Enhancing PEEK Implant Performance: Role of Hydroxyapatite Coatings and Mechanotransduction in Osseointegration and Cell Response

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Abstract

Background and objectives

Polyetheretherketone (PEEK) is emerging as a promising material for bone replacement applications, especially in cases of degenerative joint diseases and bone fractures. Its high biocompatibility and elastic modulus of approximately 4.5 GPa, which is closer to that of natural bone (ranging between 4 and 20 GPa), make it a favourable choice compared to other implant materials. However, PEEK's limited osseointegration often leads to implant failure over time. This study aims to enhance the PEEK-bone interface by applying a hydroxyapatite coating, which is expected to improve osseointegration and potentially reduce inflammation associated with implants.

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Materials and Methods

Stoichiometric hydroxyapatite feedstock (MEDICOAT) was applied to PEEK as supplied through a cold spray deposition technique. Four PEEK surface types were evaluated: grinded PEEK, sulfonated PEEK (SPEEK), hydroxyapatite-coated PEEK (HA-PEEK), and sulfonated, hydroxyapatite-coated PEEK (S/HA-PEEK). Unmodified PEEK samples were polished with SiC P600 abrasive paper. SPEEK samples were prepared by polishing PEEK samples with SiC P600 abrasive paper, followed by immersion in 95% (v:v) sulfuric acid (HSO) for 90 seconds. HA- PEEK samples were polished with SiC P600 and then coated with HA. Lastly, S/HA-PEEK samples were polished with SiC P600, treated with 95% sulfuric acid for 90 seconds, and then coated with HA.

To assess the cytocompatibility and bone tissue formation potential of these surfaces, murine embryonic chondrocytes (1) were cultured on direct contact with the four PEEK samples. Cells (0.5×106 cells/sample) were seeded onto the PEEK sample surfaces maintained in a biotriboreactor under dynamic culture conditions for 21 days, with a cyclic compressive load applied at a frequency of 0.5 Hz and an amplitude of 75 μm. Both static and dynamic culture conditions were assessed, measuring metabolic activity, cytotoxicity, mineralization, and rheological properties. Additionally, histological analyses were conducted to provide deeper insights into cellular responses and to predict tissue behaviour.

Results

Initial static culture results after 24 hours of contact demonstrated good biocompatibility across all materials, with cytotoxicity levels remaining very low ($< 5\%$). Although no significant differences in cell viability were observed between materials, sulfonation unexpectedly resulted in a higher cell rate, whereas HA-coated samples, which were expected to promote cell proliferation, did not exhibit a similar increase (2). While cell proliferation continued in static cultures, dynamic cultures exhibited a marked reduction in metabolic activity without affecting cell viability. This decline may suggest the initiation of a differentiation process induced by mechanotransduction, as has been documented in previous studies involving mesenchymal stem cells (3). Mechanical loading applied between days 3 and 10 was shown to stimulate extracellular matrix (ECM) production. Confocal imaging revealed substantial extracellular matrix (ECM) formation under dynamic conditions, despite a lower cell proliferation rate compared to static cultures. This suggests that mechanotransduction could play a key role in promoting a well-structured ECM, reinforcing tissue integrity and encouraging collagen synthesis.

Comparisons between materials in both static and dynamic cultures showed that HA coatings did not outperform uncoated materials in terms of metabolic activity or cytotoxicity. Interestingly, sulfonated materials exhibited the highest cell proliferation rate under both culture conditions, suggesting that sulfonation may be more effective than HA in enhancing cell adhesion and proliferation under the current experimental conditions.

Rheological assessments revealed a 10-fold increase in ECM storage modulus from day 3 to day 21. Early measurements showed variability in amplitude and phase shift across samples, indicating a predominantly viscous behaviour. In contrast, later measurements demonstrated converging amplitudes and minimal phase shifts, suggesting progressive matrix stiffening.

Despite these promising *in vitro* findings, commercially available HA coatings did not meet the expected performance, highlighting the need for more effective biomimetic coatings. The observed decrease in metabolic activity under dynamic conditions suggests that changes in cell signalling related to differentiation rather than cytotoxicity may be occurring, an area that warrants further investigation.

Conclusion and Perspectives

This study provides an initial framework for analysing cell behaviour at the bone-implant interface in response to mechanical stimuli. The findings suggest that mechanotransduction plays a role in supporting bone tissue formation, although cell proliferation is less pronounced under dynamic conditions. While neither sulfonated nor coated materials demonstrated significantly superior performance, there is potential to enhance the current coatings. Future research should include a more comprehensive comparison of coating effects using additional sample types. Another important avenue for investigation would be the tribological properties of the samples, as these are critical for understanding performance at the bone-implant interface. Insights into how these materials behave under mechanical loading and friction could provide valuable information on their long-term stability and integration. Notably, the release of PEEK particles due to suboptimal tribological behaviour may trigger an inflammatory response, potentially leading to implant rejection, an issue highlighted by Milinkovic et al. (2022) (4).

Key words: Polyetheretherketone (PEEK), Bone-Implant Interface, Hydroxyapatite Coating, Osseointegration, Mechanotransduction, Cytocompatibility, Rheological Properties.

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