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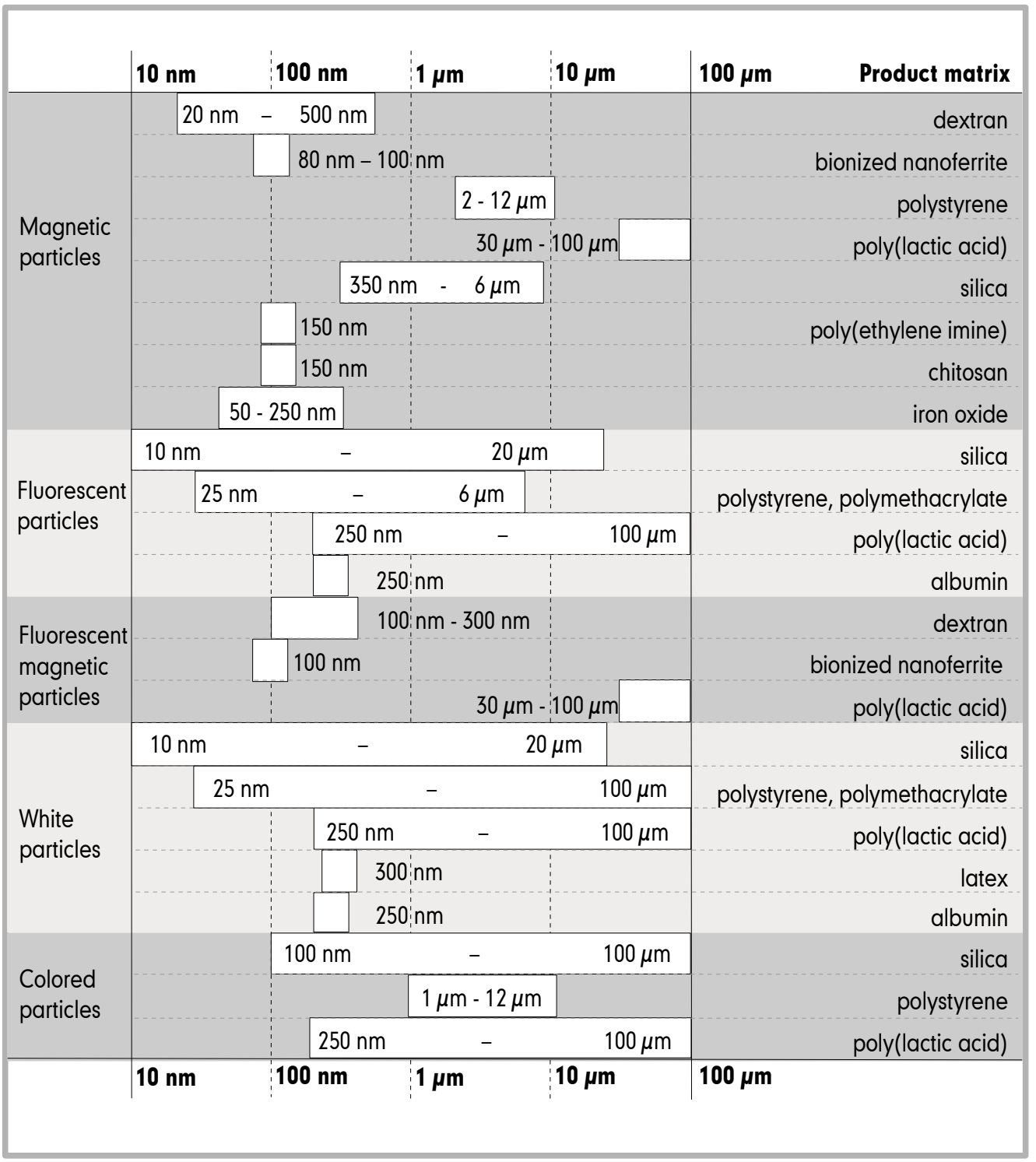

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9 Magnetic nanoparticles for stem cell tracking in soft tissue engineering approaches

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Magnetic resonance imaging emerged as an excellent tool to track implanted stem cells in soft tissue engineering approaches. Kasten et al. and Siegmund et al. reported in consecutive *in vitro* and *in vivo* studies the feasibility of using BNF-Starch and nanomag®-D-spio nanoparticles, both 100 nm in diameter and coated with poly-D-lysine, for MRI-based stem cell tracking in a soft tissue engineering approach [1-3].

