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The Instilled Antipodal- Implant Related Modifications

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Abstract

The Implant-tissue interface is a zone of transition between the superficial surface of a surgical implant and adjoining bony or soft tissue. Typically, implant- tissue interface generates a complicated and dynamic environment with cogent mechanical and biological interactions between the implant and encompassing tissue wherein aforesaid features define the quality of the implant-tissue interface. Ultimately, comprehensive integration of the implant within circumscribing tissue is necessitated to ensure extensive stability and longevity of the implant-tissue interface.

KEYWORDS: Implant, Haemorrhage, Osteoconduction, Cartilage, Haematoma

INTRODUCTION

Implant stability is categorized as primary or mechanical stability that is immediately achieved by the implant following appropriate tissue positioning. Specific tissue conditions significantly affect primary stability during the implantation process and secondary stability accompanies biological integration of the implant and is obtained within a significant duration through the integration process [1,2]. Appropriate integration of an implant within the tissue is contingent on primary and secondary stability which is essential for preliminary and extended surgical outcomes [1,2]. Integration of an implant within enveloping tissue pertains to characteristics of the implant and constitution of encompassing tissue. Implant insertion engenders tissue injury with haemorrhage into the implantation site followed by activation of wound healing [1,2]. Haemorrhage is a preliminary, significant aspect of the healing process as blood contributes to growth factors and cellular material necessitated for tissue repair. Circulating blood cells and platelets configure a fibrin matrix which provides a scaffold for regenerating tissue and enmeshes the implant. With tissue healing, an integrated implant strengthens the implant-tissue interface. Well vascularized, perfused tissues heal and integrate efficaciously, in contrast to avascular tissues such as cartilage [1,2].

DISEASE PATHOGENESIS

The orthopaedic implant integrates upon a bone surface contingent to the ability for osteoinduction osteoconduction and osseointegration [1,2]. Osteoinduction refers to an implant's capacity to activate undifferentiated and pluripotent cells to metamorphose into osteogenic cell lines. Osteoconduction is an implant's ability to permit cellular adherence, proliferation and migration along the surface with consequent deposition of bone upon the extraneous surface, intrinsic pores and interconnected channels of the implant (Figure 1 and Figure 2) [3,4].

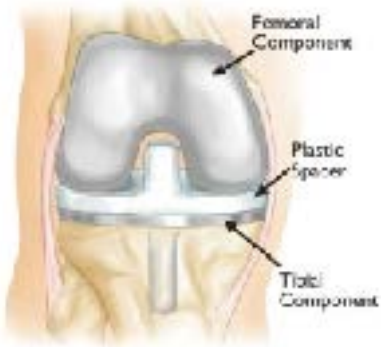

Figure 1. Implant related changes enunciating implant positioning at the knee joint between femur and tibia [11]

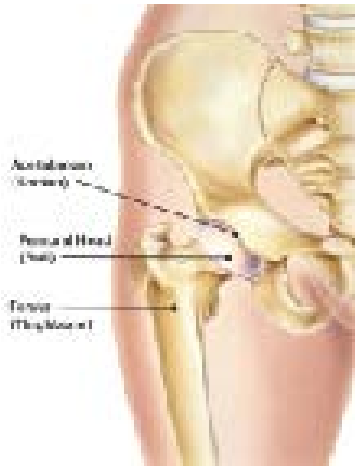

Figure 2. Implant related changes exhibiting appropriate placement of the implant between femoral head and acetabulum [12]

