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Biocompatibility of Dental Materials

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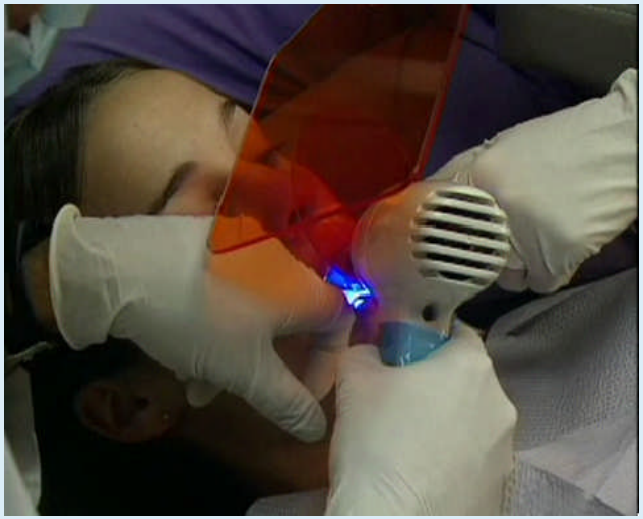
INTRODUCTION

Any material or device that is to be used or placed within the body has to be evaluated for biocompatibility to ensure it is safe for human use



BIOCOMPATIBILITY

Definition:

BIOCOMPATIBILITY IS THE ABILITY OF A MATERIAL TO PERFORM WITH AN APPROPRIATE HOST RESPONSE IN A SPECIFIC APPLICATION

(Williams 1987)

Biocompatibility involves two components:

(i) General aspect: "BIOSAFETY"

This concerns and deals with the exclusion of deleterious effects of a biomaterial on the organism itself (toxicity at the cellular level)

(2) Specific aspect: "BIOFUNCTIONALITY"

This concerns and addresses the need of a material not only to be free from damaging effects on the host at the cellular level, but also to be able to elicit a beneficial host-response for optimal functioning of the medical device

BIOCOMPATIBLITY OF MATERIALS USED IN DENTISTRY-KEY ELEMENTS

•Any dental materials used in the oral cavity should be harmless to all oral tissue: gingiva, mucosa, pulp, and bone

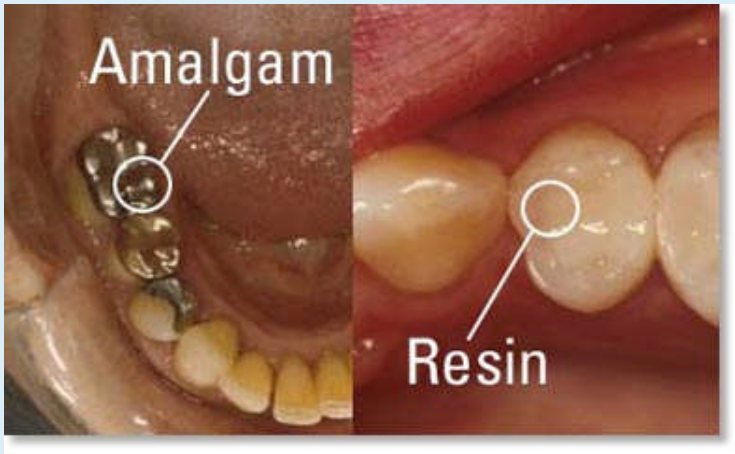
•Material should contain no toxic, leachable, or diffusible substance that can be absorbed into the circulatory system, causing systemic toxic responses/toxicity (including teratogenic or carcinogenic effects) e.g.substances released intraorally from dental alloys and other dental materials

• Material should be free of agents that could elicit sensitization or an allergic response in a sensitized patient

Tissue-material interface for dental applications

- **Those contacting soft tissues in the mouth**
- **Those contacting hard tissues in the mouth**
- **Those affecting the vitality of pulp**
- **Those affecting root canal filling**

e.g
Monomers in denture base materials
Allergic reactions to alloys containing nickel
Phosphoric acid- used as an etchant for enamel
Mercury in dental amalgam



Side effects to dental materials are rare and those reported in restorative materials may show a toxic, irritative, or allergic reactions.

This may be manifested as local and/or systemic.

• Local reactions involve the gingiva, mucosal tissues, pulp, and hard tooth tissues

•Systemic reactions are expressed generally as allergic skin reactions

•Side effects may be acute or chronic

OFTEN THE RISK IS GREATER TO THE PRACTITIONER THAN THE PATIENT!

- **Time dependent exposure when material being manipulated or during setting**

- **Effects can range from cumulative irritation to severe allergenic responses**

- **Inhalation of particulates during surgical procedures can activate immune cells**
(e.g dust from alginate impression materials, also some products containing lead and tin)

Biocompatibility relates to the overall performance of the (bio) material

- **When a biomaterial is placed in the body a 'two-way' biological interaction takes place**

1. **The effect the body has on the material (implant)**

2. **The effect the material (implant) has on the body**

EFFECT THE BODY HAS ON THE IMPLANT MATERIAL

1. PROTEIN ADSORPTION

Extent dependent on material properties

2. ENVIRONMENTAL

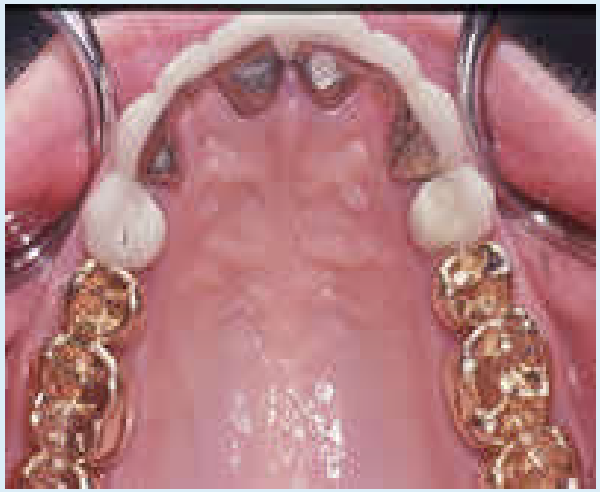
Saliva has corrosive properties, and bacteria are ever present

