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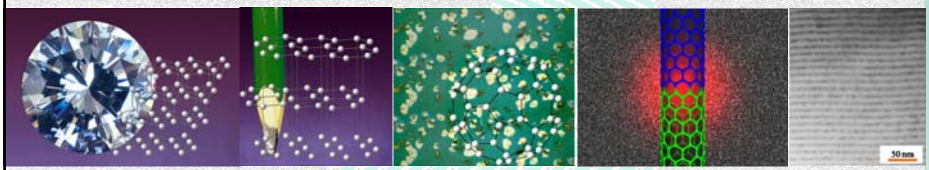
Biomaterial



CARBON

J.M. Lackner, W. Waldhauser

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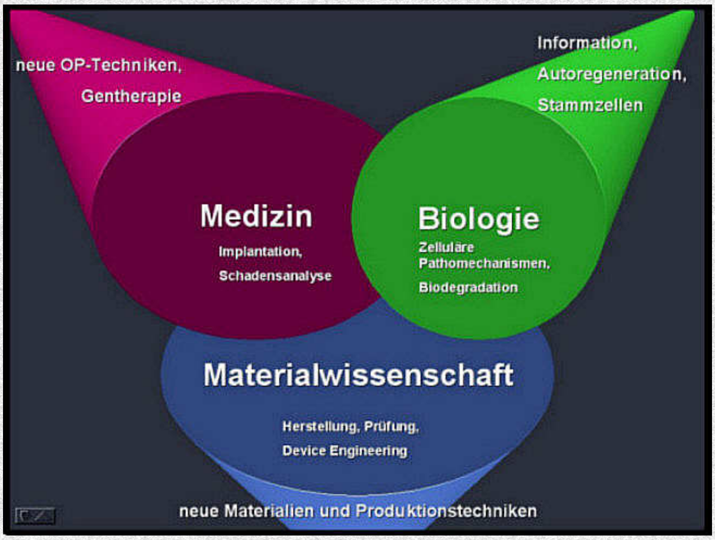
Preamble – Biomaterial research

INTERDISCIPLINARITY



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Contents

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Contents

1. Biocompatibility – Aspects of biomaterial-tissue interaction
2. Bulk biomaterial „carbon“
3. Surface coating biomaterial „carbon“
4. Conclusions

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Biocomptibility – Aspects

- Primary aspects and definitions
- Biofunctionality – Implant design
- Biomaterial – tissue interaction
- Host response

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Biomaterials

= artificial / synthetic materials with biocompatibility for the contact duration to the biosystem (tissue, body fluids)

≠ materials of biological origin

=> Medical equipment and devices (syringes, catheters, etc.), Implants

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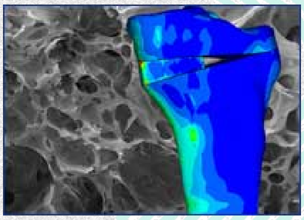
Biocompatibility

= compatibility between a technical and biological system

(1) Structural compatibility:
Adapting the implant structure to the (geometrical, mechanical, etc.) behavior of the donee tissue



(2) Surface compatibility:
Adapting chemical, physical, biological and morphological surface properties to the donee tissue

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Development in Biomaterials

Generation	*Materials*	*Body reaction*
1	Industrial materials	Distinct foreign body reaction (inflammation)
2	Inert materials	No reaction
3	Bioactive and metabolic inductive	Triggering of natural tissue growth
4	Cell-material compounds (vital-avital)	Scaffolds with cultivated cells

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Biocompatible materials features

1. Absence of carcinogenicity (the ability or tendency to produce cancer)
2. Absence of immunogenicity (absence of a recognition of an external factor which could create rejection
3. Absence of teratogenicity (ability to cause birth defects)
4. Absence of toxicity

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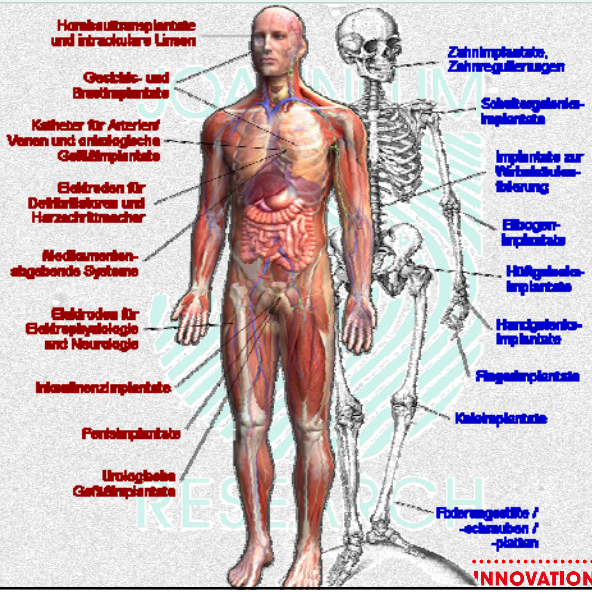
Implants – Overview



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Biofunctionality - Aspects

- Load transmission (e.g. bone healing – screws, nails, etc.)
- Joint replacement (tribology, friction – lubrication – wear, hip, knee, ellbow, shoulder, finger)
- Fluid transport (catheders, bypasses, stents, etc.)
- Optical and acoustic transmission (lenses, cochlea implants, etc.)
- Control of drug-delivery (drug-eluting stents, wound care, etc.)

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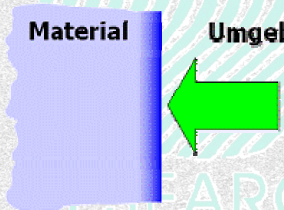
Biomaterial – tissue interaction

Proteins, cells and tissue sense:

- Surface physical properties (roughness, porosity, etc.)
- Surface chemistry (hydrophilicity, dissolution – corrosion, etc.)
- Bulk mechanical properties (elasticity, compliance, etc.)
- Bulk geometry (edges, etc.)



