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POROUS CERAMIC DENTAL IMPLANT FOR IMPROVED OSSEOINTEGRATION: AN EX-VIVO STUDY

Dentistry

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ABSTRACT

The predictability of osseointegration is of utmost importance for the long-term success of dental implants. Titanium is the current standard of care; however, owing to its bio-inert nature and the risk of inflammatory reactions, the search for bioactive alternatives is warranted. Porous ceramics have exhibited attractive surface chemistry, osteoconductive ability, and decreased propensity to bacterial adhesion. The purpose of this study was to assess cytocompatibility and ability to osseointegrate of porous ceramic dental implants in an ex-vivo model. Porous ceramic implant were used to culture with human placental mesenchymal stem cells (hPMSCs). The cells were evaluated for cell survival on days 1, 3, and 5 with an MTT assay. Viability, adhesion, and cytoskeletal organization were tested by live–dead staining and rhodamine-phalloidin/DAPI staining. For osseointegration evaluation the bone samples were harvested and prepared for histology. Newly formed bone was recognized by hematoxylin and eosin (H&E) staining and Type I collagen deposition inside the porous network was observed by Masson's Trichrome staining. Porous ceramics maintained high viability and proliferative ability for longer duration of hPMSC. Live–dead staining indicated a high density of viable cells throughout the porous structure, and cytoskeletal staining exhibited improved actin filament alignment and intercellular attachment. Histological observation showed that the new bone matrices were formed, the collagen deposition was sufficiently available, and there was complete bone–implant interface with minimal formation of fibrous tissue. Porous ceramic implants showed good cytocompatibility, osteoconductivity and ability for bone ingrowth, these indicate the potential of porous ceramic implants as a promising next-generation dental implants.

KEYWORDS

Ceramic Implant, Human Pulmonary Mesenchymal Stem Cells (HPMSC) Introduction, Osseointegration, MTT assay

INTRODUCTION

The bioinert nature of titanium implants presents its limitations on osseointegration, potentially concerning in clinical situations such as those with compromised bone metabolism. Dentoalveolar osseointegration is an essential cornerstone for long-term success of dental implants (Jin et al., 2025; Kapat et al., 2017; Seesala et al., 2024). Titanium is a biocompatible material and due to its capability of passivating oxide layer (Al_2O_3) formation, it has an excellent capacity of overcoming corrosion; however, in some conditions this passive oxide layer can cause fibrous encapsulation which may compromise bone-implant interactions (Albrektsson et al., 2023; Seesala et al., 2024; Trindade et al., 2016). In addition, continuous exposure to the biological media can lead to ion leaching and wear debris, resulting in inflammation reactions and peri-implant bone loss (Popa et al., 2015).

A similar important matter is the stress shielding effect due to huge modulus difference between metallic titanium (100–120 GPa) implant and host-living cortical bone (10–30 GPa) (Niinomi et al., 2016; Seesala et al., 2024). In this scenario, bioactive ceramics like alumina, zirconia and hydroxyapatite have emerged as potential candidates due to their chemical stability, high modulus of elasticity, intrinsic wear resistance, osteoinductivity and biocompatible properties. Unlike titanium, widely used ceramics are able to promote direct bone apposition at the implant surface (Hisbergues et al., 2009; Kapat et al., 2017) due to surface chemistry and the ability of these materials to grow a “bone-like” apatite layer under physiological conditions. In fact, because of their dielectric properties and low bacterial affinity, they have even proven to be less susceptible to peri-implantitis (Chiou et al., 2023). Unfortunately, the dense version of this material has high stiffness and is inherently brittle, disqualifying it for any load bearing duty.

Porous ceramic implants could be a strategy to face these challenges. The incorporation of porosity not only lowers the elastic moduli to those closest to the natural bone but also generates interconnected channels that offer paths for vascularization, diffusion of nutrients and ingrowth/infusion of bone; which are vital parameters for successful osseointegration (Eliaz, 2019; Liu et al., 2021; Seesala et al., 2024). Recent literature demonstrates pore sizes in the range from 100–500 µm are most conducive to bone ingrowth (remodelling), with larger interconnected porosity promoting angiogenesis and enhancing implant fixation (Somo et al., 2015). Moreover, the pore structure and surface topography of porous ceramics play a key role in cell adhesion, proliferation, and differentiation required for initiation and maintenance of bone-healing cascade.

