

# MP06-12 The correlation between Local Atherosclerosis of the Prostatic Arteries and Chronic Inflammation in Human Benign Prostatic Enlargement

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## Abstract

**Objective:** The relationships between prostate size and the degree of chronic inflammation induced by local atherosclerosis were investigated.

To elucidate the pathogenesis of benign prostatic enlargement (BPE) in humans due to chronic inflammation caused by atherosclerosis.

**Methods:** The present cohort included 50 subjects who underwent robot-assisted radical prostatectomy (RARP) in a prospective study. The presence or absence of local atherosclerosis in the prostatic arteries removed during RARP was evaluated by microscopic assessment. Chronic inflammation in the prostate was judged according to both the density and the extent of inflammatory cells. The expression of lectin-like oxidized-low density lipoprotein receptor-1 (LOX-1) and the infiltration of macrophages in the prostate, which are high in arteriosclerosis, were investigated by immunohistochemistry.

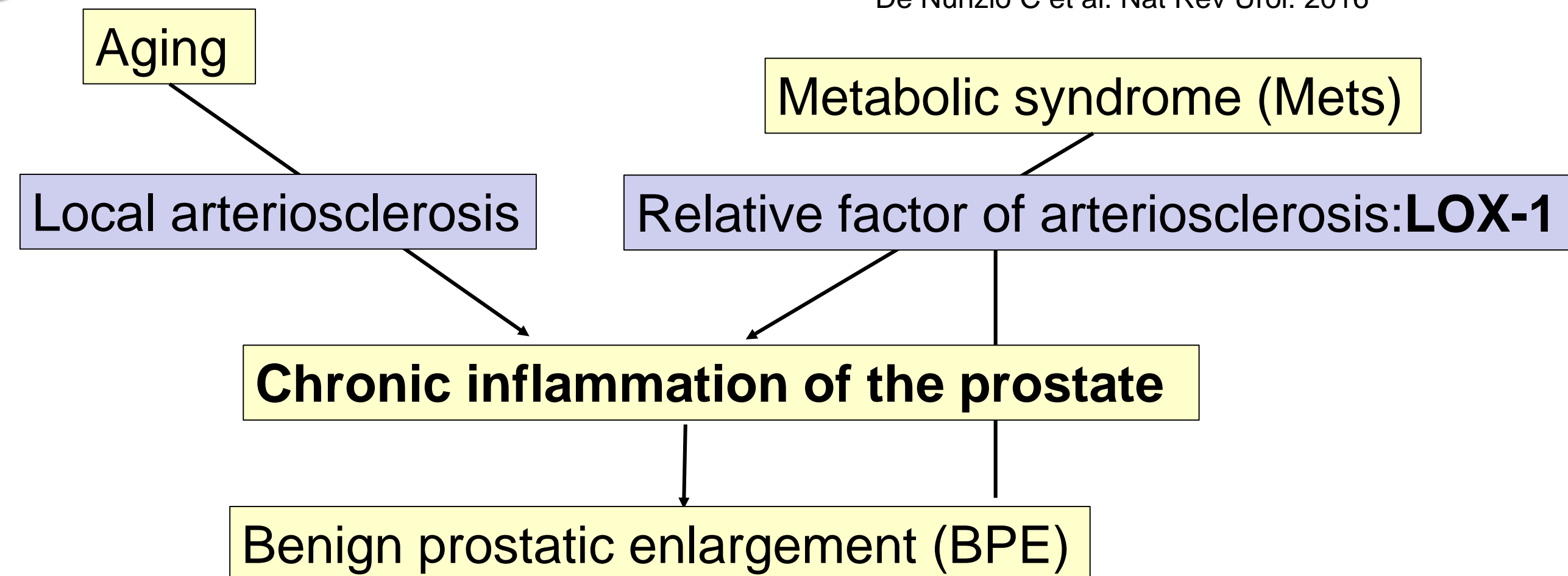
**Results:** Local atherosclerosis was observed in 28% (14/50). Prostate size and the inflammation score were significantly increased in the presence of atherosclerosis ( $P=0.006$ ,  $P<0.001$ , respectively). There was also a significant increase of LOX-1 in the epithelial and stromal cells of the prostate in the presence of atherosclerosis (all,  $P<0.001$ ). Concerning the presence of macrophages, subjects with arteriosclerosis had significantly more positive expression of ionized calcium-binding adapter molecule-1 (IBA-1), a marker of macrophages, than subjects without atherosclerosis ( $P<0.001$ ).

