PREDETERMINED BIO-PHYSICAL INTERACTIONS BETWEEN CORTICALIS AND SURFACE LAYER OF REPLACEMENT

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Abstract: Provision of a long-term functional stability of the inanimate implants in the live surroundings is a complex and quite an uneasy task.The development of replacements for a human skeleton follows the path of proposal and investigation of such materials whose mechanical properties are very similar to biomechanical properties of a bone tissue and whose biophysical and biochemical interactions with the surrounding living tissue do not cause necroses, or do not lead to any initiation of other pathological processes.

Biophysical/Biochemical fixation of replacements to the tissue depends dominantly: a) on the mechanical and chemical properties the implants and the tissue; b) on the stress-strain distributions in tissue and replacement, c) on the organization and stability of collagen molecules adsorbed to modified surfaces of replacements.

Our activities were aimed at the proposal and the bio-mechanochemical investigation of the collagen mediator films connecting the polymer matrix made from COC (cycloolephin) with the cortical bone.

Introduction

The long-term functional stability of thereplacements is dependent on the mechanical properties of the implant, on the type of materials, on the chemical composition of its surface, on the type of a CPH mediator and on remodelling limits [1] of the cortical bone.

The physical compatibility of the replacement with the bone tissue can be achieved or significantly improved by surface modification of implant. In this way specific functional groups can be introduced promoting protein adsorption and subsequent good cell adhesion and growth.

The objective of this work is to find the principal regulators of the biophysical and biomechanical stability of composite replacements in tissue, having the matrix from cycloolefin copolymer (COC). In particular, the research activities were focused on collagen adsorption which is transferring the dominant loads from implant into bone tissue, on behaviour and predetermined orientation of fibroblasts and osteoblasts, on plasma modified surfaces and on regulation of the CPH mediators (collagen – proteoglycans - growth hormones).

Materials and Methods

a) Regulation of mechanical properties

The fundamental condition for bone modelling around the stem and for the organization and stability of collagen molecules adsorbed to the stem surface is to ensure the physiologically natural level of stresses in the wall of diaphysis.

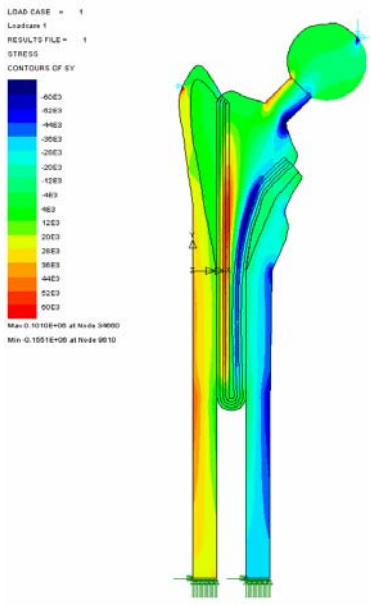

Figure 1: The translation of normal stresses (the dark strips) from surface layer of composite hip replacement to the central longitudinal stem axis. The lowering of normal stresses in the surface layer of stem

The elastic properties of the surface of the implant (its surface layer) must be identical or close to the

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elastic properties of a cortical bone. The surface layer has been made from a polymer matrix COC (cycloolefin) and reinforcing glass/carbon fibres with a resultant modulus of elasticity E = 20 GPa. The effect of the "strain-stress shield" of a rigid stem on a cortical bone has been reduced by the application of a composite stem with the gradient of elastic properties. The stress analyses were realized by FEM at 3D models, Fig.1.

b) Surface modifications of the Topas COC 8007 polymers and their relation to the collagen immobilization

In order to provide physical bonds between the surface of an artificial replacement and the atoms of collagen, the surfaces of the Topas COC (*cycloolefin*) 8007 polymer matrix were modified by the action of oxygen and nitrogen plasma [2].

When the plasmatic modification was conducted in the microwave oven, the surfaces with the *highest hydrophilicity were obtained* when the oxygen or nitrogen pressure was 1 Pa, with a double exposure taking place always for 5 seconds.