Therefore, the purpose of this study was to design a porous ceramic dental implant that mimics trabecular bone in both structure and mechanical properties. This study utilizes a new fabrication technique to produce these implants with high porosity and manipulated pore interconnectivity, and probes the in-vitro performance of these implants (specifically their cytocompatibility) as well as their ability to more securely integrate into surrounding bone. Results: To understand the initial cellular response, human placental mesenchymal stem cells (hPMSCs) were used to determine in vitro cell viability, adhesion and morphology over the ceramic surfaces using those parameters like MTT assay, live-dead staining, cytoskeletal visualization.

Although porous structures of titanium based have been tried before but with limited success (Kapat et al., 2017), research on the application of porous ceramics as root-form dental implants is relatively scarce. When coupled with a suitably designed porous architecture, the inherent material characteristics of ceramics result in a double benefit by providing both mechanical compatibility and biological functionality. In this way, we may greatly reduce the limitations of traditional metal-base implants such as stress shielding, inflammatory reactions, and bio-performance to do a better job of reflecting on-the-job selection standards for biomaterials in dental implantology.

The current study posits that porous ceramics with bioactive properties and porosity-tuneable mechanical functionality can act as potential future materials for dental implants. The study will investigate the biocompatibility, osseointegration quality of bone through several experiments.

MATERIALS AND METHODS

Material

The porous ceramic structure was obtained from the work of Seesala V S et al. (2021). Briefly, the method of preparation was as follows: Porous alumina implants were fabricated using a dough-based extrusion–lamination technique. Alumina powder (SG4000, Almatis) was combined with vinyl polymer binder (4 wt%), stearic acid (2 wt%), and alcoholic solvent to obtain a dense ceramic dough. A second mixture of lower viscosity was prepared by incorporating NaCl particles (100–700 µm, Merck) as porogens. Dense layers were

extruded through a stainless steel die, while porous sheets were laminated onto dense substrates or shaped using CAD-generated replica molds. After drying, porogens were leached in deionized water at 45 °C for 2–7 days to yield interconnected porous structures. (Seesala et al., 2021)

Cell Culture And Viability Assay

The in vitro cytocompatibility of porous ceramic implants was determined with human placental mesenchymal stem cells (hPMSCs) after approval by the Institutional Ethical Committee. UV-sterilized ceramic and titanium control samples were seeded with 4.7×10^5 cells and cultured for the indicative culture time points (1, 3 and 5 days), actively proliferating at a constant temperature of 37°C in an incubation chamber with humidity of approximately 85% and CO_2 concentration regulated to maintain a level of ~5%. The cells were cultured in DMEM (Gibco, Invitrogen) supplemented with 10% FBS and 1% penicillin-streptomycin.

Measurement of Cell Viability by MTT Assay Then, 0.1 mL of MTT reagent (0.5 mg/mL) was added to each well at indicated time points and followed by incubation for an additional 4 h at 37°C. And formazan crystals were dissolved by 200 µL DMSO, followed by measuring the absorbance at 595 nm using a microplate reader (Byonoy, Germany). Cell viability (%) was calculated as follows:

$$\%\,\text{Cell Viability} = [(Abs_{sample} - Abs_{blank}) / (Abs_{control} - Abs_{blank})] \times 100\,\%$$

Positive controls (tissue culture-treated wells) and blank (DMSO).

Live-Dead Staining

Cell viability and proliferation were determined with live-dead staining over time. The cell samples used were washed gently with PBS at 1 day, 3 days and 5 days incubation with ceramic implant sample after which 40 µL of live-dead staining solution was added. The samples were then incubated for 20 mins at physiological conditions (37°C, 5% CO_2). Post staining, the samples were rinsed with PBS and then imaged under a Carl Zeiss Axio Observer Z1 fluorescence microscope at excitation wavelengths of 488nm (for live cells) and 546 nm (for dead cells). Images by fluorescence were used to monitor viability, distribution and colonisation of hPMSCs over ceramic surface.

