Biocompatibility tests

Test article preparation is a critical variable in the conduct of the biocompatibility tests

Therefore, it is important to understand how the test articles compare to the medical device in its final finished form (e.g., sterile, if applicable).

Use of Medical Device in Final Finished Form or Representative Test Article

When biocompatibility testing is necessary, the Agency recommends testing medical devices in the condition that they will be used, whenever possible. This could include final, packaged devices, or as sterilized by an end user, if appropriate

If the medical device in its final finished form cannot be used for biocompatibility testing, a test article (e.g., coupons or “representative components”) may be considered.

The representative test article should undergo the same manufacturing and sterilization processes, have the same chemical, physical, and surface properties, and have the same ratio of component materials as the medical device in its final finished form.

In situations where differences exist between the medical device in its final finished form and the test article, additional information describing how these differences could impact study findings should be provided.

For example, when testing an individual device component, a low-level tissue response could be observed, but when all of the components are tested within a medical device in its final finished form, a more robust tissue response could occur. If there are differences between the medical device in its final finished form and the representative test article, additional information may aid in determining the appropriateness of the selected test article.

For example, extraction and surface characterization techniques may be appropriate to demonstrate that the surfaces are equivalent in geometry and surface properties, and that the chemicals leaching from the test article display the same kinetics, chemical identity and relative quantity as those eluting from the medical device in its final finished form.

Testing of In Situ Polymerizing and/or Absorbable Materials

For devices made from in situ polymerizing and/or absorbable materials, we recommend that test article preparation be representative of the device in its final finished form

In addition, we recommend that biocompatibility be evaluated for the medical device in its final finished form as well as at various time points over the course of polymerization and/or degradation to ensure that starting, intermediate, and final degradation products are assessed.

Should biocompatibility assessment of the materials during degradation be needed, preparation of test articles using in vitro degradation methods may be considered with appropriate technical justification

Test articles degraded in vitro may be used for biological testing, and/or chemically analyzed to show that the material breaks down into intermediate or final degradation products that are known to be non-toxic at the levels present.

However, depending on the materials of manufacture and the degradation testing conditions, accelerated degradation testing may not result in the same intermediate or final degradation products and therefore may not be acceptable

For in vivo tests for devices made of in situ polymerizing or absorbable materials, the assessment time points would depend on the polymerization and degradation kinetics

We recommend that assessments be targeted to demonstrate how the device materials degrade over time and continue until the absorbable material and/or its degradation products are no longer present in the tissue (e.g., microscopically), if possible.

Alternatively, it may be acceptable to provide a rationale for ending the study earlier, if the rationale includes an estimate of the percentage (%) of absorbable material remaining in the tissue, and confirmation that a steady state biological tissue response is achieved.

For in vitro biocompatibility tests conducted with extracts of an in situ polymerizing or absorbable device, chemical analytical testing of the extract may be useful to determine whether the extract is representative of leachables during the polymerization or degradation processes,

and if multiple biocompatibility tests with different extracts are needed to represent different stages of the polymerization or degradation processes

If test articles are pre-polymerized prior to extraction, unreacted constituents that may be available during physiologic polymerization may or may not be available for extraction from a pre-polymerized test article.

For systems that may not be polymerizable in traditional extraction media, alternative approaches may be necessary

Connective tissue -- Connective tissue (CT) is one of the four basic types of animal tissue, along with epithelial tissue, muscle tissue, and nervous tissue. It develops from the mesoderm. Connective tissue is found in between other tissues everywhere in the body, including the nervous system.

They support and protect the body. All connective tissue consists of three main components: fibers (elastic and collagenous fibers),[1] ground substance and cells

Vascular elements – vessel elements like arteries, veins etc or simply blood vessels.

aseptic loosening - Aseptic loosening is the failure of the bond between an implant and bone in the absence of infection

carcinogenesis - the initiation of cancer formation.

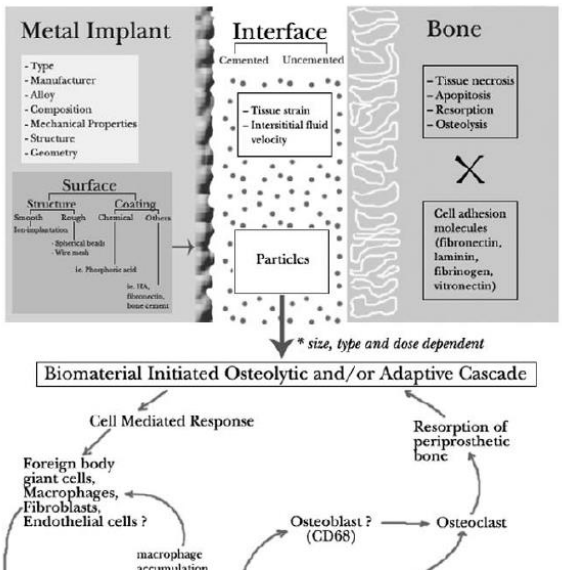
inflammation - a localized physical condition in which part of the body becomes reddened, swollen, hot, and often painful, especially as a reaction to injury or infection.