3. DEGRADATION

Enzymatic

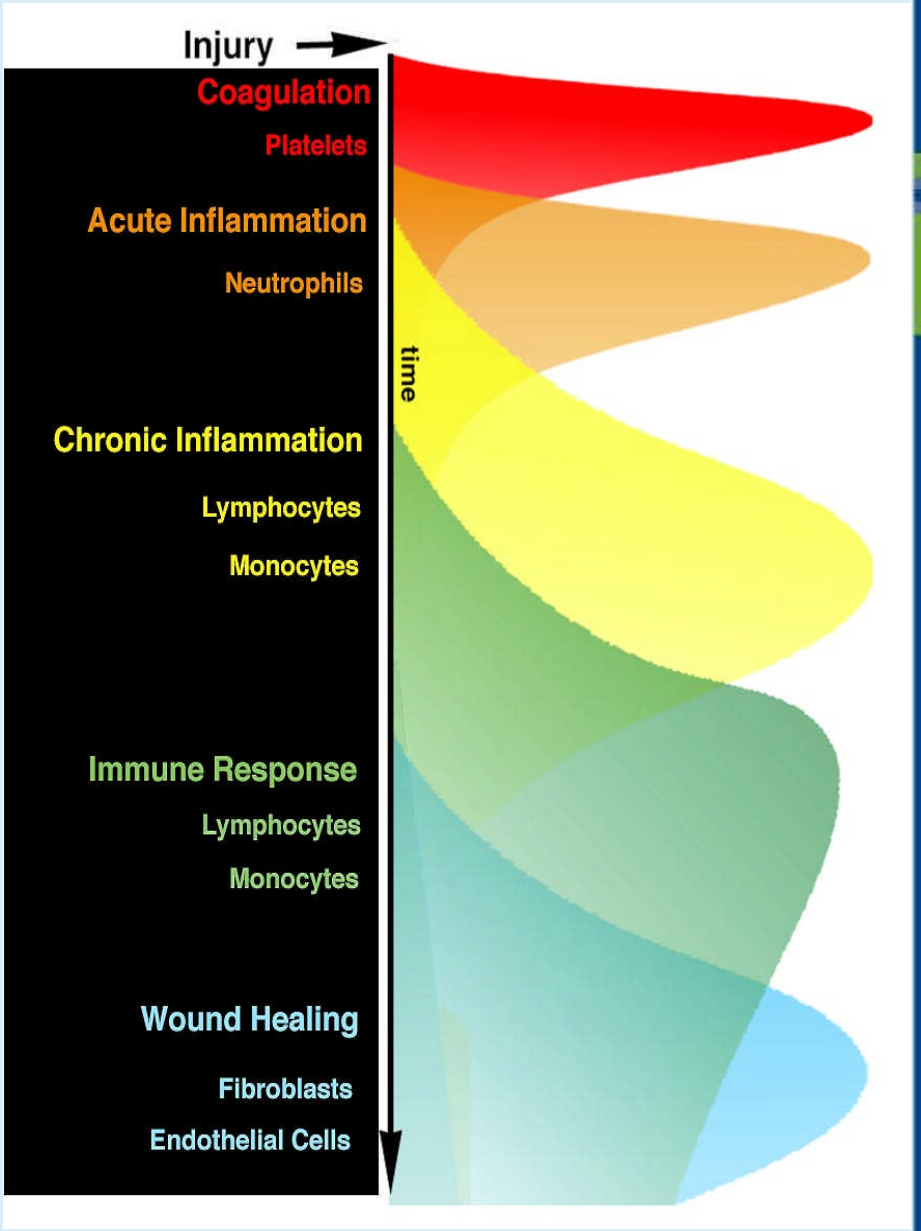
4. CORROSION

Mainly metals



EFFECT THE MATERIAL (IMPLANT) HAS ON THE BODY

1. UPSETS HOMEOSTATIC EQUILIBRIUM
2. ACUTE INFLAMMATION
3. CHRONIC INFLAMMATION
4. EVOKES AN IMMUNE RESPONSE
5. ACTIVATION OF MACROPHAGES ETC.
6. HEALING



STANDARDS & TESTING

- Until recently, almost all national & international Dental standards and tests focused on only physical & chemical aspects

- Today, all dental materials require biological testing

- Testing is based on specifications or standards established by national or international standards organization, such as the American National Standards (ANSI) or International Standards Organization(ISO)

ASSESSMENT OF BIOCOMPATIBILITY

ISO 10993 –under the general title
" Biological evaluation of medical devices"is divided into different parts:
Part 1: Guidance on selection of tests
Part 2: Animal welfare requirements
Part 3: Tests for gentoxicity, carcinogenicity and reproductive toxicity
Part 4: Selection of tests for interaction with blood
Part 5:Tests for cytotoxicity: *in vitro* methods
Part 6:Test for local effects after implantation
Part7: Ethylene oxide sterilization residuals
Part8: Clinical investigation
Part9: Degradation of materials related to biological testing
Part10: Tests for irritation and sensitization
Part11: Tests for systemic toxicity
Part 12: Sample preparation and reference materials