Cytoskeletal And Nuclear Staining

To visualize cellular morphology and cytoskeletal organization, samples were fixed with 4% paraformaldehyde (PFA) for 20 minutes at room temperature on days 1, 3, and 5. Following fixation, cells were permeabilized with 0.1% Triton X-100 in PBS and washed three times. For cytoskeletal staining, Rhodamine-Phalloidin was applied to stain F-actin filaments, and DAPI was used to counterstain cell nuclei, according to the manufacturer's protocol (Invitrogen, USA). Fluorescence images were captured using a Carl Zeiss Axio Observer Z1 microscope. This enabled assessment of cell adhesion, spreading, and interaction with the ceramic substrate.

Histological Sectioning And Staining

Femoral bone samples containing porous ceramic implants were collected at 4 and 12 weeks post-implantation from rabbit model, fixed in 4% buffered formaldehyde and decalcified for four weeks in 10% EDTA solution. Tissues were fixed in paraformaldehyde, dehydrated through graded alcohol series and xylene, then embedded in paraffin wax. Thin sections (5–7µm) were cut in a rotary microtome (Leica RM2125 RTS, Germany).

Two staining protocols were employed: 1) Hematoxylin and Eosin (H&E) staining for cellular morphology and early bone matrixomics. 2)Masson's Trichrome (MT) staining showing the collagen fiber (blue/green) and fibrous tissue (red). The histological images were imaged by bright-field microscopy (Carl Zeiss Axio Observer Z1).

RESULTS

In Vitro Cytocompatibility Assessment

MTT Assay (Cell Viability and Proliferation) MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) was used to test the proliferation and viability of cells. The proliferation of hPMSCs on porous titanium and porous ceramic surfaces was measured on days 1, 3, and 5 by MTT assay. Cytocompatibility was acceptable for both materials, and cell survival rates increased over time in a stepwise manner. Porous ceramic implants, however, consistently led to significantly greater cell viability than the titanium top control. Both groups had similar viabilities on day 1, indicating good cell attachment in the beginning. After 3 days, viability was significantly promoted on ceramics, while cells had higher metabolic activity than on titanium. By day 5, ceramics reached the maximum survivability, reflecting increased proliferation and good surface interactions. These findings indicate that the bioactive surface chemistry presented by the porous ceramic promotes greater cell activity than the bioinert titanium surface.

Live-Dead Staining

Live-dead stained cells fluorescence imaging showed a marked difference between the two substrates. After 1 d, the vast majority of the living cells (green fluorescence) were found in both titanium and ceramic composites with live cells as the predominant type, indicating that there was no visible species influence on the initial cytocompatibility. On day 3, ceramic implants showed a dense infiltration of viable cell spreading spreading across the porous network, when titanium surfaces were the less populated. At day 5, ceramics were covered with confluent layers of viable cells that invaded the pore architecture and with very few dead cells (red fluorescence). In contrast, viable cells were found with titanium samples although in less cell population than with ceramics. These results suggest that porous ceramics are more favorable environment for the survival of sustained cells and colonization.

Cytoskeletal And Nuclear Staining

Rhodamine-phalloidin/DAPI staining also demonstrated the good interaction between hPMSCs and ceramic implants. Fluorescent microscopy images showed well organized actin fibers and clear nuclear staining on both surfaces with apparent morphological differences. On titanium, cells showed an elongated and less spread-out shape, with few bonding between neighboring cells. By contrast, on ceramic implants the cells mounted a robust cytoskeletal organization with a more polygonal shape of the cells and more spreading throughout the pore walls and intercellular connections. These results emphasize the better surface-compatibility of porous ceramics in adhesion, cytoskeletal alignment, and cell–cell communication.