Figure 2: Application of XPS method

After optimizing conditions for the surface modification with regard to achieving the maximum hydrophilicity of the surface, the samples were examined by the XPS method (Fig. 2) with the aim of identifying their chemistry and population of chemical groups presented on the surface.

c) Regulation of cell orientation

The cell orientations in the assumed directions of the dominant principal stresses/strains is basic condition for the same orientations of collagen fibres. The orientation of cells in the assumed directions (Fig. 3) of the dominant principal stresses/strains were carried out by means of SRCO® method (Structural Regulation of Cell Orientations), [note: the principle will be patented by Petrtýl@Adam].

The chaotic cell distribution on the COC surface is always initiated without the application of SRCO® method, generally (Fig. 4).

d) Application of mediator films on the polymer surfaces

The mediator CPH films (made from collagen, proteoglycans and growth hormones) were applied on the COC surface. The CPH films are very effective implements for acceleration of bone metabolic activities around the stem. Verifying the CPH on the COC surface (in vitro) *showed very good cell proliferation and cell differentiation.*

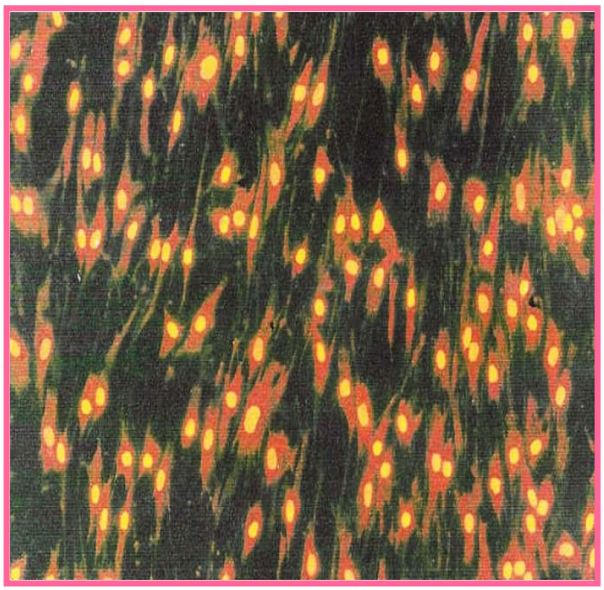

Figure 3: Structural regulation of predetermined cell orientation on the stem COC (cycloolefin) surfaces

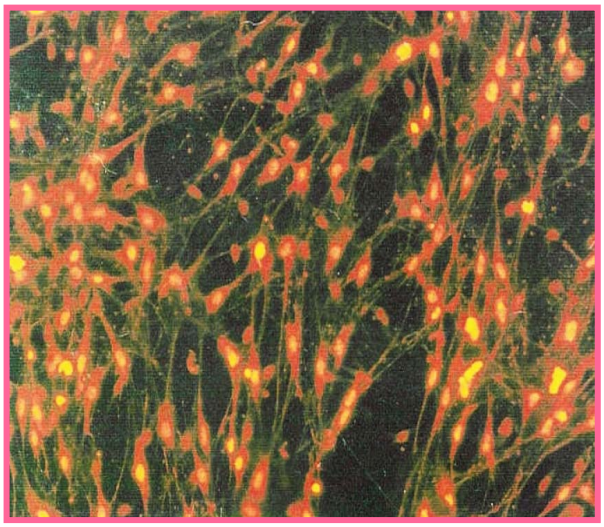

Figure 4: Chaotic cell distributions on the stem surfaces without the application of SRCO®

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e) Acceleration of the thickening of cortical bone

Thickening of the tissue substance takes place in such cases (Fig. 5) when the resultant volume change η_j of the examined tissue substance (i.e. the examined reactant component) is negative (i.e. the volume of its weight unit is reduced):

$$\eta_j = \eta_{jm} + \eta_{jch} << 0 \quad , \qquad (1)$$

where η_{jch} are volume changes initiated by primary chemical effects and η_{jm} are volume changes initiated by primary mechanical effects. The relation (1) can result from either:
(1) volume changes initiated by primary chemical effects: $\eta_{jch} << 0$, or
(2) volume changes initiated by primary mechanical effects: $\eta_{jm} << 0$.

