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Translational Model for External Volume Expansion in Irradiated Skin

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Comments
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Oksana Babchenko participated in this study as a medical student in the Senior Scholars research program at the University of Massachusetts Medical School.

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Introduction:
External Volume Expansion (EVE) treatment has gained popularity in breast reconstruction, enriching recipient sites for fat grafting. For patients receiving radiotherapy (XRT), results of EVE use vary, partly because the effects of EVE on irradiated tissue are not well understood. Based on our previous work with EVE and XRT, we developed a new translational model to investigate the effects of EVE in the setting of chronic radiation skin injury .

Methods:
Twenty-Eight SKH1-E mice received 50Gy of beta-radiation to each flank. Animals were monitored until chronic radiation fibrosis developed (8 weeks). EVE was then applied to one side for 6hrs on 5 consecutive days. The opposite side served as control. Hyperspectral Imaging (HSI) was used to assess perfusion changes before and after EVE. Mice were sacrificed at 5 days (n=14) and 15 days (n=14) after last application for histological analysis. Tissue samples were stained for vascularity (CD31) and collagen composition (Picro-Sirius red).

Results:
All animals developed skin fibrosis 8 weeks post-radiation, and changes in perfusion verified skin damage. EVE application induced edema on treated sides. Five days post-application, both sides were hypo-perfused as seen by HSI; with the EVE side 13% more ischemic than the untreated side ($p<0.001$). Perfusion returned to control side levels by day 15. Blood vessels increased 20% by day 5 in EVE versus control. Collagen composition showed no difference in scar index analysis.

Conclusion:
EVE temporarily augments radiation-induced hypo-perfusion, likely due to transient edema. Fibrosis remained unchanged after EVE, possibly accounting for the limited expansion seen in patients. It appears that EVE induces angiogenic effect but does not affect dermal collagen composition. Future efforts should focus on reducing fibrosis post radiation to allow EVE to achieve its full potential, to benefit irradiated patients.