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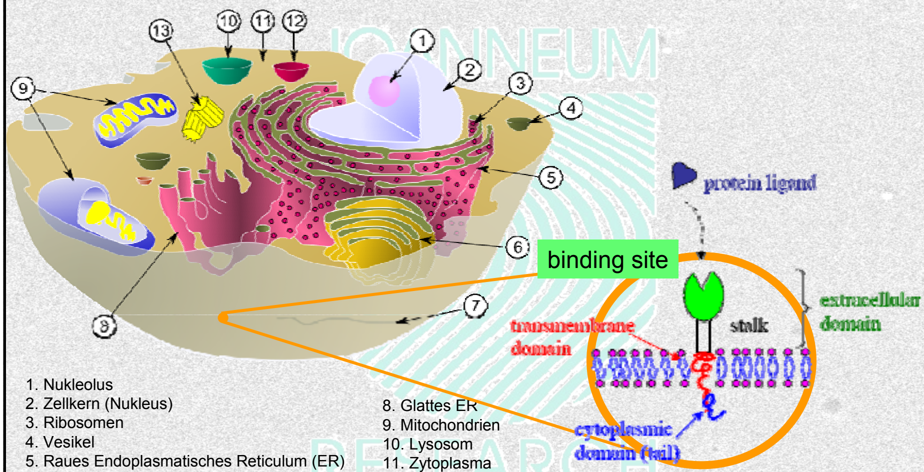
Where's interaction in/on the cell?



1. Nukleolus
2. Zellkern (Nukleus)
3. Ribosomen
4. Vesikel
5. Raues Endoplasmatisches Reticulum (ER)
6. Golgi-Apparat
7. Mikrotubuli
8. Glattes ER
9. Mitochondrien
10. Lysosom
11. Zytoplasma
12. Mikrobodies
13. Zentriolen

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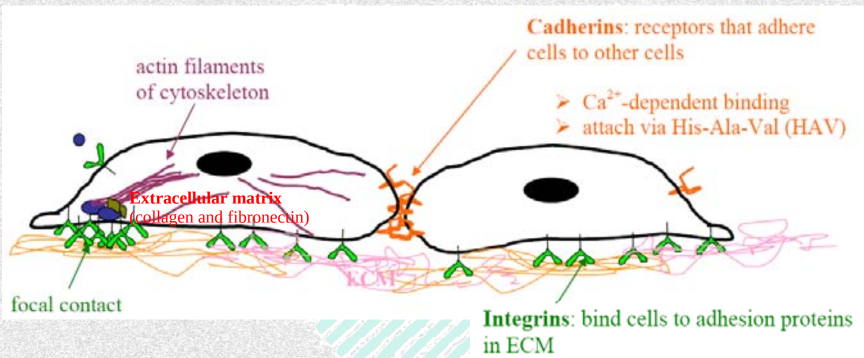
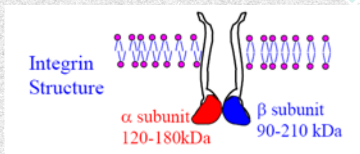
Cell adhesion to their surrounding





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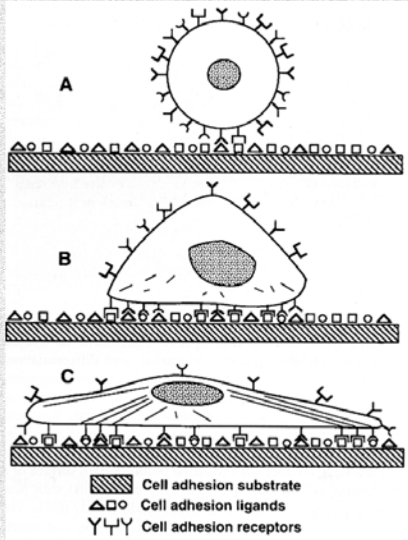
Steps in cell adhesion



(A) Initial contact of cell with solid substrate .

(B) Formation of bonds between cell surface receptors and cell adhesion ligands .

(C) Cytoskeletal reorganization with progressive spreading of the cell on the substrate for increased attachment strength .

6

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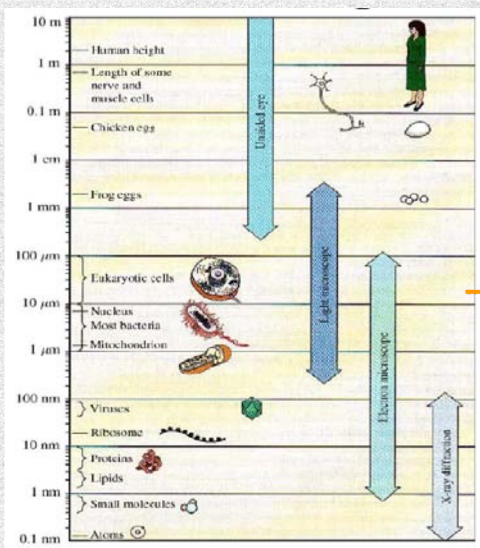
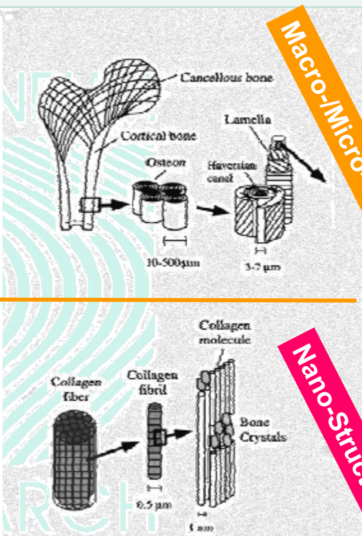
Scale of Interactions





Macro-/Micro-Structure

Nano-Structure

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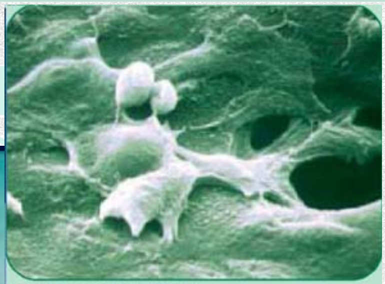
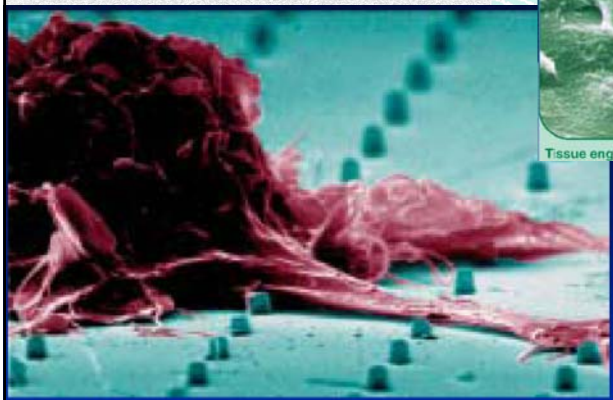
Scale of interaction



Tissue engineered epithelium



Fibroblast cell on a nanostructured surface

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Implantation – Host respone

„Body“ recognices and eradicates any foreign substance entering the body (implant, drugs, organ transplant, etc.)

