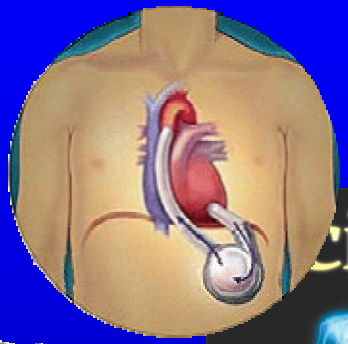
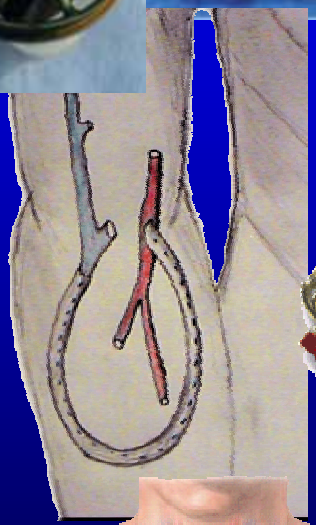
# Methods of Biomaterials Testing
# Lesson 1 - Introduction

Manfred Maitz

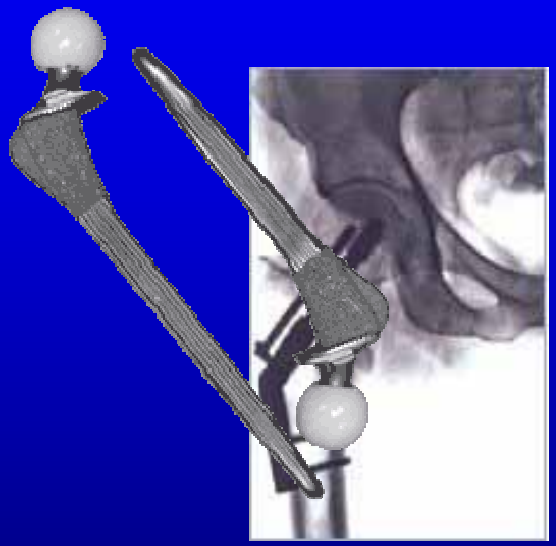
Chengdu, 24.02.2005

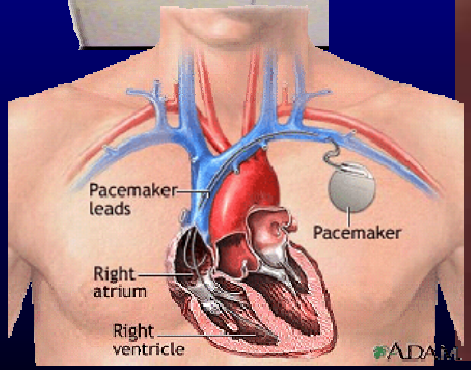
# Biomedical Devices

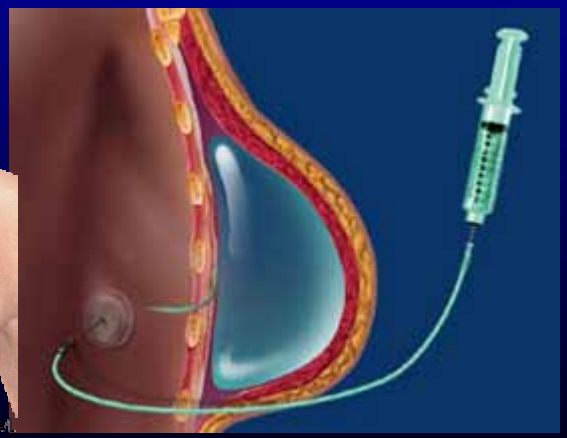


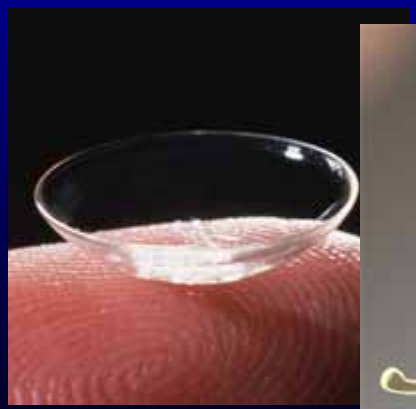


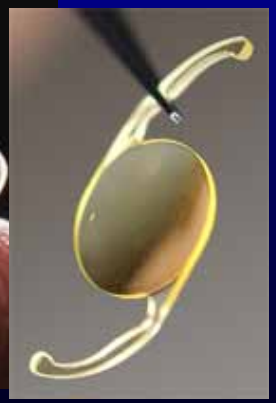










# Testing – What For?

- Conformity with (external) Standards
  - FDA, ASTM, ISO, DIN, EN…
- Quality assurance
  - Conformity with internal standards
  - “Fulfill the specifications”