Osteoinduction and osteoconduction may occur simultaneously, especially within *vivo* implants. Tissue healing occurring during implant positioning triggers an extracellular bone healing cascade which activates factors of osteoinductive growth and differentiation [3,4]. Osseointegration is a significant phenomenon inducing healing upon implant-bone tissue interface. Osteointegration engenders rigid fixation of implanted alloplastic material in the course of physiological loading of native tissue. Osseointegration is further denominated as a foreign body reaction wherein the interfacial bone is configured defensively to isolate the implant from circumscribing tissue [3,4]. Microscopic evidence of osseointegration depicts a direct contact between bone and implant [3,4]. Appropriate osseointegration of implant is associated with the direct configuration of bone upon the implant surface of 10 micrometres to 20 micrometres thickness [3,4]. The extent of osseointegration is contingent on to implant's osteoinductive and osteoconductive capacity. Failure of osseointegration may engender aseptic loosening of the implant [3,4]. Osseointegration demonstrates several biological stages denominated as the configuration of a hematoma, development of mesenchymal tissue along articulation of intramembranous (woven) bone and lamellar bone (Figure 3) [3,4].

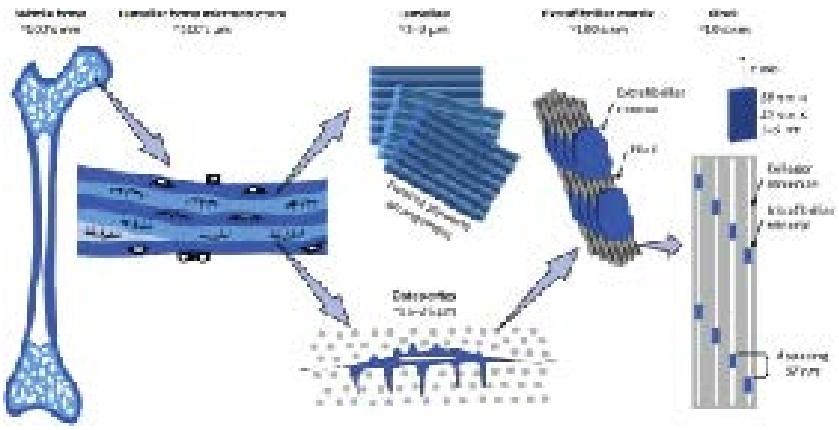

Figure 3. Implant related changes associated with the configuration of lamellar bone and extrafibrillar matrix [13]

Configuration of a haematoma commences with haemorrhage engendered by insertion of an implant. Red blood cells, platelets and inflammatory cells such as polymorphonuclear granulocytes and monocytes are deposited upon the implant surface due to extravascular migration from localized bony vasculature and bone marrow. Blood components are eventually entrapped upon the implant surface [5,6). Cellular adhesion is followed by activation and secretion of cytokines and growth factors such as Insulin-like Growth Factors I and II (IGF I and IGF II), Fibroblast Growth Factor (FGF), Transforming Growth Factor-Beta (TGF-β) and Platelet-Derived Growth Factor (PDGF). Bone Morphogenic Protein-2/7 (BMP-2/7) of the TGF-β family of growth factors depicts superior osteoinductive capacity [5,6]. Vascular clotting is initiated by coagulation factors in association with extrinsic coagulation initiator tissue factor discerned in osteoblasts. Platelet activation induces various morphological and biochemical alterations such as platelet adhesion, aggregation, induction of phosphotyrosine, elevated intracellular calcium and hydrolysis of phospholipids [5,6]. Activated platelets and inflammatory cells secrete diverse chemo-attractants which engage fibroblasts and configure a fibrin matrix that functions as a biological and osteoconductive scaffold. The scaffold stimulates osteogenic cells for articulating bone around the implant, a phenomenon designated as osteoinduction (Figure 4) [5,6].