Testing of materials

All dental materials should be subjected to

1.Primary cytotoxicity screening test- to assess any toxic effect at the cellular level

2.Secondary test- to evaluate tissue response (appropriate cell response)

Having passed both 1 and 2

3. Animal tests

4. Clinical trial in humans

ASSESSMENT OF BIOCOMPATIBILITY

ISO Part 5:Tests for cytotoxicity: *in vitro* methods

Many tests available, can assess cell number, growth rate. Cell metabolism, gene up-regulation, tests are relatively simple, reproducible, inexpensive, rapid

Can examine:

- Nature of the cell- materials interaction
- The ability of cells to retain phenotype and functionality
- Can test large number of samples; novel and commercial
- Can test biofunctionality with appropriate cell model for both soft and hard tissue

The ISO 10993 does not specify any single test but aims to define a testing scheme which requires decisions to be made in a series of steps which should lead to the selection of the most appropriate test methods

Types of test regimes recommended:

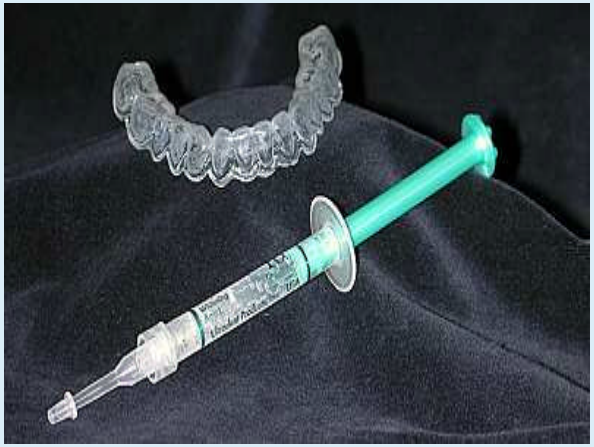
- **Indirect contact (Extract)**
- **Direct contact**

Choice is dependent on:

- **Type of sample to be tested**
- **Potential site of use**
- **Nature of use**

CYTOTOXICITY TESTS

The material to be tested should be representative of the components in the final product and the final product



Requirements for biocompatibility testing methods

- **SPECIFICTY**

Appropriate cells for material being tested

- **SENSITIVITY**

Methods used should be sensitive and suitable for *in vitro* cell culture

- **QUALITY CONTROLS**

Both negative and positive and also, material and cell culture control

- **ISO-10993 GUIDELINES**

Part 5 : *in vitro* methods

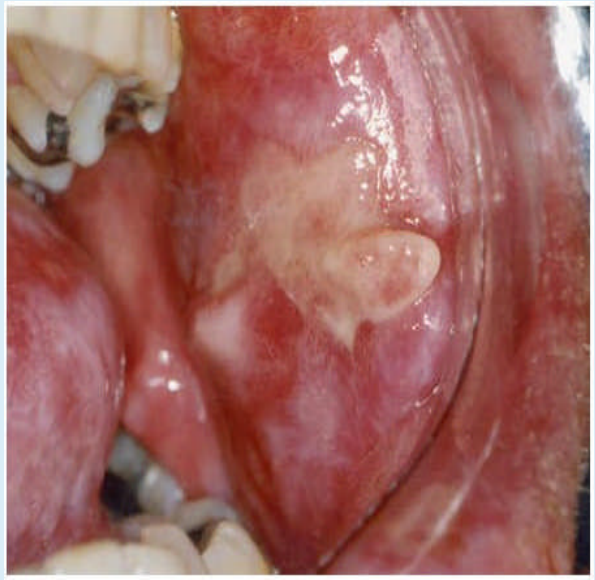
Biocompatibility of common dental restorative materials

LOCAL REACTIONS

- **No major adverse effects reported**

- **Lichenoid/white or red erosive lesions in the oral mucosa reported in direct contact with dental amalgam, composite and other restorative materials**

Interestingly, no evidence of hypersensitivity to dental restorative materials has been reported in patients with oral lichen planus



RESIN-BASED COMPOSITES

- **Few documented systemic adverse effects**
- **Associated with numerous organic compounds, effects of which are unknown**
- **Incomplete polymerisation leads to degradation, leaching, imperfect bonding**
- **Polymerisation shrinkage**
- **Adverse local pulp and dentin reactions, development of recurrent caries, and pain**
- **Increased plaque adhesion and Lichenoid episodes reported**

GLASS INOMER CEMENTS

- Few documented systemic adverse effect
- Very little irritant effect on pulp reactions, usually followed by rapid recovery
- When used as luting agent, liners are advocated
- Hydraulic pressure/etching during placement may irritate pulp
- No undue reactions reported in gingival tissue
- Good adhesion, minimal leakage at margins,

Overall, good biocompatibility !