„body“ = tissue (lymphoid), cells (leucocytes) and biomolecules (antibodies)

Any substance, not seen to have body origin, = potential threat

=> eliminated („walled off“) to prevent interaction with normal tissue function

Cell indicators for host response:
=> Biomolecules (proteins, etc.)

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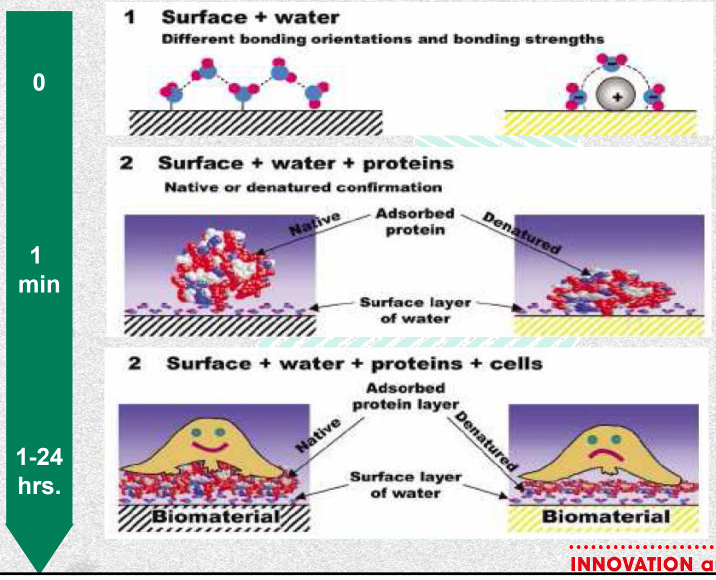
Host response – Micron scale



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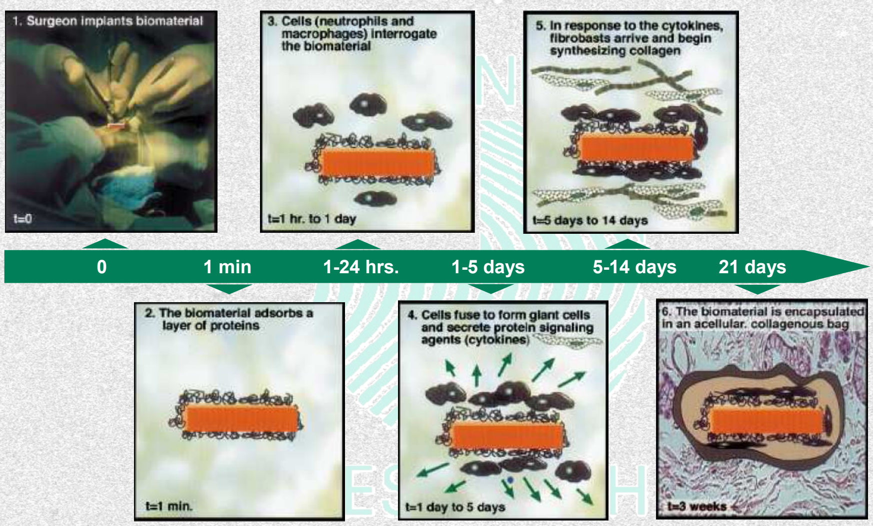
Host response – macro scale



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Host response - regeneration

Regenerative capacity of cells following injury:

Category	*Normal rate of replication*	*Response to stimulus / injury*	*Examples*
Renewing / labile	high	Modest increase	Skin, intestinal mucosa, bone marrow, bone
Expanding / stable	low	Marked increase	Endothelium, fibroblasts, liver cells
Static / permanent	none	No replication, replacement by scar	Heart muscle cells, nerves

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Host response - effects

- Acute inflammation
- Chronic inflammation
- Scarring

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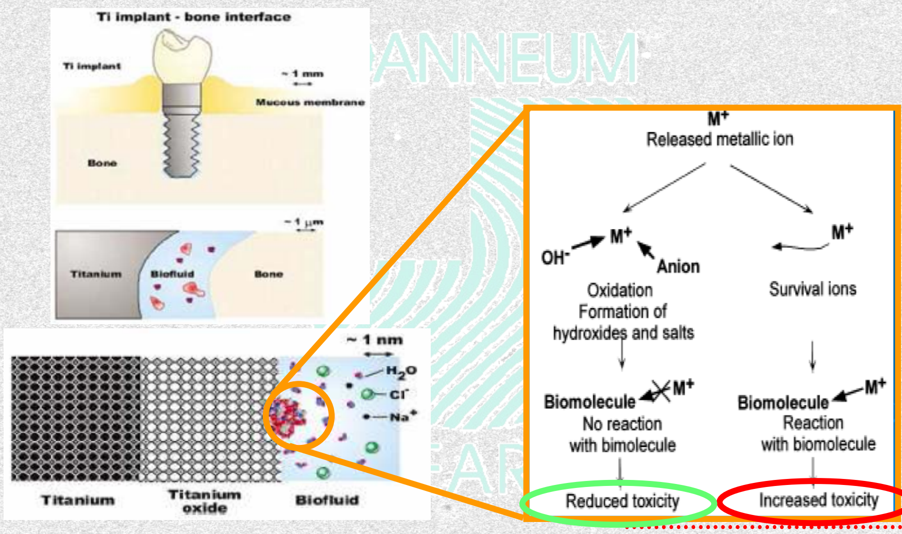
Host response – Bone



