Response to: Thoughts on Tissue Stromal Vascular Fraction for Early Scar Healing

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Letter to the Editor

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We would like to thank Sun and Zhao for their response and comments[1] on our randomized clinical trial studying the effect of tissue-stromal vascular fraction (tSVF) on early scar healing.[2] Their first comment is that the histologic evidence for an extracellular matrix in tSVF that functions as a scaffold is lacking. However, we feel there is enough evidence presented: the presence of an extracellular matrix in tSVF—isolated by the fractionation of adipose tissue (FAT) procedure—has clearly been demonstrated by Masson's trichrome staining in this study. In a previous study, we were able to decellularize tSVF (obtained by means of the FAT procedure) and to isolate extracellular matrix, which was entirely free of cells.[3] This decellularized extracellular matrix was then digested with pepsin and turned into a self-assembled hydrogel. Multiple experiments subsequently demonstrated the capability of such an extracellular matrix–derived hydrogel to bind and release paracrine factors from adipose-derived stromal cells (ASCs) in a controlled fashion over time.[3] These results show that adipose extracellular matrix functions as a scaffold.

The second comment is that mechanical fractionation of adipose tissue will reduce the viability of ASCs, a claim that is based on the authors being unable to culture ASCs derived from tSVF by an explant technique. Their findings, however, in our opinion do not justify this conclusion because enzymatic isolation of tSVF derived from mechanical fractionation still yields large numbers of ASCs. In contrast to enzymatic isolation, mechanical isolation preserves all cell-cell connections, including connection to the extracellular matrix and small vessels.[4] Therefore, in tSVF, ASCs are still attached around vessels as pericytes and/or vascular precursor cell types.[5] Hence, using an explant technique to extract ASCs from tSVF is significantly more difficult than just culturing ASCs present in a single cell suspension of cellular SVF. One might even speculate that the viability of ASCs after mechanical isolation is even better than after enzymatic isolation because

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ASCs remain in their natural niche. Recently, a cleaved caspase-3 staining of freshly isolated tSVF showed no cell death in the first 24 hours after mechanical isolation in our laboratory (unpublished data). A disadvantage of mechanical vs enzymatic isolation of SVF is that mechanical isolation might be more variable because of performance variability among clinicians. Therefore, not all isolated tSVF will be free of adipocytes. Yet, not all adipocytes stain positive for perilipin A in tSVF, suggesting the presence of "ghost" adipocytes, which are disrupted cells with their shape still intact.[2]

Our prospective study has clearly demonstrated an accelerated early scar healing by a single injection of tSVF in the wound after mammoplasty at 6 months postsurgery. This accelerated wound healing effect, however, was no longer detectable at 12 months postsurgery. This observation might indicate that a single injection of tSVF is not that effective for accelerated wound healing in the long term. Multiple injections with tSVF are probably necessary to obtain long-term results. In situations with disturbed wound healing, such as chronic diabetic wounds, perianal fistulas, etc, however, a single injection of tSVF appears to be more effective.[6] In these situations, healing inflammation plays a central role.

Disclosures

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