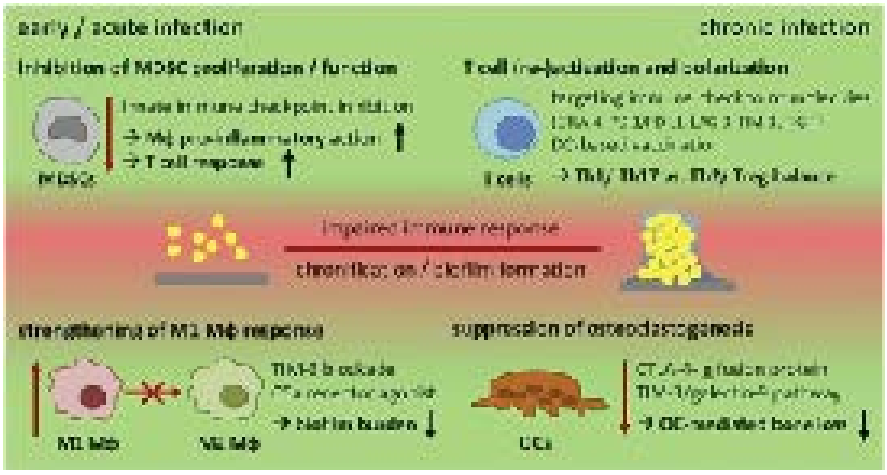

Figure 4. Implant related changes delineating cytokine-mediated acute and chronic inflammation arising at the implant-bone interface [14]

Coagulation commences within one hour of implantation and granulation tissue is usually generated within two hours. Fibrin matrix deposited upon the implant surface is gradually metamorphosed into a poorly mineralized osteoid matrix which structurally simulates bone cement lines and laminae. The osteoid matrix articulates a continuous layer of approx. 0.5 millimetre thickness predominantly comprised of calcium, phosphorus, osteopontin and bone sialoprotein [5,6]. Transformation of fibrin matrix into incompletely mineralized osteoid commences within twenty-four hours following implantation. The metamorphosis is predominantly mediated by macrophages which activate wound vascularization, mesenchymal stem cells migration and eradication of necrotic cells [5,6]. An attenuated superficial osteoid layer of the implant gradually calcifies wherein incriminated osteoblasts synthesize and secrete a collagenous matrix chiefly composed of type I collagen. Following calcification, endothelial cells and mesenchymal stem cells infiltrate the osteoid, especially within non-calcified spaces [4-6]. Vascularization of osteoid due to invading endothelial cells appears to be a significant component of osteogenesis and predominantly influences osseointegration [4-6]. Osseous fragments of 35 micrometres to 220 micrometres magnitude engendered during implantation are incorporated within the contemporary, regenerated implant-tissue interface [5,6]. Osseointegration or osteogenesis appearing directly upon the implant surface is denominated as direct osteogenesis and osseointegration arising from circumscribing, peripheral bone is designated as distance osteogenesis [5,6]. Direct osteogenesis and distance osteogenesis may occur simultaneously and are demarcated. Mineralized osteoid gradually metamorphoses into the space-occupying woven bone which maintains the integrity between host bone and implant and provides preliminary mechanical support to host bone during loading [6,7]. Woven bone serves as a scaffold for cellular attachment and bone deposition. Aforesaid preliminary processes of bone configuration commence within ten days of implantation [6,7]. Gradually, woven bone remodels into compact, lamellar bone within three months of implantation. During remodelling, newly generated osteons surround the implant with a long axis parallel to the surface [6,7]. Osseointegration of an implant is contemplated to be complete with the emergence of an attenuated layer of bone of approx. one millimetre magnitude constituted of osteoclasts, osteoblasts, mesenchymal stem cells along with lymphatic and vascular articulations circumscribing and extending from the implant surface [6,7].