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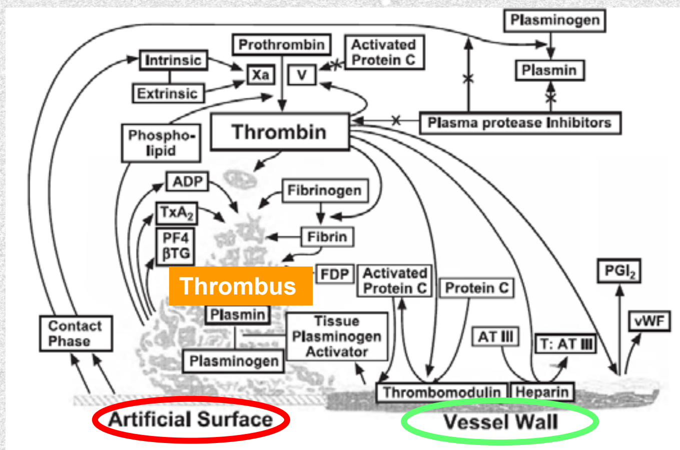
Host response - blood



Integrated hemostatic reactions between a foreign surface and platelets, coagulation factors, the vessel endothelium and the fibrinolytic system

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Bulk carbon biomaterials

- Pyrolytic carbon
- Carbon fibres (composite materials)

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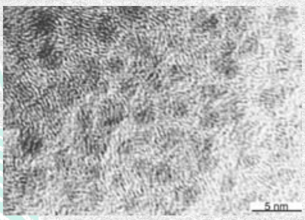
Pyrolytic Carbon (PyC)

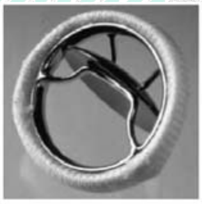
Manufacturing:
High temperature pyrolysis / thermal decomposition of hydrocarbons and subsequent recrystallization of elemental carbon

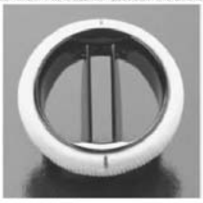
=> High mechanical strength (fatigue) and chemical resistance



TEM image of unalloyed PyC with turbostratic carbon crystals

Applications:
Artificial joints (rarely used)
Heart valves (main use)


Bjork Shiley - Tilting Disk


On-X Bileaflet

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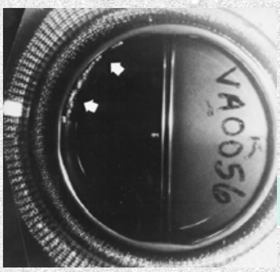
PyC - Biocompatibility

Generally high:

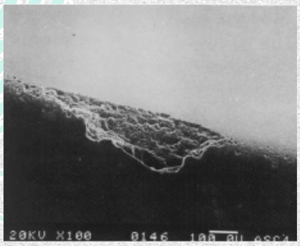
Test description	Protocol	Results
Klingman maximization	ISO/CD 10993-10	Grade 1; not significant
Rabbit pyrogen	ISO/ DIS 10993-11	Nonpyrogenic
Intracutaneous injection	ISO 10993-10	Negligible irritant
Systemic injection	ANSI/AAMI/ISO 10993-11	Negative—same as controls
Salmonella typhimurium reverse mutation assay	ISO 10993-3	Nonmutagenic
Physicochemical	USP XXIII, 1995	Exceeds standards
Hemolysis—rabbit blood	ISO 10993-4/NIH 77-1294	Nonhemolytic
Elution test (L929 mammalian cell culture)	ISO 10993-5, USP XXIII, 1995	Noncytotoxic

Biocompatibility problems



Cavitation

Pitting



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Carbon fibre composites (CFC)

Carbon fibre manufacturing:
Carbonizing or graphitizing of poly(acrylnitrile) fibres under tension at high temperatures and pressures

Applications:
Carbon fibre embedded in polymeric matrix (e.g. epoxy based)
=> Joint replacement (hip)

Carbon fibre embedded in bone cement
=> fracture healing

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Contents

1. Biocompatibility – Aspects of biomaterial-tissue interaction
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4. Conclusions

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Surface coating biomaterial carbon

- Three-dimensional surface structures
  – Carbon nanotubes
- Two-dimensional surface structures
  – Plasma polymers and DLC coatings

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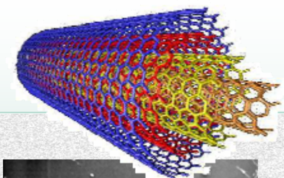
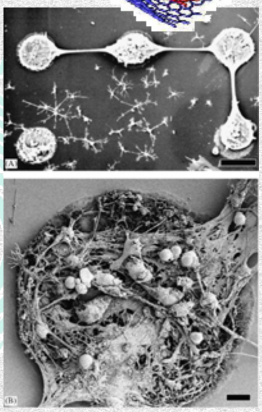
Carbon nanotubes

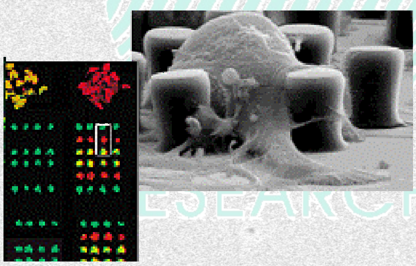


Manufacturing:
e.g. PVD / CVD growth

Applications:
- Cell tracking and labeling
- Sensing cellular behavior -->
- Cytotoxicity



neuron bridging an array of carbon nanotubes thereby creating neural networks.



Cell chips

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Biomaterials Volume 28, Issue 2, January 2007, Pages 344-353

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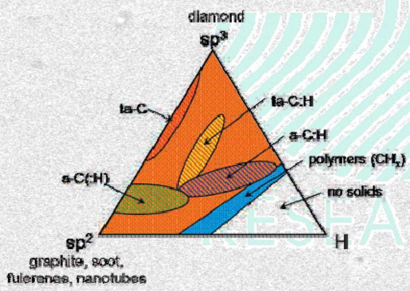
Surface coatings

Demands

Film thickness: as thick as necessary – as thin as possible

Stability: no delamination, no cracking
(otherwise: irreversible change of surface chemistry)

Carbon-based coatings



- Plasma polymers
- „DLC“

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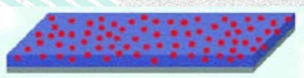
Plasma deposition

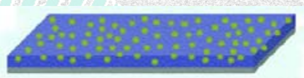
Effects of plasma on surfaces:

Ablation:
Removing surface layers

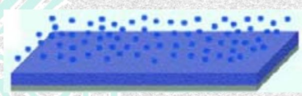
Implantation:
Sub-surface burying of atoms
(O, N, metal atoms etc.)