Note: In this regard, it is necessary to emphasize that *the sign of the prevalent volume change of the examined reactant components will predetermine whether either thinning or thickening of the tissue substance will take place*.

Taking into consideration that, out of the steady states, volume changes η_{jch} and η_{jm} are in very distinctive disequilibrium, the following relations apply

in case /1/: $|\eta_{jch}| >> |\eta_{jm}|$, (2)
and in case /2/: $|\eta_{jch}| << |\eta_{jm}|$. (3)

The process of the tissue substance thickening in the j^{th} biochemical reaction caused by volume changes $\eta_{jch} << 0$ or $\eta_{jm} << 0$ is regulated by stress changes $\Delta p = p - p_e$ (in the bone tissue element). The above-shown two cases /1/ and /2/ will be further analyzed in detail with respect to stress changes $\Delta p = p - p_e$.

Let us consider the case in which, in the j^{th} biochemical reaction of the remodelling in the bone tissue around the stem, the volume changes of the examined reactant components initiated by primary chemical effects are much less than zero, i.e.:

$$\eta_{jch} << 0 \quad , \qquad (4)$$

and, simultaneously, consider that the tissue substance is in the non-steady state, i.e.:

$$|\eta_{jch}| >> |\eta_{jm}| \quad . \qquad (5)$$

Then the total volume change of the examined reactant components is:

$$\eta_j = \eta_{jm} + \eta_{jch} << 0 \ , \qquad (6)$$

and also $$\eta_{jch} - \eta_{jm} << 0. \qquad (7)$$

Resultant speed (rate) k_j of the j^{th} biochemical reaction according to the stoichiometric equations, published by Petrtyl @ Danesova [3] is as follows:

$$k_j = A_j k_{jch} k_{jm} = A_j e^{-(\eta_{jch} + \eta_{jm}).\Delta p} . \qquad (8)$$

The actual process of the tissue substance thickening is „determined“ by stress change $\Delta p = p - p_e$. The resultant speed of the j^{th} reaction according to equation (8) is influenced by signs (*signum*) of stress changes:

$$\Delta p = p - p_e \quad . \qquad (9)$$

A) Negative stress changes

Providing that the *stress changes are negative (Fig. 5)*, i.e. $\Delta p < 0$, i.e. $p < p_e$, then the speed of the j^{th} biochemical reaction initiated by chemical effects will be considerably lower than the speed initiated by mechanical effects (according to equations (7)), i.e. $k_{jch} << k_{jm}$, and speed (rate) k_{jm} (primarily influenced by mechanical effects) will reduce (retard) speed k_{jch} (primarily influenced by chemical effects).

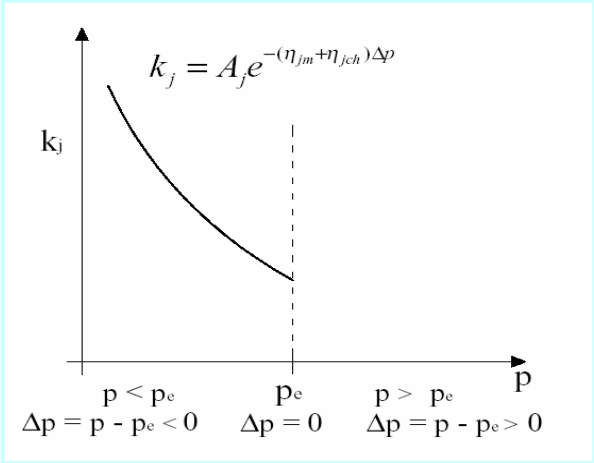

Figure 5: The speed (rate) k_j (of j^{th} biochemical reaction) is an exponential function of stress changes and volume changes of molecular mixtures. The speed (rate) is decreasing for negative Δp

The consequence is that *resultant speed k_j of the thickening in the tissue (initiated by primary volume change $\eta_{jch} << 0$) will go down if the stress decreases ($\Delta p < 0$)*, according to (6) and (8).