Contribution to osseointegration

The complicated, dynamic process of osseointegration is influenced by implant-related and host tissue-related factors. Implant-related factors are composed of implant topography, geometric outline, length, magnitude, material composition, interface distance, mechanical or architectural properties and micro or macro-motion of the implant. Additionally, bioactive surface coating of hydroxyapatite or growth factors is beneficial. Nano pores impact the proliferation, differentiation and adhesion of osteoblasts [7,8]. Host tissue-related factors are comprised of quality of adjacent bone, adjuvant therapies such as bone grafting and application of an osteogenic coating [7,8]. Systemic pharmacological agents significantly impacting osseointegration are simvastatin (β-Hydroxy β-methylglutaryl-CoA reductase inhibitor) and bisphosphonate (inhibitor of osteoclastic-mediated bone resorption). Micro-motion, magnitude and gap between implant and bone influences osseointegration. Configuration of poor bone or bone resorption with bone compression occurs due to an implant [7,8]. Miniature gaps between implant and host bone configure bone trabeculae with cogent osseointegration. Gaps exceeding 500 micrometres articulate poor quality bone and delay incorporation within the gap. Enhanced gap magnitude substantially decimates Bone Implant Contact (BIC), thereby delaying osseointegration [7,8]. Ideally, mechanical properties of the implant are required to be identical to surrounding bone which ensures adequate preservation of implant-tissue interface. Materials such as Titanium-Aluminium-Vanadium Alloy (Ti−6Al−4 V), Polyetheretherketone (PEEK) or Carbon-Fibre-Reinforced Polyetheretherketone (CFR-PEEK) are malleable and beneficial [7,8]. Material properties such as enhanced volumetric porosity, optimal pore magnitude, pore interconnectivity, pore geometry, enhanced frictional characteristics, surface energy and excellent biocompatibility of the material are features that influence osseointegration. Pore diameter of 100 micrometres permits the configuration of mineralized bone and osteocyte migration within the implant. The pore diameter of 200 micrometres to 350 micrometres aids neovascularization within superimposed implants [8,9]. Appropriate pore interconnectivity is integral for meliorating the circulation of interstitial fluid and nutrients within the implant. Porous, pure tantalum is an optimal, contemporary osseointegration metal employed for configuring implants [7, 8]. Bioactive coatings ameliorate material osseointegration. Frequently utilized coatings are constituted of calcium phosphates, Hydroxyapatite (HA), Tricalcium Phosphate (TCP), Whitlockite (WH) and Octacalcium Phosphate (OCP) [7,8]. Nevertheless, emerging factors of inferior mechanical stability necessitate the combination of coating materials with substances such as bioglass coating and silica-based coating as dicalcium silicate or tricalcium silicate [7,8]. Three-dimensional printing scans obtained by imagining modalities such as Magnetic Resonance Imaging (MRI), Modern Multi-row Detector Computerized Tomography (MDCT), Computed Tomography (CT), plain radiographs or three-dimensional scanners are employed for evaluating the anatomy of and substituting complex bone defects [7,8].

Adversities in osseointegration

Unfavourable factors implicating osseointegration are categorized as implant-related and host tissue-related factors. Implant-related factors comprise extensive micro-motion, enhanced interfacial strain, and inappropriate porosity of porous coatings, biological debris, wear and tear debris, corrosion and pertinent implant manufacture [8,9]. Host tissue-related factors are constituted of inferior quality of adjacent bone possibly arising from systemic diseases, radiation therapy and pharmacological agents such as cyclosporine A, methotrexate, cis-platinum, warfarin, low molecular weight heparins and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) [8,9]. Polyetheretherketone (PEEK) can hinder osseointegration due to the presence of a smooth surface, absence of antibacterial activity and occasional detachment of coatings [8,9]. Impaired osseointegration may engender peri-implantitis with the articulation of a circumscribing fibrous interface and aseptic extrication. Toxic Methylmethacrylate (MMA) monomers may induce severe Bone Cement Implantation Syndrome (BCIS) constituted of hypoxia, hypotension, cardiac arrhythmias, elevated pulmonary vascular resistance and cardiac arrest [8,9]. Contemporary cement comprised of calcium phosphates is associated with variable bone regeneration and degradation of calcium phosphates, restricted tissue ingrowth contingent to pore magnitude, lack of mechanical strength and inflammatory reaction arising due to degradation of synthetic polymers [8,9]. Additionally, degenerative and inflammatory conditions such as osteoporosis, rheumatoid arthritis, advancing age, nutritional deficiencies, smoking and renal insufficiency may decimate the efficacy of osseointegration [8,9]. Thus, pre-implant osteogenesis declines with dwindling quantification and activity of osteogenic cells, enhanced osteoclastic activity, imbalanced localized anabolic and catabolic factors and impaired vascularization of peri-implant tissues [8,9].