Radical / peroxide formation



Deposition
(plasmapolymerization,
metal / ceramic PVD & CVD)



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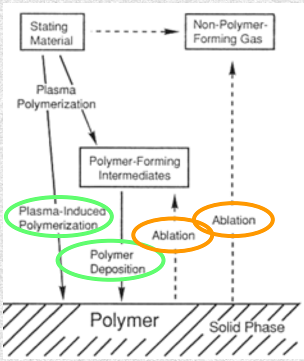
Plasma polymers

Deposition of polymerizable gases in glow discharge plasma:

e.g.: methane – ethylene - acetylene



Properties:
+: homogenous films
high variety of polymers, even from one monomer

-: complex mechanisms (control?)
mixture of structures

Applications:
- stents
- contact lenses

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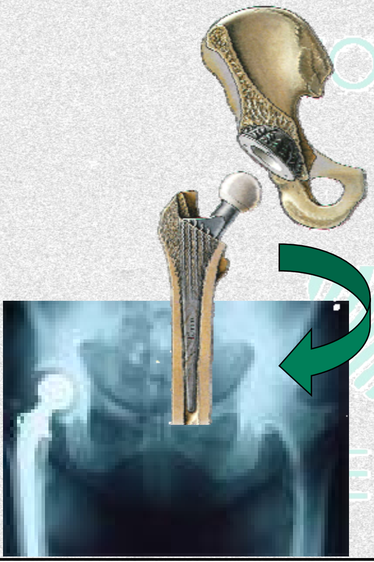
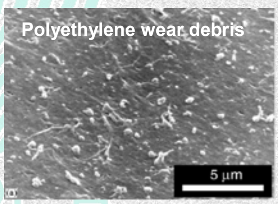
Bone contact – Artificial joints



Polyethylene wear debris is the main factor limiting the lifetime of the implants

Aseptic loosening, wear debris initiates inflammatory response
=> osteoclast cells activation
=> bone resorption



