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A paper-based oxygen generating platform with spatially defined catalytic regions☆

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ABSTRACT

A flexible, parchment paper/PDMS based platform for local wound oxygenation is fabricated and characterized. The platform consists of a PDMS microfluidic network bonded to a parchment paper substrate. Generation of oxygen occurs by flowing H_2O_2 through the channels and chemically decomposing it via a catalyst embedded in laser-defined regions of the parchment paper. PDMS is bonded to parchment paper using partially cured PDMS followed by a brief air plasma treatment, resulting in a strong bond. For pressures below 110 Torr the parchment paper is observed to be impermeable to water and hydrogen peroxide. The oxygen permeability of parchment paper is measured to be 1.42 μL/(Torr mm^2 min). Using a peroxide flow rate of 250 μL/min, oxygen generation in the catalyst spots raises the oxygen level on the opposite side of the parchment paper from atmospheric levels (21%) to 25.6%, with a long-term (30 h) generation rate of 0.1 μL O_2/min/mm^2. This rate is comparable to clinically proven levels for adequate healing. Device and material *in vitro* biocompatibility is confirmed with NIH 3T3 fibroblast cells via alamar blue assays.

1. Introduction

Suboptimal oxygenation of the wound bed is a major healing inhibitor in chronic wounds [1–4]. A chronic wound is one which does not heal in an orderly or timely manner (i.e. three months) due to an inadequate healing microenvironment. Unlike acute injuries that receive sufficient oxygen via a functional blood vessel network, chronic wounds often suffer from a lack of a proper vascular network incapable of providing sufficient oxygen for tissue growth. While the lack of oxygen may trigger vascular regeneration [5], the severity and depth of wounds can prevent adequate regeneration, causing wound ischemia [6].

Modern medical treatment of hypoxic chronic wounds typically employs hyperbaric oxygen therapy [7–11], which requires bulky equipment and often exposes large areas of the body to unnecessarily elevated oxygen concentrations that can damage healthy tissue. Hence, such methods require very careful and periodic oxygen administration to avoid hyper-oxygenation of tissue surrounding the wound. In a more practical approach, recent research has endorsed transdermal oxygen therapy (TOT) as a viable and effective method for oxygenating a hypoxic wound [12–16]. A variety of wound dressings can be used to create an enclosure around a wound which can entrap oxygen generated from an external source (e.g. oxygen tank), restricting oxygen exposure to only the wound region while reducing the amount of healthy tissue that is exposed to hyper-oxygenation.

One of the latest embodiments of TOT technologies is a handheld system (EPIFLO, Ogenix, Ft. Lauderdale, FL) that concentrates oxygen from the environment and pumps it through a piece of tubing that it feeds into the wound dressing [17,18]. The system is capable of producing oxygen continuously at a rate of 3 mL/h for up to 15 days (at atmospheric pressure), which has been shown to be sufficient for an expedited healing process. This product is definitely an improvement over previous systems, as it allows for patient mobil-

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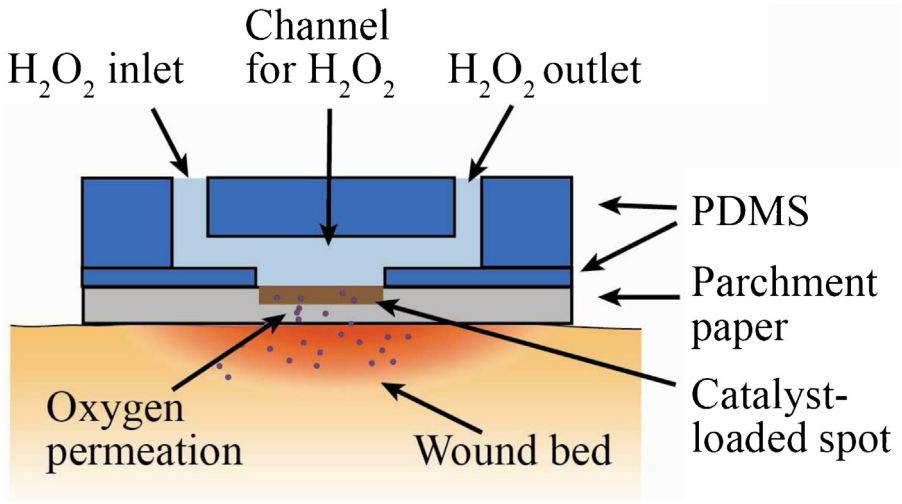

Fig. 1. Cross-sectional schematic of the oxygen-releasing platform at a single catalyst-loaded spot.

ity and limits oxygen exposure to the wound bed. However, the system is still bulky, expensive, and does not provide a means to selectively deliver oxygen to the hypoxic regions within the wound. The treatment of such wounds would greatly benefit from the use of a localized method for oxygen delivery with improved spatial and temporal precision.