Histological elucidation

Debris within the implant-bone interface may arise from the metallic component of the joint and appears as grey-black, irregular fragments which may frequently be incorporated within histiocytes, a feature especially denominated with titanium implants. The Polyethene component of the joint appears as thread-like particles of up to 20 microns, may be confined within histiocytes and are discernible with polarized light (Figure 5 and Figure 6) [5,6].

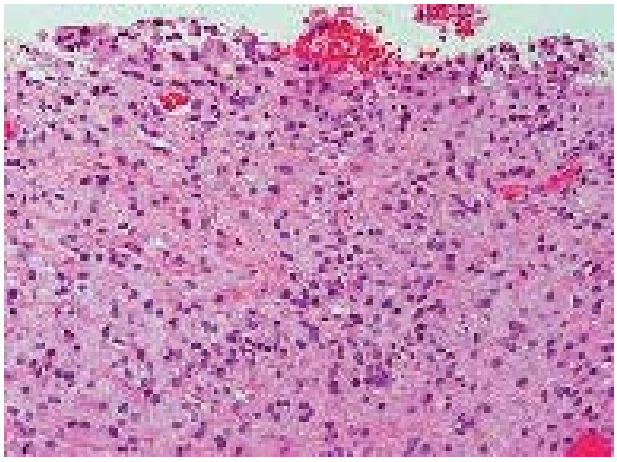

Figure 5. Implant related changes depicting an intense neutrophilic efflux admixed with fibrinous exudate and red cell extravasation [15]

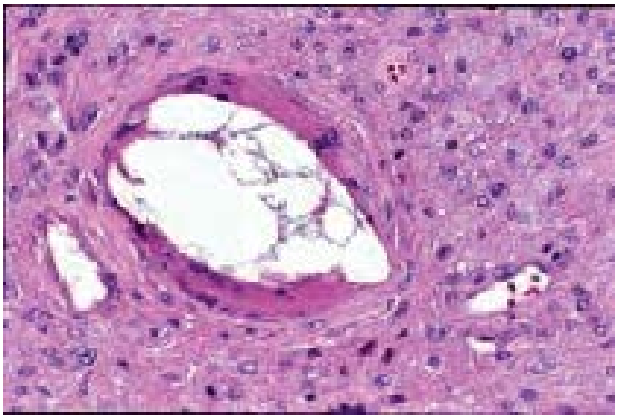

Figure 6. Implant related changes demonstrating inflammatory cell exudate and a superimposed fibrinous exudate [16]

Methyl methacrylate is exemplified as grout and dissolution of the material during histological processing may display the substance as irregular holes varying from 1 micron to 100 microns in magnitude. Silicone rubber employed for implants emerges as a bosselated, faintly yellow, refractile substance that lacks birefringence [5,6]. Placement of aforesaid implants is accompanied by significant histiocytic infiltration and evokes a giant cell reaction [6]. Implants may engender aggressive metallosis which erodes the bone and incites joint failure [6]. The frozen section may be employed for morphological assessment of infected joints accompanied by significant infiltration of neutrophils. Additionally, superimposed fibrinous exudate is admixed with an intense inflammatory cell infiltrate [6,7].

Adherence in bone implants

Bone and implant interaction demonstrates primary stability and secondary stability. Primary stability, designated as mechanical stability, is inadequate with the immediate placement of the implant into the bone. Proportionate primary stability is contingent on several factors such as surgical technique, implant design, the texture of implant surface, loading, micro-motion and texture of encompassing bone [6,7]. Primary stability remains unaffected by osseointegration. Implants with inferior primary stability demonstrate micro-motion exceeding 150 micrometres, elevated tensile and shear stresses and fibroplasia with the characteristic configuration of fibrous interface enveloping the implant. Secondary stability is additionally designated as biological stability and enhances with the configuration of new bone which circumscribes and is contiguous with the implant. Secondary stability ensures the long-term stability of the implant-bone interface and is concurrent with osseointegration [6,7]. The aforementioned factors impacting osseointegration are applicable in the generation of adequate secondary stability and the interdependent variants may occur simultaneously [6,7].