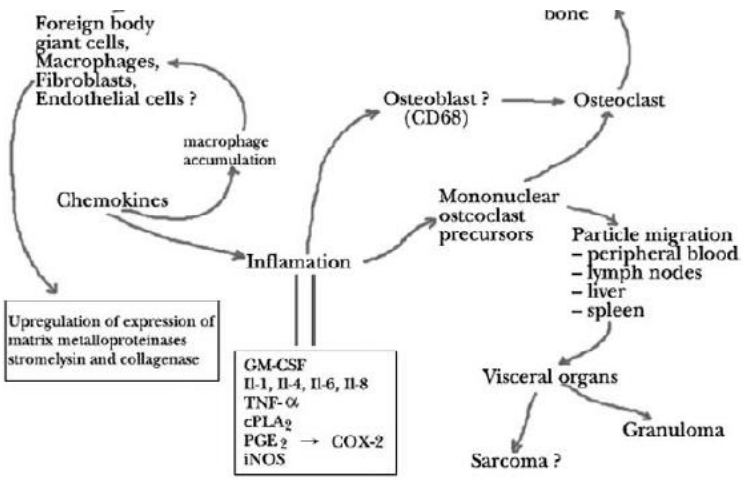
bone marrow depletion - is the decrease in production of cells responsible for providing immunity (leukocytes), carrying oxygen (erythrocytes), and/or those responsible for normal blood clotting (thrombocytes).[1]Bone marrow suppression is a serious side effect of chemotherapy and certain drugs affecting the immune system such as azathioprine.[2] The risk is especially high in cytotoxic chemotherapy for leukemia.

Uncemented - unsettled

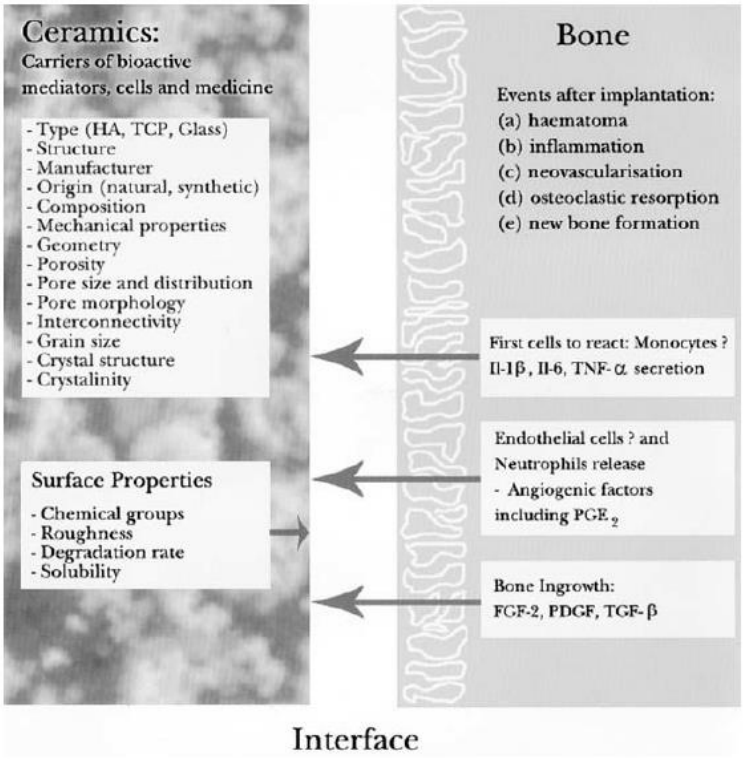
endoprostheses - An artificial hip joint is an implanted prosthesis (endoprosthesis) to replace the functions of the hip joint after a loss of functionality