In this work, we present a low-cost alternative for continuous O_2 delivery consisting of an inexpensive, paper-based, biocompatible, flexible platform for locally generating and delivering oxygen to selected hypoxic regions. The platform takes advantage of recent developments in the fabrication of flexible microsystems, including the incorporation of paper as a substrate [19–22] and the use of inexpensive laser machining process [23–25]. The use of paper simultaneously provides structural flexibility as well as selective filtering functionality, i.e., it allows for oxygen to pass through while preventing aqueous solutions to reach the tissue. The laser machining enables the precise definition of oxygen generating regions that match the hypoxic wound profile. Together these two technologies enable the development of a low-cost patch/wound-dressing with customized, wound-specific oxygen generating regions.

2. Design and fabrication

The platform consists of a flexible microfluidic network bonded to a parchment paper substrate, as illustrated in Fig. 1. A key feature is the use of a laser-patterned parchment paper as the primary structural/functional substrate. Parchment paper is a hydrophobic material by design; however, it can be ablated using a CO_2 laser to selectively create hydrophilic regions [26]. This technique is applied to define an array of hydrophilic spots. The natural mesh structure of the paper allows the spots to be embedded with chemicals suspended in an aqueous solution. For the present application, the spots are loaded with a chemical catalyst, MnO_2. When H_2O_2 is injected through the microchannel network, it reaches the spot array, and is decomposed by the catalyst, resulting in oxygen generation [27–29]:

$$2H_2O_2 \rightarrow 2H_2O + O_2$$

The generated O_2 diffuses through the paper and oxygenates the wound bed directly below the catalyst spot for as long as H_2O_2 flows in the microchannel. The use of a biocompatible structural material allows the platform to be integrated into commercial wound dressings that are in contact with the wound bed.

The fabrication process of the oxygen generating platform is shown in Fig. 2. It consists of making laser-defined patterns on parchment paper, creating microchannels on a PDMS substrate, and bonding the layers together. The entire procedure is straightforward and requires no complex cleanroom processing. First, the catalyst spot pattern is laser-ablated onto a parchment paper substrate (30 μm thick). The paper is then dipped (1 s) into a 0.1N $KMnO_4$ aqueous solution followed by a dip (1 s) in a 0.1N KI aqueous solution. This results in the deposition of $KMnO_4$ and KI only onto the ablated pattern. The two reactants yield MnO_2 via the following reaction

$$KI(aq) + 2KMnO_4(aq) + H_2O(l) \rightarrow KIO_3(aq) + 2KOH(aq) + 2MnO_2(s).$$

Next, PDMS (polydimethyl siloxane, Dow Corning Sylgard 184) is spin-coated on a silanized silicon wafer and cured on a hotplate (100 °C, 20 min) for a final thickness of 200 μm. The PDMS is transferred onto an acrylic substrate and laser-machined to create through-hole regions with the same pattern as the catalyst. The patterned PDMS is exposed to air plasma (75 W, 1 min) in a plasma etcher (PLASMOD, Tegal Corporation, Richmond, CA), stamped onto uncured PDMS, and partially cured on a hotplate (65 °C, 5 min). Next, the PDMS is bonded to the patterned parchment paper by plasma-treating both materials and bringing them

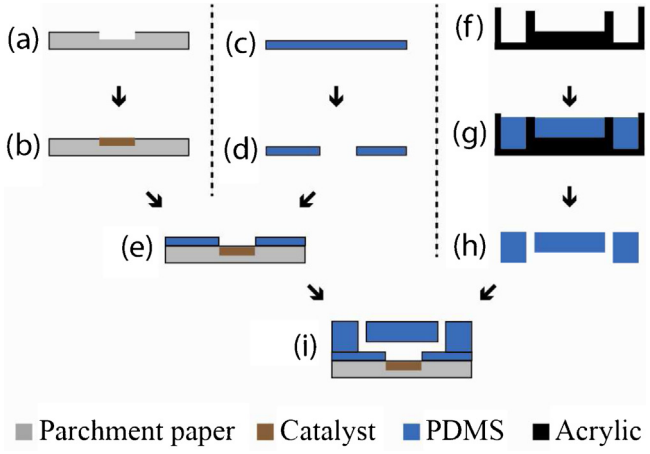

Fig. 2. Fabrication procedure (a) laser-pattern parchment paper, (b) deposit catalyst, (c and d) laser-machine 200 μm thick PDMS, (e) bond paper to PDMS by stamping partially-cured PDMS, (f–h) mold PDMS microchannels, (i) bond the PDMS microchannels to the paper substrate after plasma treatment.