islets due to hypoxia is common in almost all modes of islet transplantation- micro-encapsulation devices, macro-encapsulation devices, and tissue-grafts transplantation. Several approaches to improve oxygenation in these transplantation devices are thus being tested (1-4). However, because of the lack of available technologies to provide oxygen partial pressure (pO_2) assessment in and around devices, the progress is severely hindered.

O2M Technologies' platform non-invasive Oxygen Imaging technology has the potential to guide the development of islet cell transplantation therapies by providing real-time high accuracy pre- and post-implantation pO_2 maps in and around devices *in vitro* and *in vivo* (5-6). O2M's preclinical small animal oxygen imager, JIVA-25 (Figure 1A), provides average pO_2 values in sample volumes (up to 40 mm) as well as three-dimensional pO_2 maps with high spatial (0.5 mm, isotropic), temporal (1-10 min), and pO_2 (1-3 torr) resolution. For reporting oxygen concentration, JIVA-25 uses oxygen-dependent relaxation rates of trityl radicals OX063 or its deuterated version OX071 (Figure 1B). The pO_2 is linearly related to R_1 (Figure 1C). JIVA-25 uses spin-echo based T_1 inversion recovery method for mapping absolute pO_2. For the measurements, samples can be loaded vertically or horizontally (Figure 1D-1F).

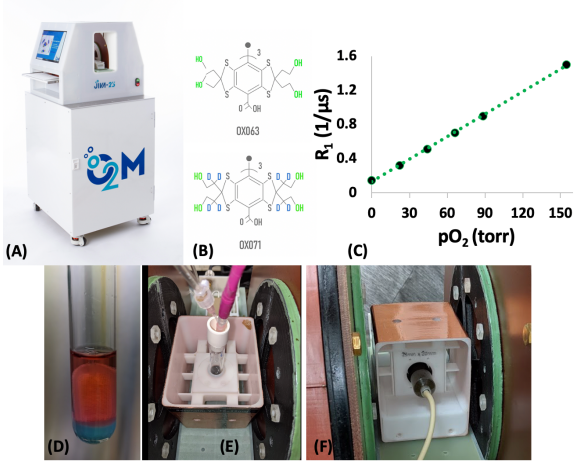


Figure 1: (A) JIVA-25 Instrument. (B) hydroxyethyl tetrathiatriarymethyl radical OX063 and OX071, (C) Example calibration curve at 25 mT, the oxygen in the sample (PBS at 37 °C) was set at 0, 3, 6, 9, 12, and 21% and R_1 were measured when the equilibrium was reached. (D) A 20 µL TheraCyte devise in a 16 mm tube, (E) Example *in vitro* measurement set up for vertical access resonator, (F) example *in vitro* measurement for horizontal access resonators inside JIVA-25.

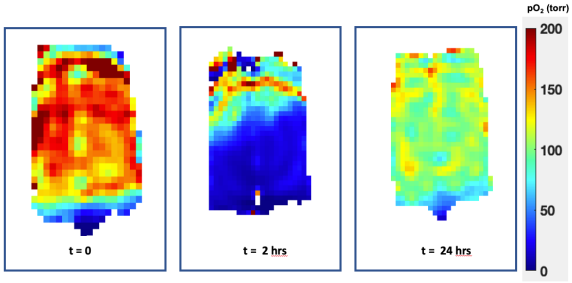
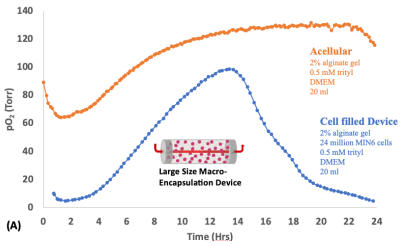


Figure 2: pO_2 maps of 10 million beta TC6 cells loaded 20 µL TheraCyte device in a 16 mm test tube at different time points during a 24-hour experiment. The incubator gas mixture (95% air and 5% CO_2 was circulated on top of the sample throughout the experiment. The temp was kept at 37 (± 1) °C.



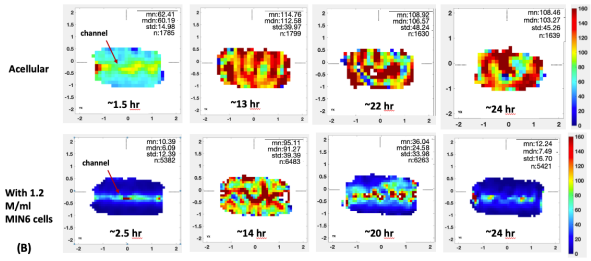


Figure 3 (A): Average pO_2 and (B) pO_2 maps and statistics of a large size macro-encapsulation device with a perfusion channel in the middle and filled with either only 2% alginate (Acellular) or with 24 million MIN6 cells embedded in 2% alginate as a function of time for a 24-hour experiment. The trityl concentration was 0.5 mM in the sample and 0.25 mM in the channel.

This work is the outcome of JDRF-supported "*Oxygen Measurement Core*" facility established at O2M Technologies in 2019. We performed *in vitro* pO_2 measurements of acellular and cell loaded islet cell transplantation devices at the core. These devices varied in shape, size, biomaterials, and oxygen profile. We will present key data from these measurements. Some example data are presented in Figure 2 and 3.

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