V. Saikko et al., Biomaterials 22 (2001) 1507

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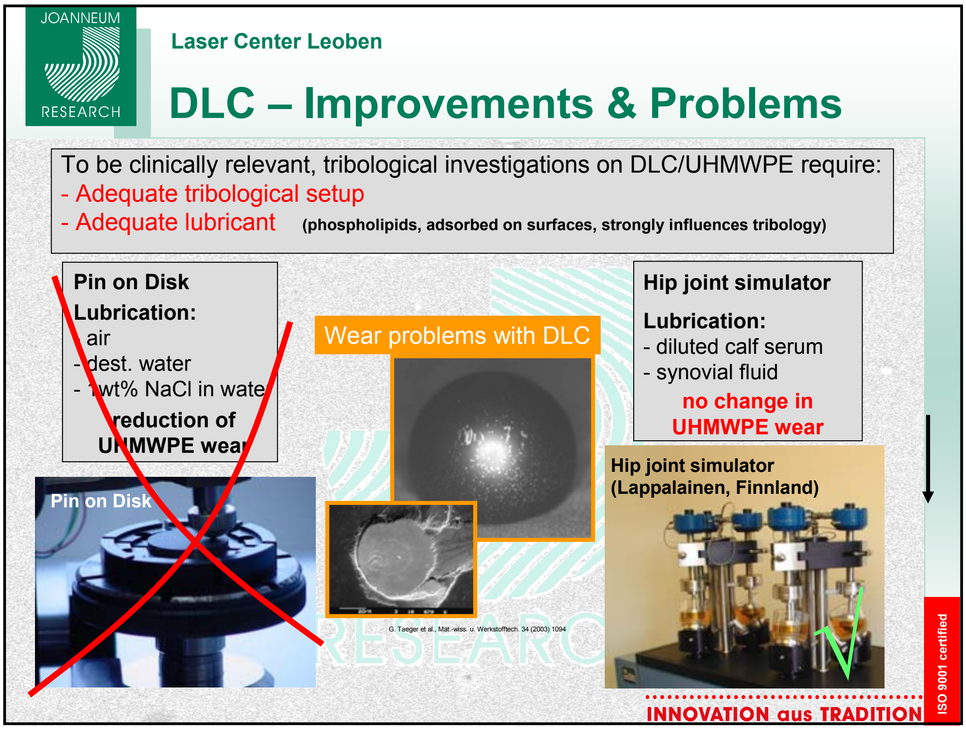
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DLC – Improvements & Problems
To be clinically relevant, tribological investigations on DLC/UHMWPE require:
- Adequate tribological setup
- Adequate lubricant (phospholipids, adsorbed on surfaces, strongly influences tribology)
Pin on Disk
Lubrication:
- air
- dest. water
- 1wt% NaCl in water
reduction of UHMWPE wear
Pin on Disk
Wear problems with DLC
G. Taeger et al., Mat.-wiss. u. Werkstofftech. 34 (2003) 1094
Hip joint simulator
Lubrication:
- diluted calf serum
- synovial fluid
no change in UHMWPE wear
Hip joint simulator
(Lappalainen, Finnland)
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DLC – Problems
ankle-joint, AISI Z5 CNMD 21 steel
coated with DLC (carbioceram™)
knee-joints coated with DLC
(carbioceram™)
=> USE NOW FORBIDDEN
Shoulder-joint, the Ti-alloy ball
coated with DLC (carbioceram™)
No medical follow-up on these products found
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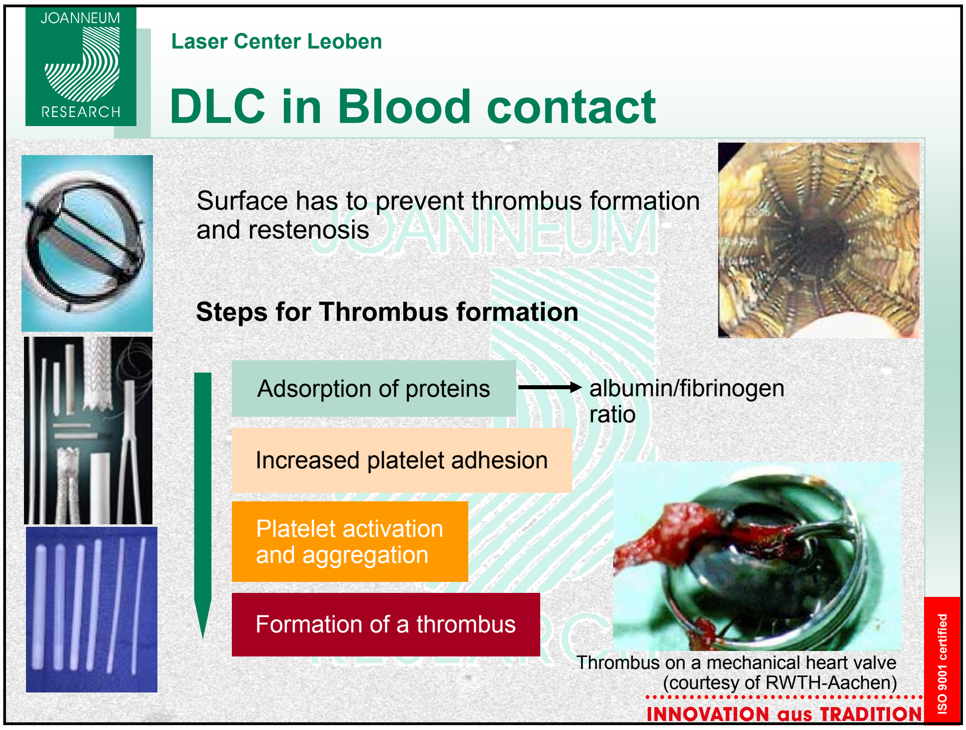
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DLC in Blood contact
Surface has to prevent thrombus formation and restenosis
Steps for Thrombus formation
Adsorption of proteins
albumin/fibrinogen ratio
Increased platelet adhesion
Platelet activation and aggregation
Formation of a thrombus
Thrombus on a mechanical heart valve (courtesy of RWTH-Aachen)
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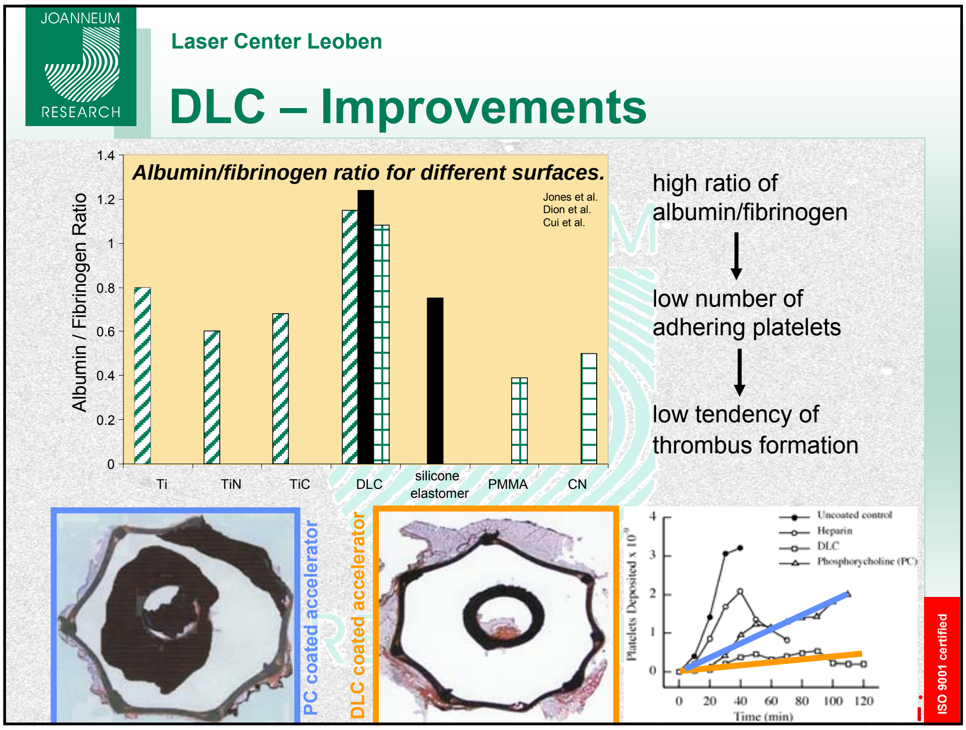
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DLC – Improvements
Albumin/fibrinogen ratio for different surfaces.
Jones et al.
Dion et al.
Cui et al.
Albumin / Fibrinogen Ratio
Ti
TiN
TiC
DLC
silicone elastomer
PMMA
CN
high ratio of albumin/fibrinogen
low number of adhering platelets
low tendency of thrombus formation
PC coated accelerator
DLC coated accelerator
Uncoated control
Heparin
DLC
Phosphorycholine (PC)
Platelets Deposited x 10^9
Time (min)
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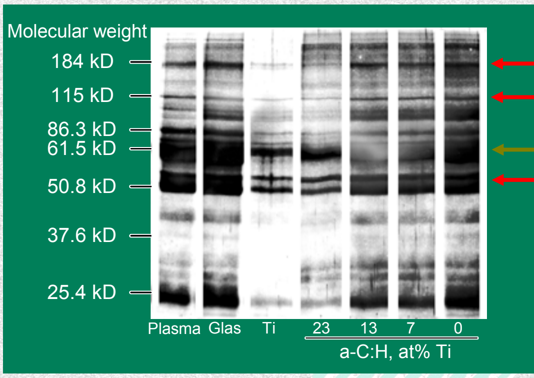
DLC - Improvements



Tunable protein adsorption

between Ti and DLC by Ti concentration in Ti-DLC.

Adsorption of human plasma proteins on a-C:H/Ti
Chromatographic analysis of the proteins. Molecular weight marker is indicated on the left side.