metal implant action

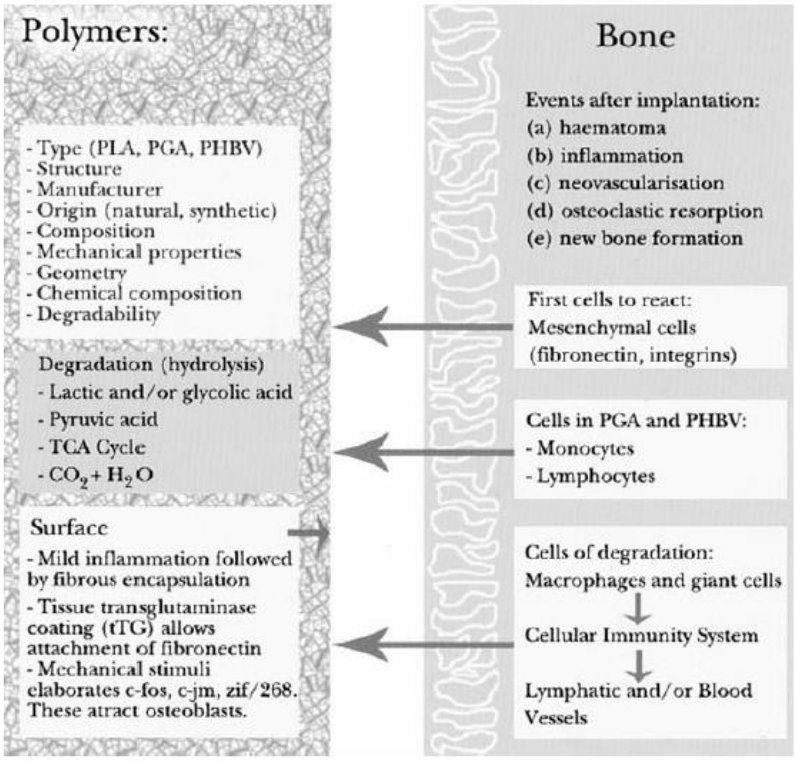



Foreign body
giant cells,
Macrophages,
Fibroblasts,
Endothelial cells ?
macrophage
accumulation
Chemokines
Osteoblast ?
(CD68)
Osteoclast
Mononuclear
ostcoclast
precursors
Particle migration
– peripheral blood
– lymph nodes
– liver
– spleen
Inflamation
Upregulation of expression of
matrix metalloproteinases
stromelysin and collagenase
GM-CSF
Il-1, Il-4, Il-6, Il-8
TNF-α
cPLA2
PGE2 → COX-2
iNOS
Visceral organs
Granuloma
Sarcoma ?

Ceramic


Ceramics:
Carriers of bioactive
mediators, cells and medicine
- Type (HA, TCP, Glass)
- Structure
- Manufacturer
- Origin (natural, synthetic)
- Composition
- Mechanical properties
- Geometry
- Porosity
- Pore size and distribution
- Pore morphology
- Interconnectivity
- Grain size
- Crystal structure
- Crystalinity
Surface Properties
- Chemical groups
- Roughness
- Degradation rate
- Solubility
Bone
Events after implantation:
(a) haematoma
(b) inflammation
(c) neovascularisation
(d) osteoclastic resorption
(e) new bone formation
First cells to react: Monocytes ?
Il-1β, Il-6, TNF-α secretion
Endothelial cells ? and
Neutrophils release
- Angiogenic factors
including PGE2
Bone Ingrowth:
FGF-2, PDGF, TGF-β
Interface

Polymer



Traumatology - is the study of wounds and injuries caused by accidents or violence to a person, and the surgical therapy and repair of the damage.

how ceramics promote healing of bone??

Ans: promoting healing of bone in clinical practice alone or in combination with other materials with their osteogenic, osteoconductive, and/or osteoinductive properties

Osteo - relating to the bones.

What about the bio activity of ceramics??

Ans: Bioactivity of ceramics is mainly limited to osteoconduction as long as they do not carry cells and/or growth factors

What is the biological response of ceramic implants??

Ans: Biological response to these ceramics follows a similar cascade observed in fracture healing. This cascade includes (1) hematoma formation, (2) inflammation, (3) neovascularization, (4) osteoclastic resorption, and (5) new bone formation.

Meaning of the above words

hematoma is an abnormal collection of blood outside of a blood vessel

Neovascularization is the natural formation of new blood vessels

In vivo??

are those in which the effects of various biological entities are tested on whole, living organisms or cells, usually animals, including humans, and plants, as opposed to a tissue extract or dead organism

in vitro??

studies are performed with microorganisms, cells, or biological molecules outside their normal biological context

biodur 108??

Type Analysis

Single figures are nominal except where noted.

Carbon (Maximum)	0.08 %	**Manganese**	21.00 to 24.00 %
Phosphorus (Maximum)	0.030 %	**Sulfur (Maximum)**	0.010 %
Silicon (Maximum)	0.75 %	**Chromium**	19.00 to 23.00 %
Nickel (Maximum)	0.10 %	**Molybdenum**	0.50 to 1.50 %
Copper (Maximum)	0.25 %	**Nitrogen (Minimum)**	0.90 %
Iron	Balance		

0.05% max nickel available upon request

What is tja??

Total joint arthroplasty

Arthroplasty --surgical reconstruction or replacement of a joint.

Flexural rigidity??

Flexural rigidity is defined as the force couple required to bend a non-rigid structure in one unit of curvature or it can be defined as the resistance offered by a structure while undergoing bending.

Stiffness is the rigidity of an object — the extent to which it resists deformation in response to an applied force

Bioactive - having a biological effect.

Fretting corrosion - Fretting refers to wear and sometimes corrosion damage at the asperities of contact surfaces. This damage is induced under load and in the presence of repeated relative surface motion, as induced for example by vibration.

Gene therapy - the introduction of normal genes into cells in place of missing or defective ones in order to correct genetic disorders.