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Proposed Regeneration Therapy for Cutaneous Radiation Injuries

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Increasing concern on systemic and local radiation injuries caused by nuclear power plant accident, irradiation for malignant tumor or under fluoroscopic procedures for heart diseases should be treated and prevented properly for life-saving and improved wound management.

We therefore reviewed our therapeutic regimens and for local radiation injuries and propose surgical methods reflecting the importance of the systemic and local conditions.

For local radiation injuries, demarcation of the lesion should be carefully determined with certain time period and sequential surgeries starting with local flap, arterialized or perforator flap and to free flap when the patients' general conditions allow. There are often undetermined wound margins in cases of acute emergency radiation injuries and the regenerative surgical modalities should be attempted with temporal artificial dermis application with angiogenic factor such as fibroblast growth factor-2 (FGF-2 or basic fibroblast growth factor, bFGF) and secondary reconstruction can be a candidate for demarcation and saving the donor morbidity.

For systemic radiation injury model, total body irradiation to a nude rat was employed. Human mesenchymal stem cells (hMSCs), angiogenic and mitogenic factor of FGF-2 and porcine derived artificial dermis was applied over the excised irradiated skin defect.

The local perforator flap was successful for reconstruction in patients who are suffering from complex underlying disease such as diabetes and anti-coagulant medication. Temporal coverage with artificial dermis and FGF-2 bring about benefit for wound bed preparation and further easier secondary reconstruction. At least one year observations after surgeries, 30 patients were uneventfully treated with minimal morbidities.

The hMSCs are now stockpile in the freezing condition and readily available for emergency use. The hMSCs are strongly proliferative even after 20Gy irradiation in vitro in contrast to the cell death of other human neuroblastoma cells (NG108-15) and rat pheochromocytoma cells (PC-12) up to 180 days. As low as 4 Gy irradiation resulted in loss of hematopoietic stem cells and differentiating macrophages in the rat bone marrow, on the other hand, the mesenchymal stem cells survived in healthy condition. The electron microscopic cell morphology of hMSCs in vitro was maintained even after 60 Gy irradiation. The immediate artificial dermis application impregnated with hMSCs and bFGF over the 20 Gy irradiated skin and soft tissues demonstrated the significant subcutaneous angiogenesis, architected dermal reconstitution and less inflammatory epidermal recovery. The fate of the grafted hMSCs was clearly demonstrated by a green fluorescent protein (GFP)-transfected hMSCs, which were differentiation to the epithelium from the outer surfaces.

Even though there are increasing therapeutic evidences of the emergent radiation-exposure cases, detailed understanding of underlying pathogenesis and rational reconstructive procedures brings about good outcomes for difficult irradiated cutaneous wound healing. In this context, the staged regeneration with a commercially available artificial dermis and FGF-2 would be one of the choices.

In systemic acute radiation injury, especially preparedness for it, the products which are available for use at hand such as FGF-2, artificial dermis and hMSCs, which are in stockpile in the refrigerators, are most effectively inducing the acceleration of cutaneous wound healing and life-saving.

Effective and sufficient reconstructions and regenerations for local and systemic radiation cutaneous injuries are proposed and available for preparedness.

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