In the first step, both nanoparticle types were evaluated *in vitro* to determine their MRI properties as well as potential biological effects on adipose-tissue derived mesenchymal stem cells (ASC). Furthermore, to determine dose-dependent effects, three different nanoparticle concentrations were used for cell labeling. In general, no cytotoxic effects or alterations in metabolic activity of ASC were detected. Furthermore, intracellular localization of nanoparticles was examined and no co-localization with nuclei or mitochondria was found. Instead, nanoparticles were associated with lysosomal structures indicating a non-specific particle internalization pathway. Regarding cell proliferation, a dose-dependent increase was observed for both nanoparticle types compared to unlabeled control cells. Evaluation of multipotent differentiation potential of ASC into the adipogenic, osteogenic, and chondrogenic lineage revealed an overall, dose-dependent decrease due to nanoparticle application. In general, effects were more pronounced for BNF-Starch nanoparticles even at much lower concentrations than for nanomag®-D-spio nanoparticles. In contrast, MRI-properties of BNF-Starch nanoparticles in terms of R2* values were much better compared to nanomag®-D-spio nanoparticles.

In the second step, both nanoparticle types were tested under *in vivo* conditions. ASC were loaded with both types of nanoparticles (25 µg Fe/ml nanomag®-D-spio, 10 µg Fe/ml BNF-Starch) and seeded on collagenous three dimensional scaffolds which were implanted subcutaneously in the back region of severe combined immunodeficient mice (SCID mice, n=69). As control group, cell seeded scaffolds without nanoparticles were implanted. MRI scans were performed at several time points from 24 hours up to four months postoperatively and constructs were explanted afterwards for light microscopic histomorphometric analyses.

As a result, nanoparticle loaded cells showed a high contrast in MRI (t2-tse-sequence) and could be detected inside the implanted scaffold (Fig. 1). Cells of the control group could not be separated from the surrounding tissue. The contrasting effect of both nanoparticle types was observed even after four months in a stage of total resorption of the scaffolds. Nanoparticles could be detected inside the scar tissue. Histomorphometric analysis showed iron oxide containing cells inside the constructs using Prussian blue staining. Except six mice which had to be excluded because of perioperative complications, animals of all groups did not show any signs of infection or other complications. Regarding the shrinkage of implanted scaffolds, no significant differences where observed between nanoparticle loaded groups and the control group.

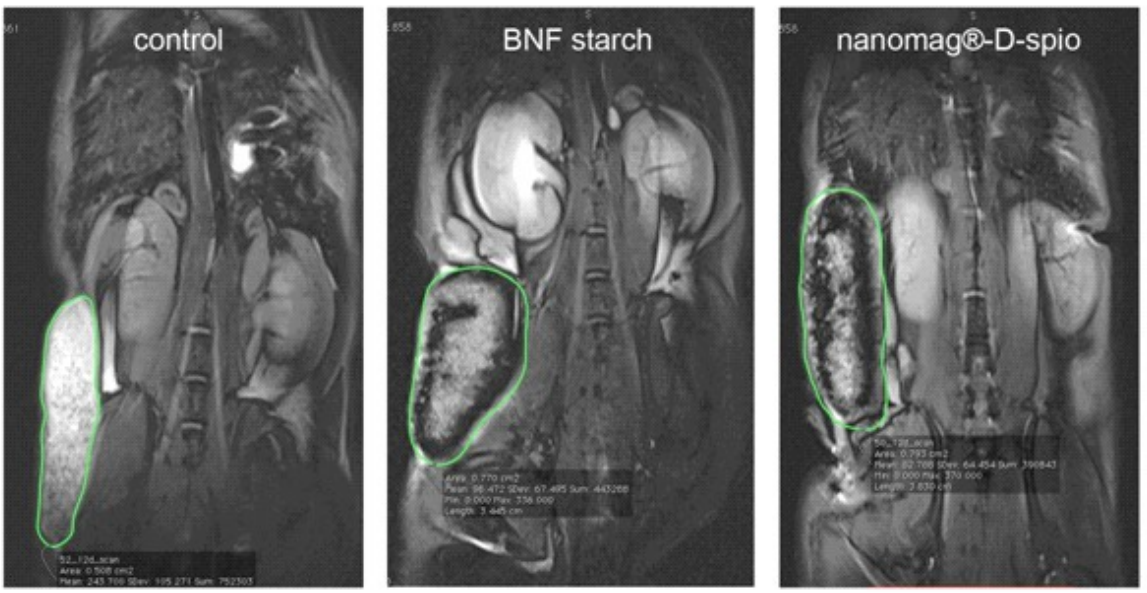

Fig. 1 : *In vivo* MRI scans of nanoparticle-labeled ASC.
T2-tse-maps (coronary views) of collagen scaffolds implanted in SCID mice are shown 12 days after implantation. Scaffold borders are marked with a green line. Only BNF-Starch and nanomag®-D-spio-labeled ASC lead to a high contrast on collagenous scaffolds compared to control cells.
MRI scans were performed by using a 7.1 T MR system (ClinScan, Bruker Corp., Billerica, MA, USA) in cooperation with the Department of Radiology and Neuroradiology, Greifswald University Medical Center.

References

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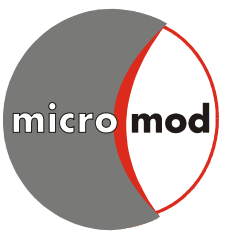

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