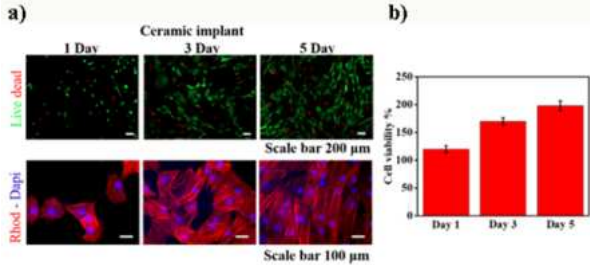

Figure 1: Cytocompatibility of porous ceramic implants.

a) Fluorescence microscopy images showing live-dead staining of hPMSCs cultured on porous ceramic (top panels) for 1, 3, and 5 days. Live cells are indicated in green (calcein-AM) and dead cells in red (ethidium homodimer-1), demonstrating high viability and progressive colonization of both implant surfaces, with ceramic implants supporting denser viable cell coverage. Rhodamine-phalloidin (Rhod) and DAPI staining images (bottom panel) illustrate actin cytoskeleton (red) and nuclei (blue), showing enhanced cell spreading, alignment, and intercellular connectivity on porous ceramic surfaces. b) MTT assay results at days 1, 3, and 5, revealing significantly higher viability and proliferation with ceramic implants.

Histological Evaluation of Bone Ingrowth

Hematoxylin and Eosin (H&E) Staining

Sections of bone samples harvested following implantation showed extensive tissue ingrowth around ceramic implants. Ceramic implants had considerable homogeneous bone in-growth, in which newly formed osteoid tissue extended into the porous structure. The tissue–implant junction seemed to be continuous with minimal fibrous tissue, indicating that an appreciable host integration was established.

Masson's Trichrome (MT) Staining

These findings were supported by MT staining, which revealed intense blue-green staining representing mature collagenous bone matrix formation around ceramic implants. High collagen and ordered bone matrix deposition in ceramics indicates a high osteoconductive activity of ceramics.

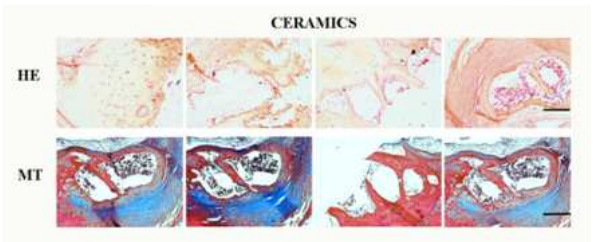

Figure 2: Histopathological Evaluation of Improved osseointegration: Representative histological sections of bone–implant interfaces demonstrating improved osseointegration with porous ceramic dental implant. Hematoxylin and Eosin (H&E) staining reveals extensive new bone formation (Upper Panel) infiltrating the porous ceramic structure (S), with minimal fibrous tissue encapsulation and a continuous bone–implant interface. Masson's Trichrome (MT) staining (Lower panel) highlights dense collagen deposition and mature bone matrix (blue/green) within the ceramic pores, indicative of enhanced osteoconductivity and bone remodelling.

DISCUSSION

These ex-vivo experiments, in this study, investigated the cytocompatibility and osteointegration properties of porous ceramic dental implants. We tested hPMSC as a model showed normal cell viability, improved cytoskeletal alignment, and active proliferation over the entire culture period. Histological assessment also verified the presence of abundant bone in the porous structure with dense collagenous deposition and intimate contact between the implant and the host bone, which indicated that the porous ceramics exhibited excellent osteoconductive function.

Our in vitro results are consistent with previous publications, which demonstrated in vivo, that ceramic implant surfaces induce addition/better biological activity compared to bioinert metals. Ceramics, such as zirconia or bioactive glass composites have been shown to promote cell adhesion, spreading and osteoblast differentiation (Aldhuwayhi, 2025). Research has shown that zirconia has low bacterial adhesion, high biocompatibility, and an anti-inflammatory profile, leading to better peri-implant health (Bosshardt et al., 2017; Shrivastava et al., 2025). These characteristics are consistent with our live–dead staining results indicating mostly viable cells with increasing colonization on porous ceramics.

