IV. Conclusion

Endothelial and monocytic cells appear to play a key role in the initiation and progression of atherosclerosis and restenosis via the upregulation of inflammatory cytokines. The proliferation of VSMCs induced by injury to the intima of arteries is still an important etiologic factor in atherosclerosis and restenosis. However, the role of SMCs is not fully understood in mechanism of restenosis. NF-κB plays a pivotal role in restenosis after angioplasty and the aim of the present clinical trials was to be the effective reduction of activated NF-κB for preventing restenosis. Breuss et al concluded that balloon angioplasty-induced activation of NF-κB contributed to lumen loss likely via the induction of an inflammatory response and a decrease in the rate of apoptosis [Breuss et al, 2002]. Specific and more potent inhibitors of NF-κB might therefore be a useful therapeutic measure to improve clinical outcome after balloon dilatation. Synthetic double-stranded DNA with a high affinity for NF-κB, known as a 'decoy', had been shown to significantly suppress the activation of inflammatory factors and had been used in the treatment of acute myocardial infarction and cardiac rejection [Morishita et al, 1997; Suzuki et al, 2000]. Using a rat model, Yoshimura et al demonstrated that the NF-κB decoy successfully inhibited neointimal formation after arterial balloon injury [Yoshimura et al, 2001]. Furthermore, Low-dose radiotherapy (LD-RT) was known to exert an anti-inflammatory effect, but the knowledge of the underlying molecular mechanisms is still scarce [Kern et al, 2000]. LD-RT of stimulated human endothelial cells is followed by NF-κB activity and caused an increased secretion of TGF-β1 [Rodel et al, 2004]. UV-C inhibited TNF-induced NF-κB transactivation, indicating that this was a dominant effect [Campbell et al, 2004]. In our study, cultured VSMCs were irradiated with γ-ray (2 Gy) leading to decreased expression of at 1 day after radiation (p < 0.05, compared with untreated cells), whereas at 2, and 3 day after γ-radiation the expression

increased on radiated-cells which was similar to the expression on nonirradiated cells. At 2 and 3 day the level expression in radiated-VSMCs was similar to that in nonirradiated cells and did not reach statistical significance. The increasing expression of NF-κB was observed and leaded to the induction of an inflammatory response at 2 and 3 day after radiation because NF-κB might play a role in radioprotection. As a result, the expression of VCAM-1 and ICAM-1 might subsequently be involved in the cascade of events resulting in inflammatory responses, such as leukocyte infiltration. The radiation-induced or -deduced expression of NF-κB may be related to the time course, the types of radionuclide, or the dosage of radiation. In addition, the expression of NF-κB detected by cDNA microarray was not significant different compared to each group in our study.

Several studies during the last years have shown that VSMCs also express the cellular adhesion molecules (i.e., ICAM-1 and VCAM-1) in atherosclerosis and restenosis except for endothelial cells. Shimizu et al reported that the expression of ICAM-1 and VCAM-1 were found in the inflammatory cells and SMCs in the neointima of injured vessels investigated in the porcine coronary injury model at 1 week after angioplasty by immunostaining [Shimizu et al, 2004]. UVB radiation suppressed the TNF-α-induced expression of ICAM-1 on cultured human umbilical vein endothelial cells [Yamawaki et al, 1996]. UVB radiation inhibited their ability to activate T cells through selective effects on the expression of ICAM-1. Besides, in cultured HMECs irradiated with 2.5-40 mJ/cm^2 of UVB, ICAM-1 was upregulated at 24 h post-irradiation and no change was seen in expression of VCAM-1 [Rhodes et al, 1996]. ICAM-1 expression was depleted following UVA radiation in epidermal keratinocytes [Treina et al, 1996]. However, IR causing to the induction or reduction of adhesion molecules in restenosis was underestimated. In our study we are interested in the role of adhesion molecules in porcine received angioplasty and/or brachytherapy. As a result, we found that the expression of ICAM-1 in coronary artery cells treated by angioplasty

(PTCA only group) was 2 folds higher than that without PTCA treatment (in sham control group). However, the expression of ICAM-1 in Re188 group was similar to that in sham control group. It means that PTCA treatment increased the expression of adhesion molecules not radiation treatment. However, the expression of ICAM-1 in the PTCA group was similar to that in PTCA/Re, and Re/PTCA groups. There was no significantly different among three groups. Therefore, PTCA/Re and Re/PTCA groups leaded to the same expression of ICAM-1 from our data and were not able to recognize the effect of radiation between PTCA/Re and Re/PTCA groups for the injury wall treated with PTCA. The expression in three groups was 2 folds higher than that in the sham control group ($p < 0.001$). Besides, the expression of ICAM-1 in the β-radiation (20 Gy) only group was 2 folds lower than that PTCA/Re group, and Re/PTCA group. It represented that the inhibition of ICAM-1 activation induced by PTCA was contributed by radiation and this dosage (20 Gy) may be decrease inflammatory response in porcine model.

As a result, we found that the expression of VCAM-1 in coronary artery cells treated with the angioplasty (PTCA only group) was 2 folds lower than that in cells without PTCA (in sham control group) ($p < 0.01$). It meant that PTCA leaded to decrease the expression of adhesion molecules. However, the expression of VCAM-1 in the PTCA group was similar to that in PTCA/Re and Re/PTCA group. There was no significantly different among three groups. Therefore, PTCA/Re and Re/PTCA group leaded to the same expression of VCAM-1 from our data and were not able to recognize the effect of radiation between two groups for the injury wall treated with PTCA. The expression in three groups was 2 folds lower than that in the sham control group ($p < 0.001$). Besides, the expression of VCAM-1 in the β-radiation (20 Gy) only group was 1.5 folds lower than that in the PTCA/Re group, and Re/PTCA group. It represented that the inhibition of VCAM-1 was contributed by radiation and this dosage (20 Gy) may be decrease the inflammatory response in porcine

model.

However, the expression of ICAM-1 and VCAM-1 detected by cDNA microarray was not significant different compared to each other.