GOLD FOIL AND CAST ALLOYS

- Inert, sensitivities are rare
- Potential pulp reactions due to condensation
- Rare allergic reactions to alloy metals

CERAMICS

- No known reactions except wear on opposing dentition and restoration
- Good biocompatibility- but no long-term data on biocompatibility available

Most reported adverse effects of dental materials are allergic reactions:

Large number of dental materials contain components that are common allergens e.g

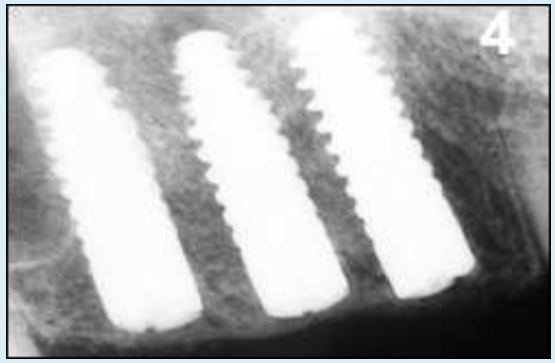
Mercury, eugenol, chromium, cobalt, components of resin-based materials, formaldehyde-containing materials, methyl methacrylate

Extent of toxicity dependent on

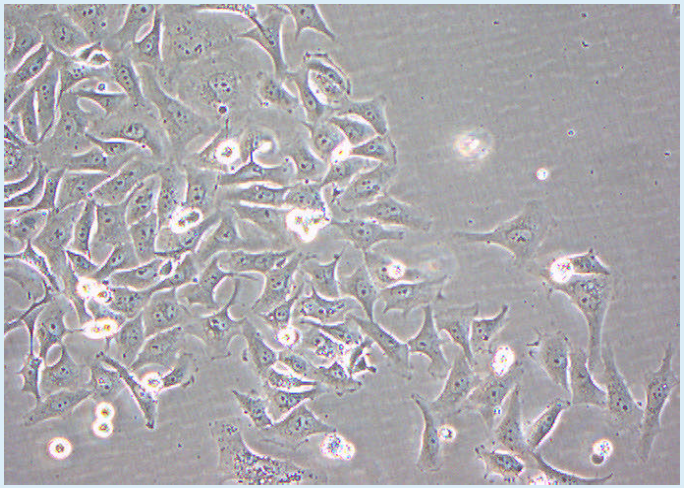
CONCENTRATION & LENGTH OF EXPOSURE

Biofunctionalilty:Cellular interactions

- Interactions between material (or implant) and surrounding tissue are complex

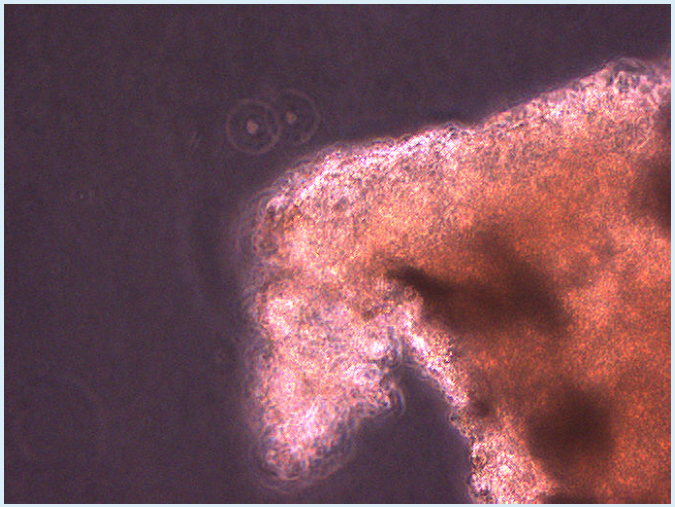


- Restorative materials may elicit responses from pulp, gingiva and oral mucosa

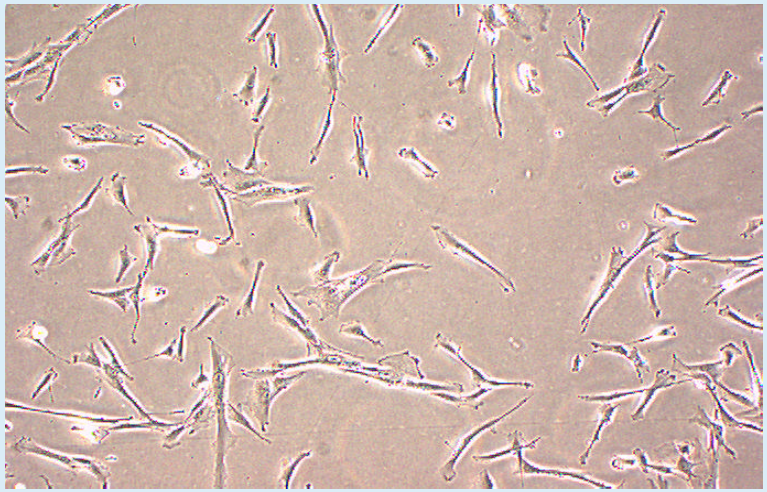


Different cell types involved

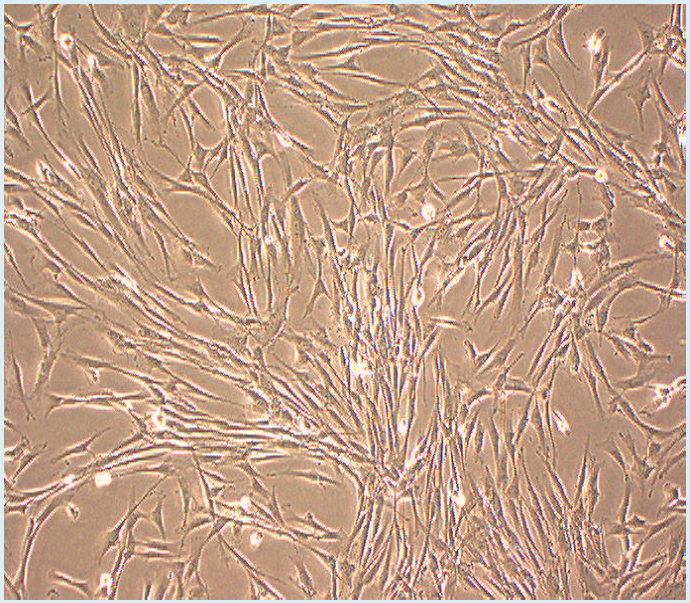
Cell harvesting from dental pulp



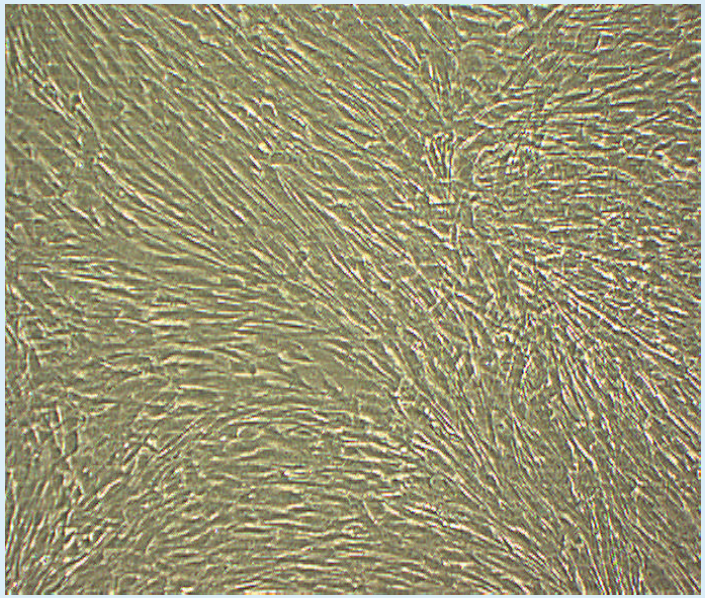
Dental pulp tissue explant



Migrating cells 2-3- days



Expanding cells 7days in culture



Confluent cultures 28 days

Augmentation of Bone defects in dentistry

- **Preparation of good bony layer prior to implantation is mandatory to ensure long term success of implant**

Treatment modes are dependent on defect size

- **Bone substitutes (e.g bone matrix, TCP, HA) have been used - usually characterized by long healing time 6-12 months to achieve sufficient bone regeneration**

- **The success of these materials is whether they can give rise to *de novo* bone and remodelling that is necessary for the primary stability of endosseous implants**

Commercially available bone substitute materials for shortening therapy protocols