The MTT assay also proved that porous ceramics sustained cell growth for time. Analogous trends have also been found in studies that have used both porous zirconia scaffolds and bioactive glass-chitosan composites, where the chemically active surface of the material results in high protein adsorption and integrin-mediated cell adhesion (Rahaman et al., 2012; (Rahaman et al., 2011; Skallevold et al., 2019). Also, cytoskeletal staining in our study showed a filigree actin filament structure and extensive intercellular connections, with published data stating that ceramic surfaces promote osteoblast spreading and cytoskeletal alignment compared to smooth or bioinert materials (Kapat et al., 2017; Rokusek et al., 2005).

Histological evaluation also helped to confirm osseointegration. Among the staining profiles, active bone remodelling was indicated by extensive collagen deposition which was identified by Masson's Trichrome, while H&E staining revealed bone matrix formation directly within the porous network of the implants. These results corroborate previous work demonstrating that porous ceramics allow mineralized bone growth into and osseo-integration of the implant surface (Rahaman et al., 2011). The decreased fibrous tissue response observed in our study is also in line with previous studies that have reported that ceramics induce a reduced chronic inflammatory response when compared to metal implants (Aldhuwayhi, 2025; Bosshardt et al., 2017).

In addition to these clear biological benefits, there are also mechanical limitations to overcome in the area of ceramics. Another noteworthy feature of these ceramics is their brittleness, which is a safety issue in high-load areas, where resistances to fracture play important role. Recent progress in ceramic processing and additive manufacturing has started to address this challenge where it is now possible to produce porous and functionally graded ceramic structures exhibiting enhanced strength (Guddati et al., 2019). Furthermore, hybrid modifications, for example, covering ceramics with osteoinductive ions or forming composite structures can improve biological aspects as well as mechanical properties (Tang et al., 2025).

Future outlook will focus on the development of the second generation of the ceramic implants, which include the implementation of an optimized pore architecture with customized mechanical properties. Studies on ion-releasing ceramics, and anti-microbial modification have also shown potential for reducing the risk of peri-implantitis, while promoting long-term osseointegration (Skallevold et al., 2019). Long scale clinical trials will be necessary to confirm biological advantages obtained in our ex-vivo model and the place of ceramics used as routinely as classical implant materials.

In conclusion, our study demonstrates that porous ceramics enhance good biological responses in terms of cell survival, osteoblastic attachment, cytoskeletal arrangement and bone matrix apposition. These results emphasized once again the biological potential of porous ceramics for the next-step dental implant material but the mechanical reliability and clinical translation required further development.

CONCLUSION

This ex-vivo experiment proves the potential of porous ceramic dental implants to promote osseointegration and formation of new bone. Porous Ceramics could both integrity cell viability, shear proliferation and complete cellular cytoskeleton and Analysis on histological assay demonstrate the status of proliferation and the cytoskeleton of hPMSCs. Live–dead and cytoskeletal staining demonstrated that the sintered porous ceramic surface was a suitable microenvironment for cell adhesion and interconnection. Histological examination also showed abundant presence of collagen, deposition of new bone matrix, and continuous interface between the implant and the host bone, with only mild fibrous tissue response, suggesting the excellent osteoconductive and biocompatible attributes of ceramics.

These results are in accordance with recent publications pointing to ceramics as bioactive and osteoconductive implant materials; ceramics are also less prone to bacterial colonization and inflammatory reactions. The interconnected porous microstructure of the ceramic infiltrated implants probably promoted vascularization and grow-in of tissue depositions, which are keys for long-term implant fixation.

Although the biological benefits of porous ceramics are clear, there are still some difficulties to address in the realization of their potential as they have the inherent drawback of brittleness, and mechanical reliability in a load-bearing context. Future research should further optimize the pore geometry and develop composite or hybrid configurations as well as undertake long term in vivo and clinical investigations. In general, porous ceramics is a very promising substitute for new generation dental implants, which have high chance of enhancing clinical performance.

Acknowledgement
Conflict of interest

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