INTRODUCTION and CLINICAL RELEVANCE
Conditions influencing periprosthetic healing in the early post-operative period include the surgical technique, mechanical stimuli and biochemical factors. Clinically, vascularization is of prime importance in the healing process and it was shown that angiogenesis was playing a major role in bone tissue formation.

Establishing correlations between neo-vascularization and implant fixation is challenging in clinical studies or animal models because of the multiplicity of mechanical and biological factors. Associated with experimental models, theoretical models could potentially help. In this context, theoretical models of vessels formation have been proposed for tumors but studies in arthroplasty were missing.

We hypothesized that a diffusive and reactive model of endothelial cells population could help to rank the role of random motility, haptotaxis and chemotaxis in wave front progression of endothelial cell around an orthopedic implant in the first weeks of the healing process. Transforming angiogenic factors (TAF; chemotactic factors), fibronectin factors (FF: haptotactic factors) were considered and the application was a canine experimental model.

MATERIALS AND METHODS
The motion of endothelial cells was due to random motility, chemotactic and haptotactic active migrations. Chemotaxis occurred in response to gradients of TAF and adhesion gradients of FF conditioned haptotaxis. We denoted the concentration of endothelial cells by $n$, the concentration of TAF by $c$ and the fibronectin concentration by $f$. Equation (1) was the governing equation of endothelial cell population with $D_n$, $\chi$ and $h$ conditioning the random motility, the chemotaxis and the haptotaxis respectively. The source of cells $\mathcal{Q}$ was expressed by a logistic law involving a proliferation threshold $N_c$.

$$\frac{\partial n}{\partial t} = D_n \nabla^2 n - \nabla [\chi (c) \cdot \nabla c] - \nabla [h \cdot n \cdot \nabla f] + \mathcal{Q} (n)$$

The TAF concentration was expressed by equation (2) with $D_f$ for the random diffusion and $\lambda$ for the cellular uptake in the source term $\mathcal{Q}$.

$$\frac{\partial c}{\partial t} = D_f \nabla^2 c + \mathcal{Q} (n, c) \text{ with } \mathcal{Q} (n, c) = - \lambda \cdot n \cdot c$$

Equation (3) governed the fibronectin phase with $D_f$ for the random diffusion and $(\alpha, \beta)$ for the cellular production and uptake in the source term $\mathcal{Q}$.

$$\frac{\partial f}{\partial t} = D_f \nabla^2 f + \mathcal{Q} (n, f) \text{ with } \mathcal{Q} (n, f) = \alpha \cdot n - \mu \cdot n \cdot f$$

The theoretical model was applied to the canine experimental model (stable and unloaded) presented in Figure 1. Associated with specific boundary conditions and initial conditions, it was solved using a spatio-temporal finite element method into Consol Multiphysics®.

RESULTS
Figure 2 showed the radial distribution patterns of endothelial cells population. When all biochemical factors were taken into account (Figure 2a), cells present into the host bone at $t = 0$ formed a wave front migrating toward the implant. At 10 days it reached $r = 3.7$ mm and at 35 days endothelial cells were in vicinity of the implant ($r = r_i$).

DISCUSSION AND CONCLUSION
When our results were compared to theoretical studies in soft tissue tumor, it appeared that similar trends were obtained. This confirmed that our theoretical approach could be relevant to investigate the neovascularization around orthopedic implants.

We found that chemotaxis due to TAF in initial bleeding was attracting endothelial cells initially present into the host bone, toward the implant surface. Haptotaxis conditioned by fibronectin factors favored cells adhesion to the host bone. It appeared that the superimposition of these two contradictory phenomena could influence the magnitude and the wave front velocity of endothelial cells.

We assumed that the best cell migration was found, the more tissue mineralization and implant fixation would be obtained. Associated with parametric studies our theoretical models could be used to evaluate the influence of the clinical technique including the roles of post-operative gap, the initial TAF concentration in initial blood clot and the initial concentration of fibronectin factors. These studies might contribute to the reduction of implant revisions.

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REFERENCES