•**NanoBone™** – this comprises nanocrystalline HA in silica gel matrix-designed to be used with blood to enhance plasma proteins and assist the attachment of stem cells to encourage *de novo* bone formation.
Can be used for:

- Sinus floor elevations
- Lateral and vertical augmentations
- Covering buccal fenestrations
- Socket preservation

Others include:
Osseotite™
NanoTite™
Osseospeed™
Straumann SLActive

Assessment of Biofunctionality of bone contacting implants

Reasons for modifying the surface:

- Surface modifications play a significant role in the interaction and success of the implant to the adjacent tissue-

Study focused on the effect of different **chemical and electrochemical treatment** on the bioactivity of titanium

Anodic Spark Deposition (ASD)

- ASD is an electrochemical treatment of titanium surface for use in implantology

- This treatment aims to obtain a thickened titanium oxide layer doped with **calcium** (Ca) and **phosphorus** (P), known to enhance **osseointegration** properties of titanium implants

Protein adsorption leading to desired cell adhesion can be achieved by:

(1) Choice of material

Bioactive materials such as glasses, ceramics allow the formation of the hydroxy-carbonate-apatite (HCA) layer which favour cell adhesion

(2) Design of the implant

Shape, porosity, composite materials, incorporated factors all have an effect on cell adhesion.

(3)Surface modifications

Hypothesis

1. Surface physicochemical properties contribute important **environment cues** for subsequent bone cell adhesion by determining preferential protein adsorption onto modified surfaces, and hence enhancing osseointegration

2. Surface nano-topography plays a key role in bone cell behaviour, including cell adhesion, proliferation, and differentiation.

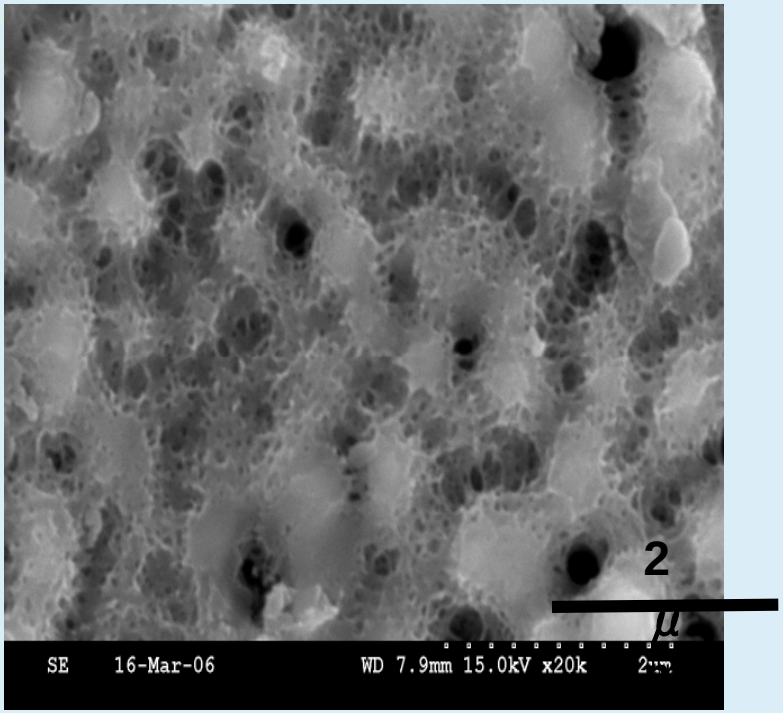
Biofunctionality of modified titanium surfaces