B) Positive stress changes

Providing that the *stress changes are positive (Fig. 6)*, i.e. $\Delta p > 0$, i.e. $p > p_e$, then the speed of the j^{th} biochemical reaction initiated by chemical effects will be considerably higher than the speed initiated by mechanical effects (according to equations (7)), i.e. $k_{jch} >> k_{jm}$, and speed (rate) k_{jm} will not substantially influence speed k_{jch}. The consequence is that *resultant speed (rate) k_j of the thickening in the tissue (initiated by primary volume change $\eta_{jch} << 0$ influenced by chemical effects) will go up if the stress increases ($\Delta p > 0$)*, according to (6) and (8), see Fig.6.

Discussion and Results

The stems with the gradient of elastic properties (GEP) eliminate the negative “stress/strain shield” and reduce the bending rigidity of system “femur-stem”. The stresses in the femur wall (with the stem having the GEP) are near to the natural distributons of stresses.

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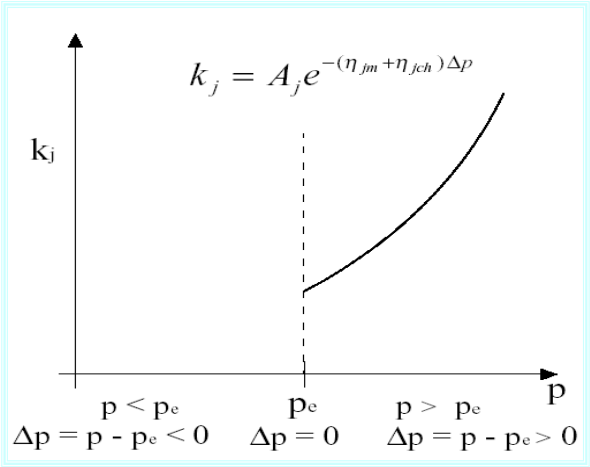

Figure: 6 The speed (rate) k_j (of j^{th} biochemical reaction) is an exponential function of stress changes and volume changes of molecular mixtures. The speed is increasing for positive Δp.

The modulus of elasticity of the investigated composite implants COC+C/Si fibres are *very similar to the modulus of elasticity of the bone tissue*, and, considering their application, they do not substantially increase the bending rigidity of the bone-implant system. The hybrid COC composites (having the surface coated with GAG) have well-controlled material characteristics. After plasmatic treatment, the components with higher values of binding energy occurred in the C 1s spectra of electrons (see Fig. 7).

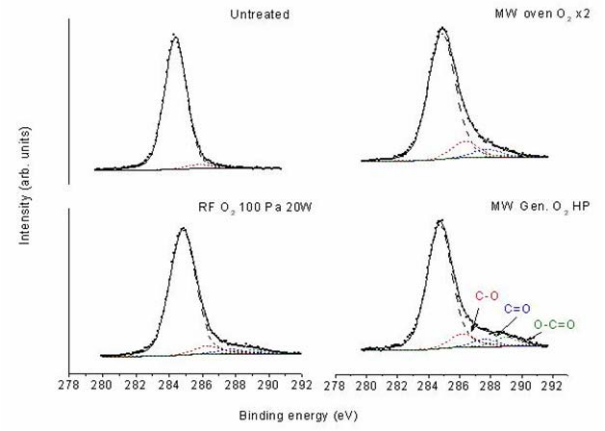

Figure 7: C 1s spectra of electrons of unmodified and modified samples

The measured C 1s spectra of electrons showed, with the exception of the mother line, at 284.8 eV, the presence of other three components with binding energies higher by 1.5, 2.9 and 4.3 eV. These components can be included in groups **C-O, C=O** and **O-C=O.** The measured C1s electron spectra of the sample after treating with the nitrogen plasma are presented on Fig 7. For examining the collagen adsorption, stable samples whose surface composition did not change in time were used. The occurrence of adsorbed collagen was identified as a line of N 1s electrons in the spectrum