Implant- cartilage interface

Implants situated within cartilage comprise scaffolds of regenerative tissue occurring within chondral or osteochondral defects. The scaffolds assist with the inlaying of bone defects and provide an optimal surface for chondrocyte adherence,

proliferation and evolution [7,8]. Implant integration within avascular articular cartilage is challenging on account of dense proteoglycans, Extracellular Matrix (EM) and extensive compressive or shear forces applicable to articular surfaces during physiological joint mobility [7,8]. Tissue implantation typically engenders necrosis of chondrocytes adjacent to the implant. Also, cellular components facilitating regeneration such as recruitment of chondrogenic progenitor cells from circulating blood or bone marrow and innate chondrocytes demonstrate a limited potential for regeneration as the cells are incompetent in migrating through the dense extracellular matrix [7,9]. Resurfacing of articular cartilage with allogeneic or autologous implants is optimal in rejuvenating physiological joint function. Articular cartilage is incompetent incomplete regeneration, especially with lesion diameter exceeding 6 millimetres [7,9]. Healing of osteochondral lesions is superior, in contrast to cartilaginous lesions due to exposure of subchondral bone with meliorated vascular and cellular migration [8,9]. Haemorrhage from subchondral bone with the subsequent configuration of a blood clot ensues following osteochondral injury and may layer bone defects of up to approx. 23 millimetres magnitude [9,10]. Subchondral blood is imbued with growth factors, mesenchymal stem cells and platelets which are a pre-requisite for cartilaginous regeneration [9,10]. Defects within the hyaline cartilage are preliminarily repaired with fibrocartilage which is mechanically and functionally inferior to hyaline cartilage on account of reduced collagen I to collagen II proportion and decreased quantities of aggrecans [9,10]. Bone defects inlayed with fibrocartilage may appear healed although tissues repaired with inferior fibrocartilage engender tissue deterioration. Fibrocartilage may undergo peripheral micro-cracking, especially between repaired tissue and adjoining hyaline cartilage. Thus, thick, dense fissures may ensue. Perpetual transition upon the implant-cartilage interface is essential for implant integration and preservation of viable chondrocytes [9,10]. Implant integration commences with tissue injury along with a necrotic band of 100 micrometres to 200 micrometres magnitude with gradual cellular apoptosis for up to two weeks and consequent expansion of the necrotic band to up to 400 micrometres. On account of restricted migration of resident chondrocytes, an implant comprised of viable stem cells or chondroblasts or chondrocytes may enhance osseointegration [9,10].

CONCLUSION

Osseointegration may commence within 10 days of implantation and may extend to up to 3 months. Cogent morphological evaluation is imperative for ascertaining osseointegration. Bone and soft tissue enveloping rejected implant may be subjected to histological assessment. Implant failure usually occurs due to infection with organisms such as *staphylococci* and is admixed with diverse inflammatory cells. Mechanical factors may engender implant rejection which is accompanied by an epithelioid granulomatous reaction along with the accumulation of necrotic debris. Bone Implant contact (BIC) can be directly assessed and measured histologically as bone tissue appears to be in contact with the implant surface. Bone Implant contact (BIC) can also be evaluated with pertinent mechanical tests such as Resonance Frequency Analysis (RFA), percussion testing, Insertion Torque (IT), Peak Reverse Torque (PRT), Cutting Torque Resistance Analysis (CRA) and assays measuring pull out, pushout, torsion and bending forces applicable to implant-tissue composites. Aforesaid methodologies can adequately assess the primary as well as secondary stability. Secondary stability may be optimally evaluated with tissue placement of the implant. Mechanical tests usually employed to measure secondary stability are pull-out, pushout, torsion, bending and Peak Reverse Torque (PRT). Mechanical tests evaluate maximum tension load, actuator displacement and construct stiffness. Torsional loading can be adopted to assess an implant or an entire construct in bone or soft tissue.

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