1. The physicochemical properties
- Surface topography using Scanning Electron Microscopy (SEM)
- Surface chemical composition using Energy Dispersive X-ray Spectroscopy (EDS)
- Atomic Force Microscopy (AFM)

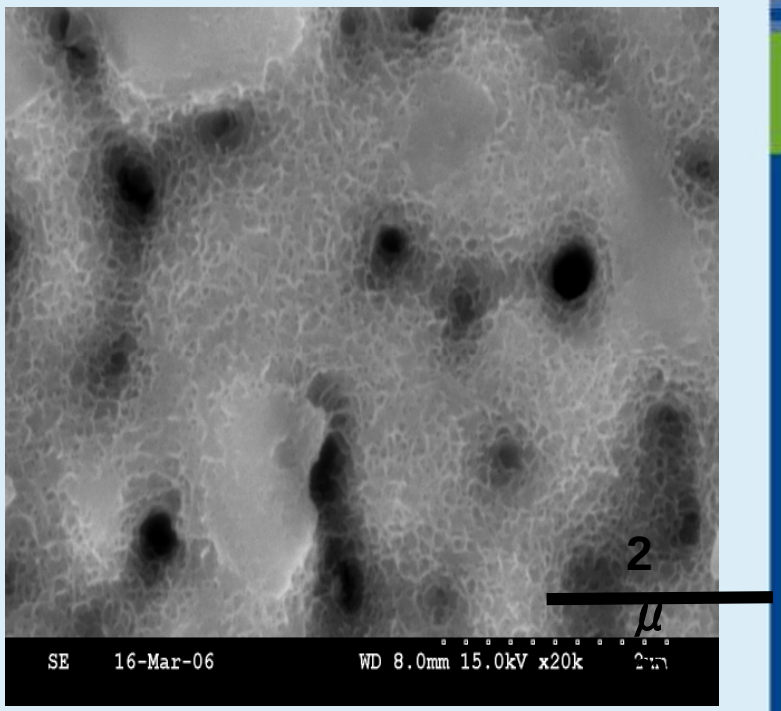
2. To assess the *in vitro* cellular response
- Cell viability (MTT assay)
- Cell Proliferation (Alamar Blue assay,DNA, protein, cell counts)
- Cell adhesion and morphologic study (SEM)