“Standardized” Testing

- Defined rules
- Defined drop-out values
- High requirements of documentation

- Gain of knowledge
  - No standards
    but requirements of statistics

“Scientific” Testing

- No defined rules
- No drop-out values
- High requirements background knowledge

# Outline of the Lecture

| Lesson | Topic |
|---|---|
| 1 | Introduction |
| 2 | Cell Culture and Tissue Engineering |
| 3-5 | Biochemical “Working Tools” |
| 6-7 | Vitality, Toxicity, Mutagenicity |
| 8-9 | Principle Biological Reactions |
| 10 | Specific Biology: Bone |
| 11-12 | Specific Biology: Blood Vessel and Blood |

**Start the Lesson with one scientific article!**

# Scientific Articles I

- Endothelialization of a non-woven silk fibroin net for use in tissue engineering: growth and gene regulation of human endothelial cells.
- Tissue response and biomaterial integration: the efficacy of in vitro methods.
- Compartmentalized coculture of porcine arterial endothelial and smooth muscle cells on a microporous membrane.
- Flow cytometry for assessing biocompatibility.
- Analysis of plasma protein adsorption on polymeric nanoparticles with different surface characteristics.
- *In vivo* leukocyte cytokine mRNA responses to biomaterials are dependent on surface chemistry.
- Antibody microarray for correlating cell phenotype with surface marker.
- Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays.
- Complement activation by IgG immobilized on methylated silicon.
- Use of an enzyme linked immunosorbent assay (ELISA) for quantification of proteins on the surface of materials.
- In situ complement activation by polyethylene wear debris.

# Scientific Articles II

- Human bone cell cultures in biocompatibility testing. Part I & II
- Culture and behavior of osteoblastic cells isolated from normal trabecular bone surfaces.
- Comparative study of the osteoinductive properties of bioceramic, coral and processed bone graft substitutes.
- Expression of selected osteogenic markers in the fibroblast-like cells of rat marrow stroma.
- Osseointegration of Ti6Al4V alloy implants coated with titanium nitride by a new method.
- Prothrombotic phenotype diversity of human aortic endothelial cells in culture.
- Measuring the degree of plasma contact activation induced by artificial materials.
- Hemocompatibility of treated polystyrene substrates: Contact activation, platelet adhesion, and procoagulant activity of adherent platelets.
- Measurement of phosphatidylserine exposure in leukocytes and platelets by whole-blood flow cytometry with annexin V.
- Stent coating with titanium-nitride-oxide for reduction of neointimal hyperplasia.

# Presentations Available

## Definitions

**Biocompatibility**

Acceptance of an artificial implant by the surrounding tissues and by the body as a whole

- non toxic
- non mutagenic/ non carcinogenic
- do not irritate surrounding structures
- do not provoke an abnormal inflammatory response
- do not induce allergic or immunologic reactions

**Biofunctionality**

Behaviour in specific biological environment

- Locally appropriate behaviour
- Adequate mechanical properties
- Appropriate optical properties
- Appropriate density
- Support of the local biological functions

- Sterilizability
- Manufacturability
- Long-term storage
- etc.

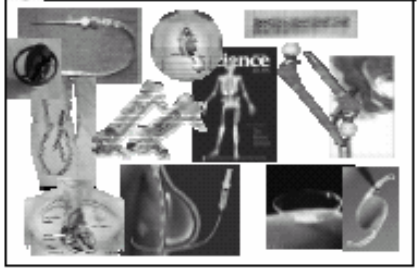
## Consequences for Testing

The difference between "Biomaterials Research" and "Materials Science" is the word "Bio"

- All testing procedures of "Materials Research"
  - Roughness
  - Surface free energy
  - Hardness
  - Corrosion/ degradation susceptibility, degradation products
  - Generation of reactive oxygen species
- Computer simulation, Finite Element Calculations
- Biocompatibility testing
  - toxicity, mutagenicity, sensitization
- Biofunctionality testing

  Set-up adequate models of the implant site and ask the right questions
  - *In vitro* (cell culture) models
  - *In vivo* (animal) experiments
- Clinical long term studies

## Every Device has Specific Requirements for Testing



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