Vascular Therapy for Radiation Cystitis

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**Purpose:** The underlying pathology of radiation cystitis is cellular and vascular damage followed by increased fibrosis and inflammation. This study was to determine if neovascular-promoting therapy could reduce the pathological changes in the bladder wall associated with pelvic irradiation.

**Methods:** Adult female Lewis inbred rats were irradiated with a single dose of 20 Gray directed at their bladder. Four weeks later, 30 rats were divided equally into one of three treatment groups for bladder wall injection of: 1) PBS (Control); 2) PBS containing 50 ng vascular endothelial growth factor (VEGF165); or 3) PBS containing 1x10^6 rat endothelial cells (EC). Age-matched non-irradiated rats (n=10) served as untreated controls. At either 1.5 or 3 months following radiation, bladders were analyzed for collagen deposition using Masson’s Trichrome staining of collagen and muscle and vascularization using Von Willebrand factor staining of ECs. Quantitative-PCR was used to examine markers of angiogenesis, hypoxia and fibrosis.

**Results:** The collagen/muscle ratio was doubled in the Control group 3 months post irradiation (p<0.05 vs. non-irradiated bladders). Both ECs and VEGF inhibited increases in collagen content (p<0.05 vs. Control). Similarly, irradiation reduced bladder wall vessel counts compared to non-irradiated controls (p<0.05) and both ECs and VEGF maintained vessel counts similar to that of non-irradiated controls (p<0.05). PCR analysis showed a higher expression of neovascular markers (CD31, KDR) in the EC and VEGF groups compared to non-irradiated controls (p<0.05).

**Conclusions:** Angiogenesis therapy may be useful in the prevention and/or treatment of the underlying pathology of radiation cystitis.