Qualitative Observations

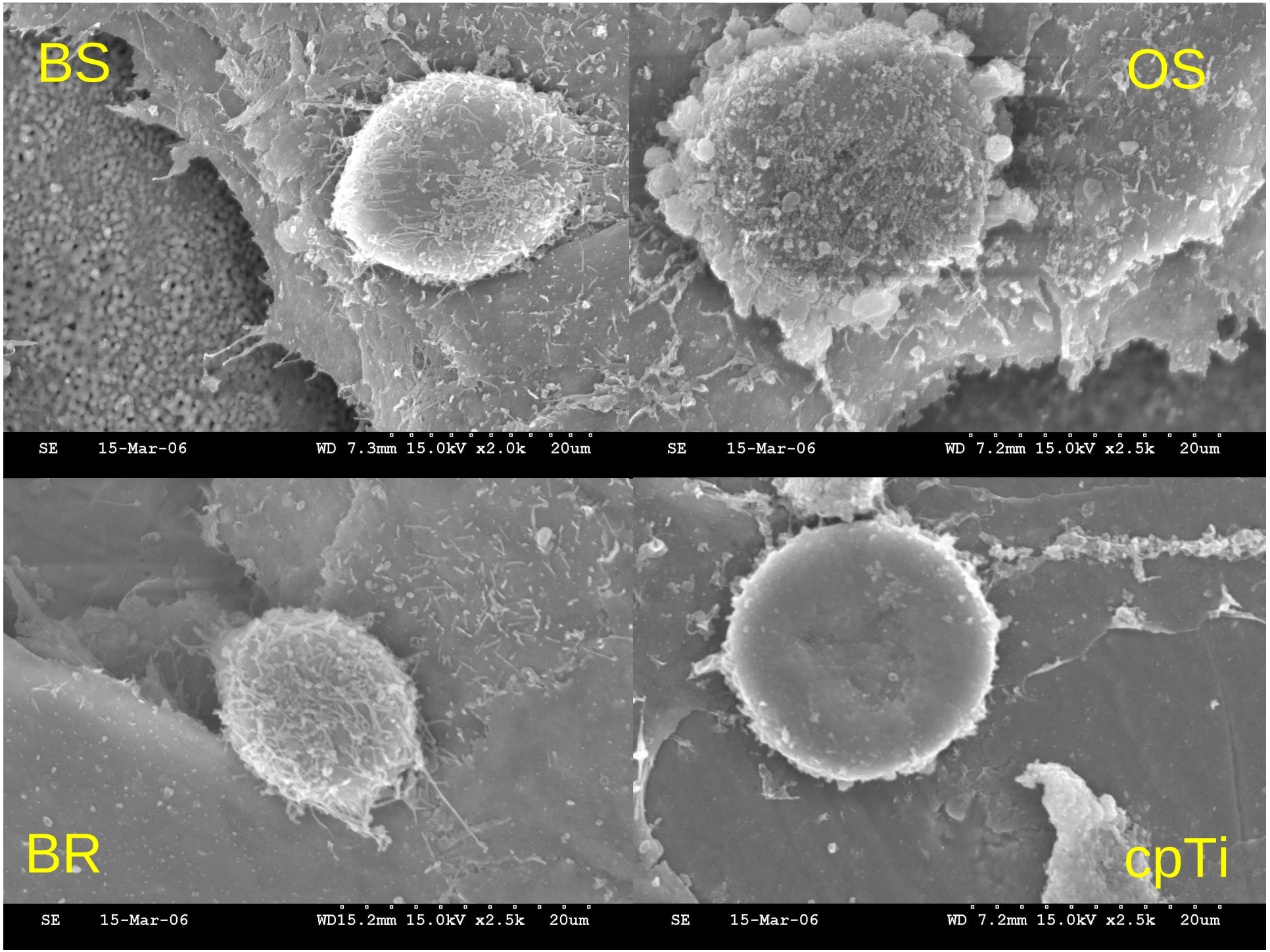
BioSpark



OsseoSpark



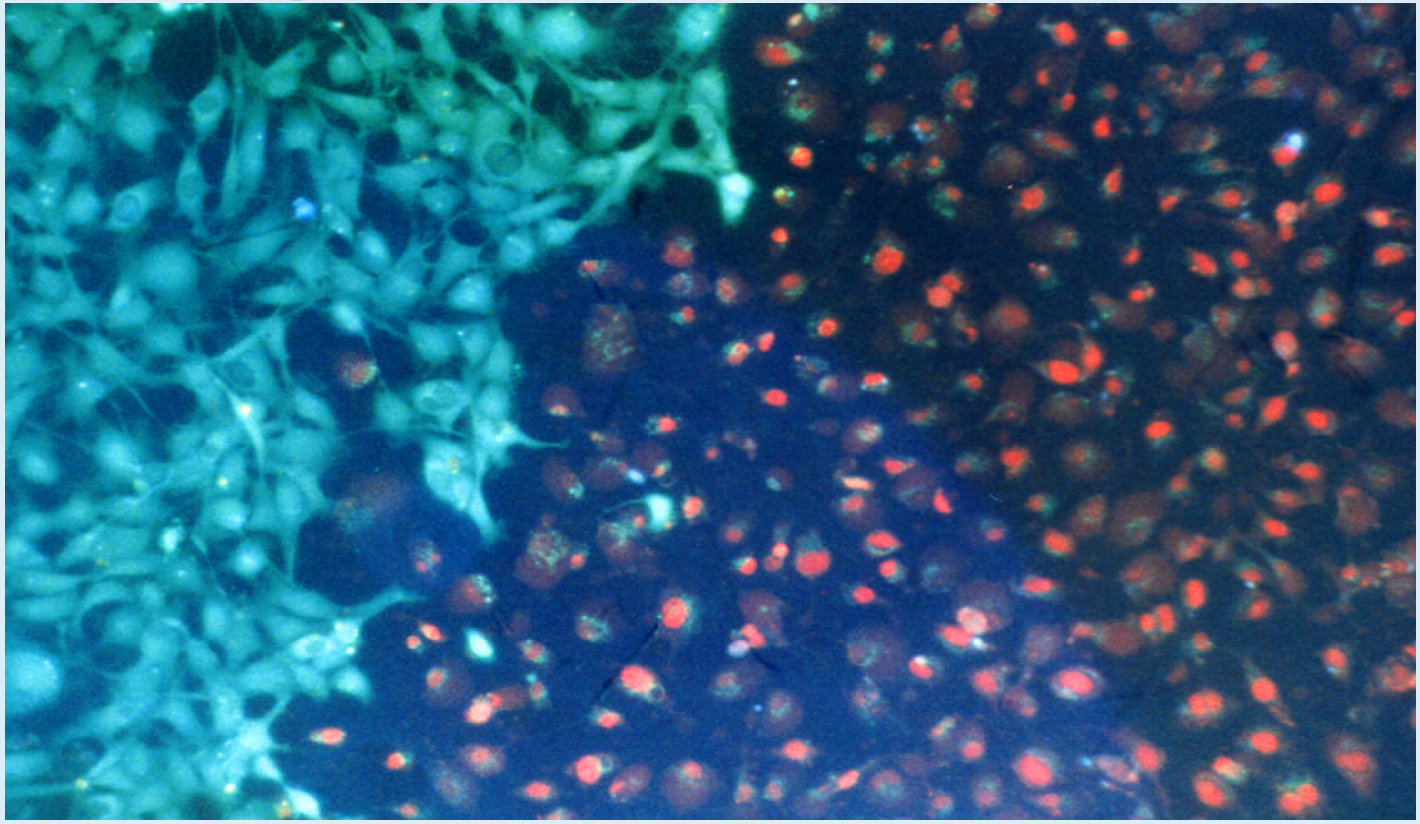
SEM comparison (x20k)


BS
OS
SE 15-Mar-06 WD 7.3mm 15.0kV x2.0k 20um
SE 15-Mar-06 WD 7.2mm 15.0kV x2.5k 20um
BR
cpTi
SE 15-Mar-06 WD15.2mm 15.0kV x2.5k 20um
SE 15-Mar-06 WD 7.2mm 15.0kV x2.5k 20um