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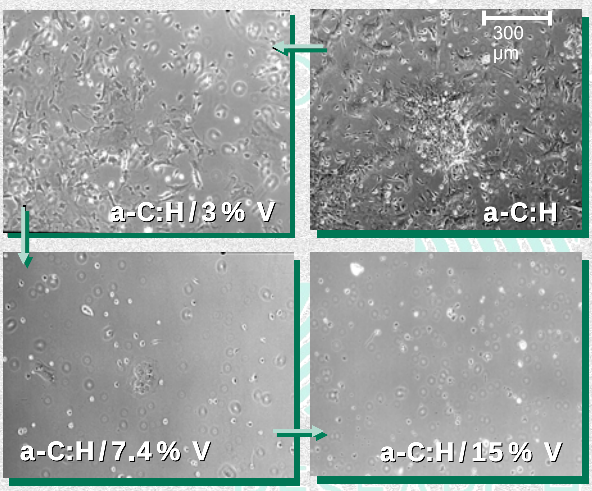
Diamond-like Carbon Coatings



after 10 days in vitro

Tunable poisoning:

Poisoning of the BMC cells due to vanadium dissolution out of the V-DLC film

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Diamond-like Carbon Coatings
Problems: Wear in hinges, Hemocompatibility
SORIN BIOMEDICA THE NETHERLANDS
CARBOFILM™ made by PVD using a pyrolytic turbostratic carbon target. Probably it is a-C.
Chrome-cobalt alloy cage, coated with CARBOFILM™
CARDIO
Titanium alloy coated with DLC
Products under development by Cardio Carbon Company Ltd.
Catheter
Carbofilm™ by Sorin Biomedica, Inc.
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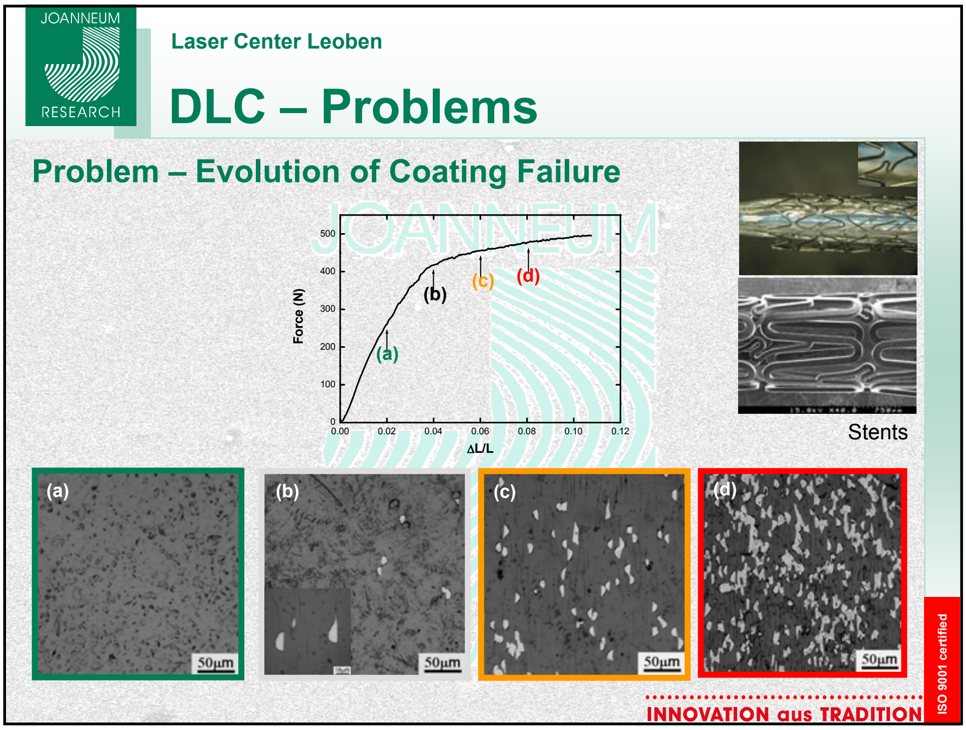
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DLC – Problems
Problem – Evolution of Coating Failure
Force (N)
ΔL/L
(a)
(b)
(c)
(d)
Stents
50µm
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Example

Own research –

Coatings for blood contact

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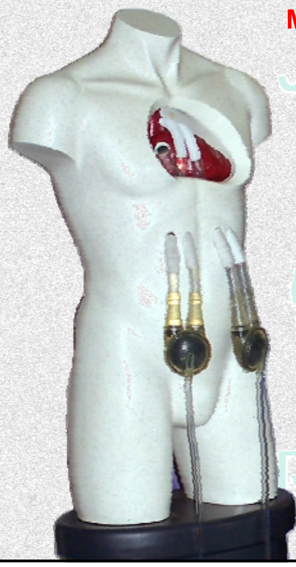
Coatings for Artificial Hearts



Medical implants – artificial hearts:

Optimization of polyurethane human implant surfaces (artificial heart) by biocompatible coatings

