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**Histological and histomorphometrical analysis of a silica matrix embedded nanocrystalline hydroxyapatite bone substitute using the subcutaneous implantation model in Wistar rats.**

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The clinical suitability of a bone substitute material is determined by the ability to induce a tissue reaction specific to its composition. The aim of this *in vivo* study was to analyze the tissue reaction to a silica matrix-embedded, nanocrystalline hydroxyapatite bone substitute. The subcutaneous implantation model in Wistar rats was chosen to assess the effect of silica degradation on the vascularization of the biomaterial and its biodegradation within a time period of 6 months. Already at day 10 after implantation, histomorphometrical analysis showed that the vascularization of the implantation bed reached its peak value compared to all other time points. Both vessel density and vascularization significantly decreased until day 90 after implantation. In this time period, the bone substitute underwent a significant degradation initiated by TRAP-positive and TRAP-negative multinucleated giant cells together with macrophages and lymphocytes. Although no specific tissue reaction could be related to the described silica degradation, the biomaterial was close to being fully degraded without a severe inflammatory response. These characteristics are advantageous for bone regeneration and remodeling processes.