

To the Editor:

Kalns et al. have addressed a fundamentally important issue in wound care: the significance of oxygen therapeutics.¹ The stated intent of this article is unclear and complicates the interpretation of benefits that can be achieved through oxygen therapy. The results of this study are unclear for the following reasons.

First, the total number of pigs used per treatment group and time point is not clearly stated; a group of two ($n < 3$) pigs shown in Table 1 is a cause for concern.

Second, the authors “hypothesized that hyperbaric oxygen (HBO) will be of benefit as a treatment adjunct to improve the success rate of compromised partial-thickness skin grafts,” but the study does not adequately test this hypothesis. None of the skin grafts in this study are “compromised.” Furthermore, the reported findings do not support that stated conclusion that “HBO offsets the oxygen deficit present in partial-thickness grafts,” because they never showed that HBO elevated pO_2 within the graft.

Third, the use of “sham anesthesia” is a less than an ideal control, especially given the aggressive HBO treatments the pig(s) received.

Fourth, based upon our interpretation of the figures and the text, the authors show statistical significance of effects between HBO- or non-HBO treated grafts at 2-, 4-, or 7-day time-points vs. nongrafted partial-thickness wounds at the time of injury/day 0. A more appropriate comparison would be between HBO-treated grafts and non-HBO-treated grafts. In that case all statistical significance seems to be lost.

We comment because this report presents a conditional departure from repeated findings establishing that oxygen therapy stimulates wound angiogenesis and that wound angiogenesis is a key component of the healing process. In view of the fact that in the entire paper there does not seem to be a single statistically significant difference between data from HBO vs. non-HBO groups, the title claim does not seem to be justified.

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RESPONSE

We agree with Gordillo et al. that the literature supports the idea that HBO increases angiogenesis during ischemic wound healing. Indeed, at the outset of this study we fully expected that HBO would increase angiogenesis and were surprised when the data showed the opposite. We believe one possible explanation for our findings is that our wounds were not hypoxic, and during treatment times they were hyperoxic, resulting in a suppression of angiogenesis. As Gordillo et al. point out, pO_2 measurements are lacking in our study, and such measurements are crucial to understanding the relationship between wound oxygenation and angiogenesis. We believe one cannot assume that all HBO regimens will invoke new vessel formation in all wounds. It appears that hypoxia, for short periods of time, is a stimulus for angiogenesis. However, prolonged hypoxia interferes profoundly with wound healing and angiogenesis. In our model the presence of hyperoxia in HBO-treated animals apparently suppressed the stimulus for angiogenesis. This emphasizes an important shortfall in our collective understanding of HBO, namely the lack of a pharmacodynamic model that describes the relationship between wound pO_2 and angiogenesis.

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REFERENCE

1. Kalns JE, Dick EJ, Scruggs JP, Kieswetter K, Wright JK. Hyperbaric oxygen treatment prevents up-regulation of angiogenesis following partial-thickness skin grafts in the pig. *Wound Rep Reg* 2003;11: 139–44.