Stability studies of nonfouling surfaces made by plasma discharge coating of FEP with tetraglyme

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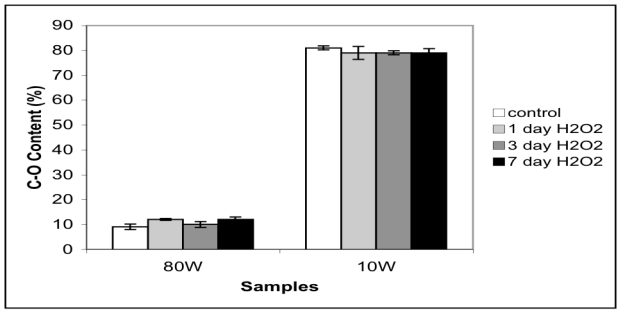
Introduction: The ability of surfaces to withstand degradation is a critical but so far poorly understood aspect of their ability to serve as useful biomaterials (1), especially for more recently developed nonfouling surfaces. Thus while PEG containing polyurethanes are well known to be subject to oxidative degradation, the stability of more recently developed nonfouling materials, including the tetraglyme based materials we have studied, is not known. Electron spectroscopy of chemical analysis (ESCA) of PEO-like tetraglyme surfaces after 30 day subcutaneous implantation in rats showed that no delamination or gross changes in surface chemistry took place, despite having large numbers of adherent monocytes (2). Here, *in vitro* studies designed to mimic the oxidative environment at the cell-material interface were conducted, in order to evaluate whether tetraglyme degradation might result from exposure to monocyte-derived macrophage release of superoxides and oxygen radicals during the foreign body response (FBR) [1]. We also repeated the earlier *in vivo* studies.

Materials and Methods: Tetraglyme (Aldrich) was RFGD-plasma deposited on 6-mm diameter FEP (gift from DuPont) disks using varying deposition powers. Samples from the *in vivo* study (1 day subcutaneous implants in rats) were fixed in Karnovsky's prior to SEM analysis. An oxidative degradation study was done by exposure to 30% hydrogen peroxide (H_2O_2) solution at 37°C for 24 hours to 7 days. ESCA was used to detect changes in surface chemistry. Tests on oxidized and control surfaces to detect changes in reduced resistance to adsorption or monocyte adhesion were also done. ^{125}I (Amersham Pharmaceuticals) labeled fibrinogen (Fg) was used for measurement of Fg adsorption from a 10% plasma solution in buffer. Primary monocytes were isolated from human blood using magnetic activated cell sorting (MACS, Miltenyi Biotech). The number of adherent monocytes was determined using a lactase dehydrogenase (LDH) assay (Boehringer Mannheim).

Results and Discussion: SEM results of explanted tetraglyme samples showed a large number of adherent cells on tetraglyme surfaces that had displayed cell and protein resistance *in vitro*. However, ESCA analysis of explanted samples indicated no significant surface degradation as ether carbon content (characteristic of tetraglyme coatings) was still present on explants, similar to previous results (2). ESCA showed no significant changes in ether carbon content after soaking in 30% H_2O_2 solution for 1, 3, or 7 days (Fig 1). Functionally, no differences were detected in Fg adsorption and monocyte adhesion of untreated (ie unsoaked control tetraglyme samples) and hydrogen peroxide-treated tetraglyme films (not shown). No significant changes were detected in the surface chemistry of the surfaces treated with peroxide, and no significant changes in protein adsorption or monocyte adhesion were observed.

Fig 1. C-O content of tetraglyme films was unchanged after extended sample incubation with H_2O_2 solutions.



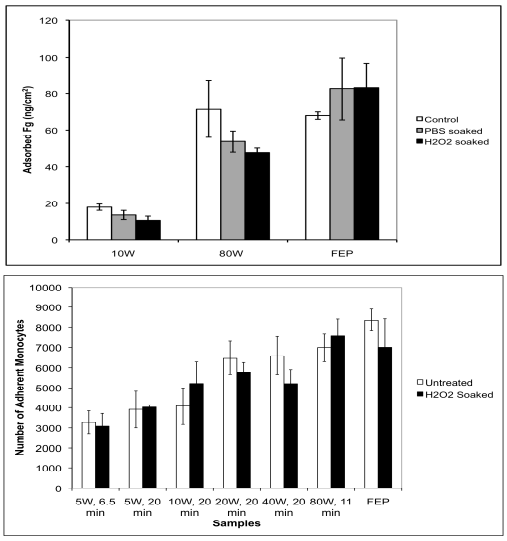


Fig 2. Protein adsorption (upper) and monocyte adhesion (lower) were unchanged after incubation in 30% H_2O_2 or PBS.

Conclusions: *In vivo* and *in vitro* studies suggest that tetraglyme films are largely resistant to ether carbon oxidation. The lack of changes in surface ethercarbon content of the films was confirmed in functional evaluation of the samples, where no significant changes were detected in the Fg adsorption and monocyte adhesion to hydrogen peroxide-treated films. These results suggest that the foreign body response to these samples, as observed in prior studies in our lab, are not a result of surface degradation or delatmination, but rather a result of an alternate mechanism.

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