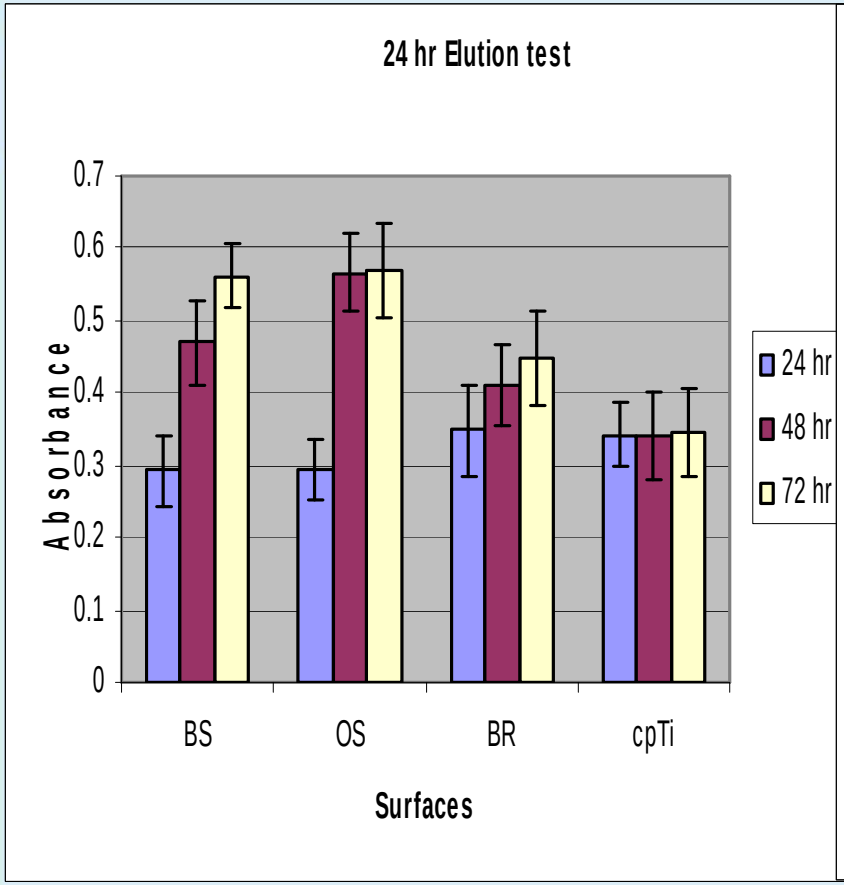
Toxic effect on cells (e.g.leachables) can cause alterations in cell membrane function

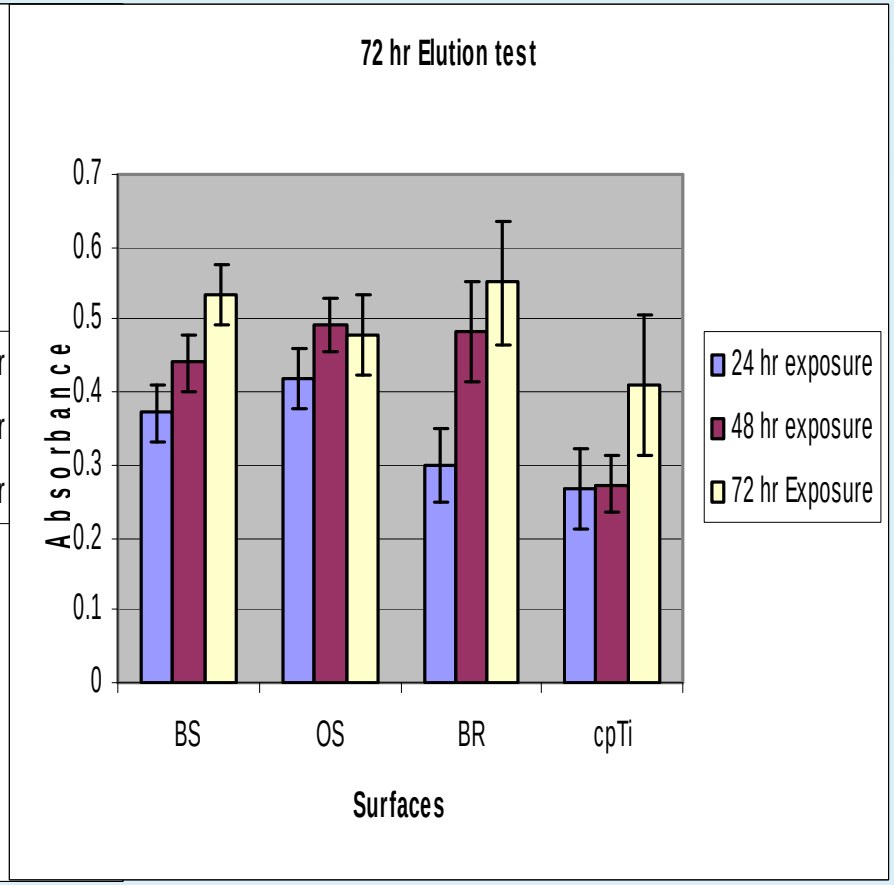
LIVE-DEAD STAIN: Photo Dynamic Therapy to kill cells on surfaces

Stained with Fluorescent agents (Calcein –AM)
Stains healthy cells –GREEN and Dead cells-RED



MTT assay results





24 hr eluant

72 hr eluant

Summary of Biofucntionality

- ASD modified titanium surfaces have a nanostructured topography enriched in Calcium and Phosphorus resulting in:
- Enhanced selective protein adsorption (fibronectin)
- High osteoblast adhesion and proliferation
- High mineralization capability
- Potentially enhancing osseointegration

CONCLUSION

- *In vitro* tests are an integral part of biocompatibility evaluation prior to *in vivo* testing

- All materials implanted in, or in contact with, the body should be biocompatible

All current dental materials in use are considered acceptable and cytocompatible, when properly handled

Adverse systemic effects are rarely documented,self-limiting and tend to be of an allergic nature

The biomaterial-tissue response should be appropriate such that the continued safe and effective performance of the material is ensured

Acknowledgements

Lertrit Sarinnaphakorn (PhD student)
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Thank you for your attention