Goal: prevention of thrombus formation

POLVAD

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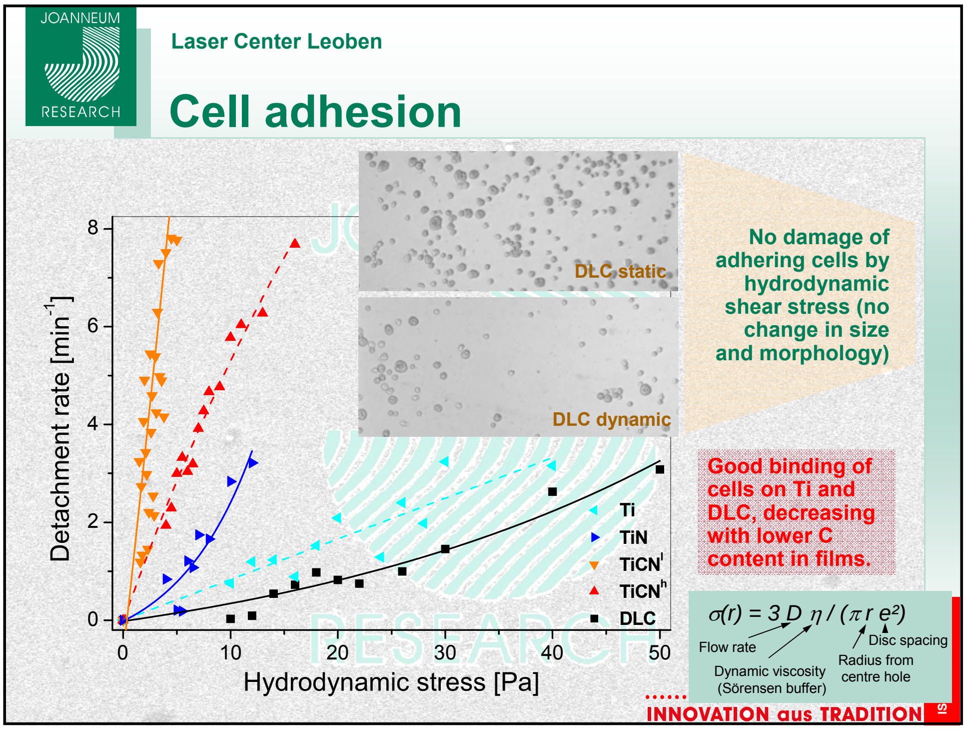
JOANNEUM
RESEARCH
Laser Center Leoben
Cell adhesion
Detachment rate [min-1]
Hydrodynamic stress [Pa]
0
2
4
6
8
0
10
20
30
40
50
DLC static
DLC dynamic
Ti
TiN
TiCNl
TiCNh
DLC
No damage of adhering cells by hydrodynamic shear stress (no change in size and morphology)
Good binding of cells on Ti and DLC, decreasing with lower C content in films.
σ(r) = 3 D η / (π r e²)
Flow rate
Dynamic viscosity (Sörensen buffer)
Disc spacing
Radius from centre hole
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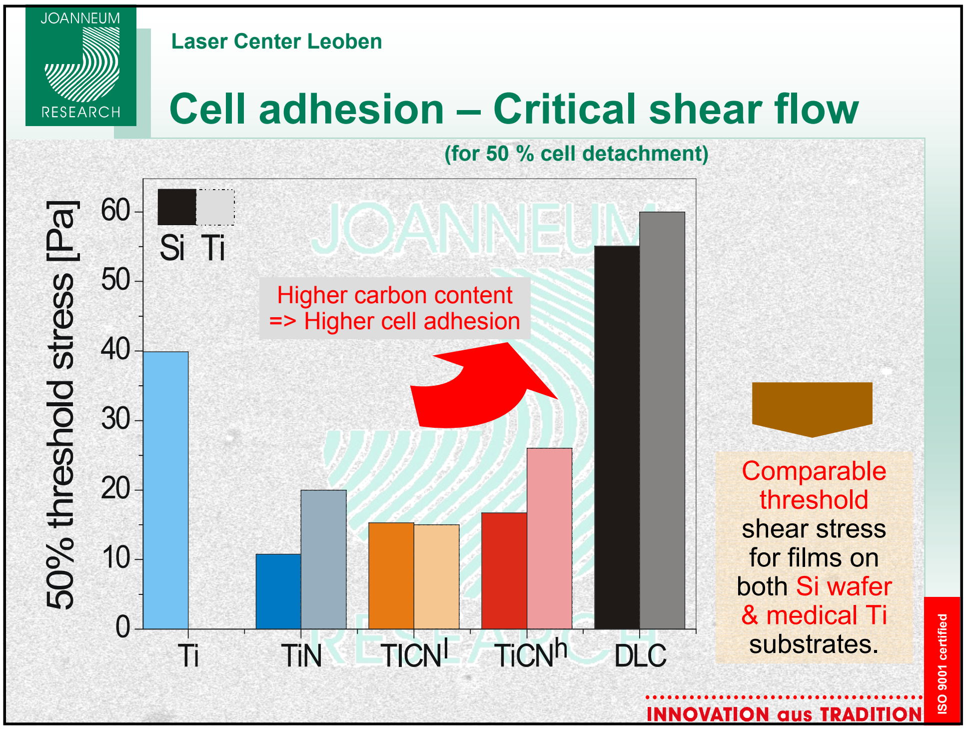
JOANNEUM
RESEARCH
Laser Center Leoben
Cell adhesion – Critical shear flow
(for 50 % cell detachment)
50% threshold stress [Pa]
0
10
20
30
40
50
60
Si
Ti
Higher carbon content
=> Higher cell adhesion
Ti
TiN
TiCNl
TiCNh
DLC
Comparable threshold shear stress for films on both Si wafer & medical Ti substrates.
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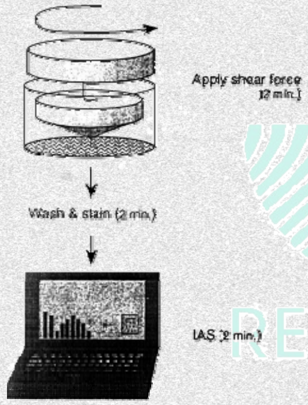
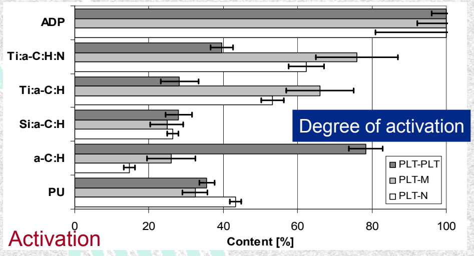
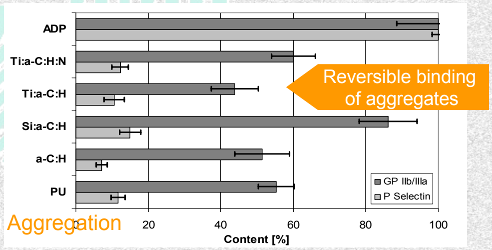
Thrombogeneity

Impact-R Test:

Activation and Aggregation of Platelets, measured by flow cytometry







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Contents

1. Biocompatibility – Aspects of biomaterial-tissue interaction
2. Bulk biomaterial „carbon“
3. Surface coating biomaterial „carbon“
4. **Conclusions**

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Conclusions

CARBON = applied BIOMATERIAL

Artificial heart valves
Stent surfaces

PROBLEMS of CARBON

Adhesion of coatings
Hemocompatibility (?)

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