We compared the adsorption on plasma modified COC sample surface with the adsorption on untreated surface in order to better understand the interactions between the polymer and the bioactive molecule. We proved that the plasma treatment leads to an *increase of oxygen content and formation of surface chemical groups such as C-O, C=O, O-C=O and even C-O-O.* Concerning the nitrogen treatment, we obtained a well oxidized surface with a ratio O/C similar to oxygen plasma. After plasma treatment, the amount of oxygen and/or nitrogen groups increases.

The modified surface exhibit enhanced adsorption of collagen and improvement of its adhesion. The stronger bonding explains the higher quantity, the better organization and the better stability of collagen molecules adsorbed on oxidized surfaces.

Conclusions

On the basis of the obtained results the following conclusions can be made:

1. The high bending rigidity of rigid (metallic) stems can be reduced by the application of a composite stems with GEP.

2. The GEP contributes the natural stress/strain distributions in the femur wall.

3. Treatment of COC surface by oxygen plasma results in production of C-O, C=O, O-C=O functionalities. The dependence of the population of these groups on the method used for modifications and on experimental conditions were investigated.

4. The long-term functional stability of the replacements of the I. and II. generation in the live tissue can be ensured by creating *the fields of active physical bonds between the binding atoms (implanted) on the surface of the artificial replacements* and the "partnership" binding atoms of the collagen molecules.

5. On plasma modified and aged COC surface the value of the measured contact angle did not depend on the method used to produce plasma. These surfaces were found to exhibit enhanced adsorption of collagen. The average thickness of adsorbed collagen layer on plasma modified and stabilized COC surface calculated from intensities of N 1s and C 1s photoemission lines amounts 1 - 2 monolayers.

6. Improvement of fibroblasts/osteoblasts adhesion on plasma modified COC surface with adsorbed collagen was found.

7. By application of the CPH mediator films, the proliferation of osteoblasts can be accelerated with the subsequent development of the osteoid and its mineralization.

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8. The speed of thickening in the tissue during the j^{th} biochemical reaction initiated by volume change $\eta_{jch} << 0$, influenced by primary chemical effects, or $\eta_{jm} << 0$, influenced by primary mechanical effects is the *exponential function* of stress changes $\Delta p = p - p_e$ in the examined bone tissue element.

9. Thickening in the bone tissue will be retarded (reduced) around the stem when the stress (load) $\Delta p < 0$ declines, both in the initiation of the thickening by volume changes η_{jch} influenced by primary chemical effects, and in the initiation of the thickening by volume changes η_{jm} influenced by primary mechanical effects.

10. When the stress (load) $\Delta p > 0$, i.e. $p > p_e$ increases, the thickening process in the bone will be accelerated around the stem, both in the initiation of the thickening by volume changes η_{jch} influenced by primary chemical effects, and in the initiation of the thickening by volume changes η_{jm} influenced by primary mechanical effects.

11. Provided that a skeleton is loaded insufficiently (i.e. if the exercises are minimal or none), the external *application of chemical substances* (for example: hormones, vitamins etc.) whose aim has been to initiate bone thickening around the stem will be more/less *ineffective*. If the exercise is insufficient, the expected thickening will be retarded and reduced.

12. Provided that a skeleton is loaded (i.e. if the exercise is maximal), the *application of chemical substances* (for example: hormones, vitamins etc.) whose aim has been to initiate thickening around the stem will be *highly effective*. If the exercises are sufficient, the expected thickening will be accelerated.

Acknowledgement

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