**Conclusions:** In human surgical specimens, chronic inflammation owing to local atherosclerosis of the prostatic arteries was significantly related to prostatic enlargement. Given the immunohistochemical analyses, the putative pathogenesis for this relationship is that LOX-1 induces macrophage infiltration, leading to BPE.

## I. Background

### Pathogenesis of the benign prostatic enlargement

De Nunzio C et al. Nat Rev Urol. 2016



### Hypothesis

Local arteriosclerosis and LOX-1 might induce BPE, because these are associated with the aging and Mets.

## II. Objective

To elucidate the pathogenesis of BPE due to chronic inflammation caused by arteriosclerosis,

1. The association between local arteriosclerosis and chronic inflammation in the prostate was investigated.
2. The association between the expression of LOX-1 and generation of BPE was investigated.

## III. / Patients and methods

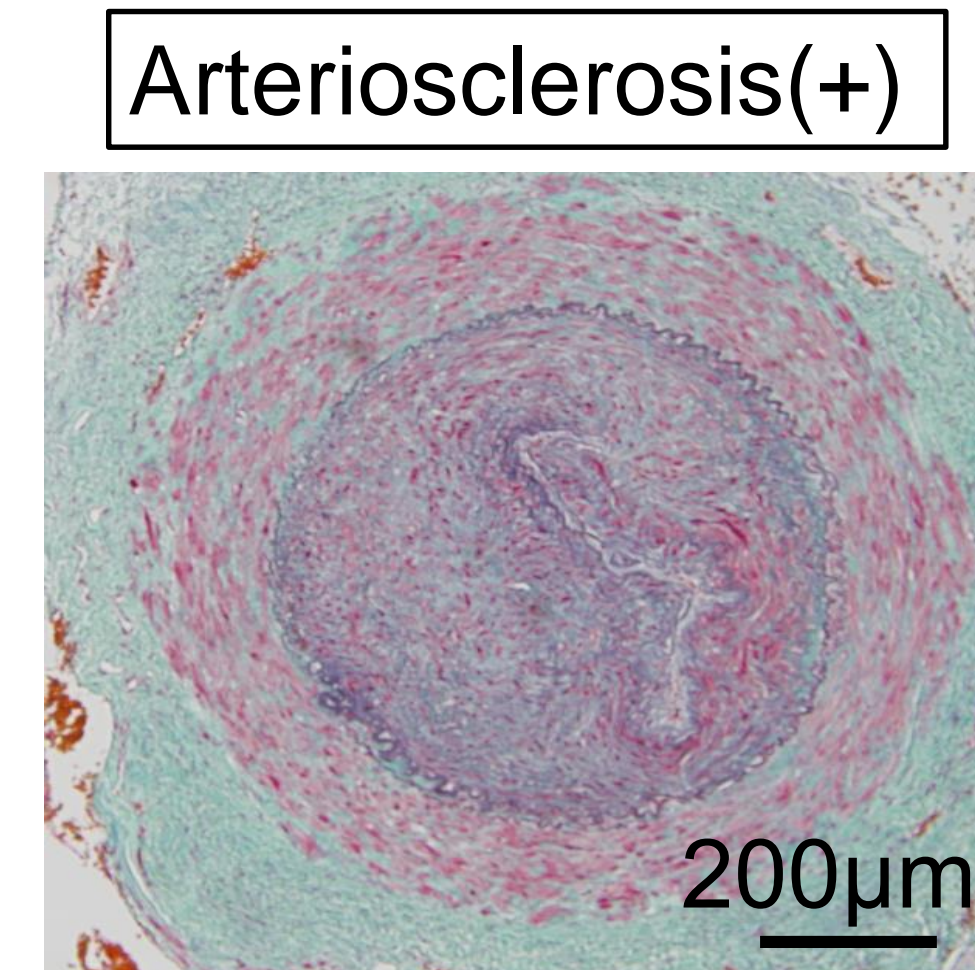
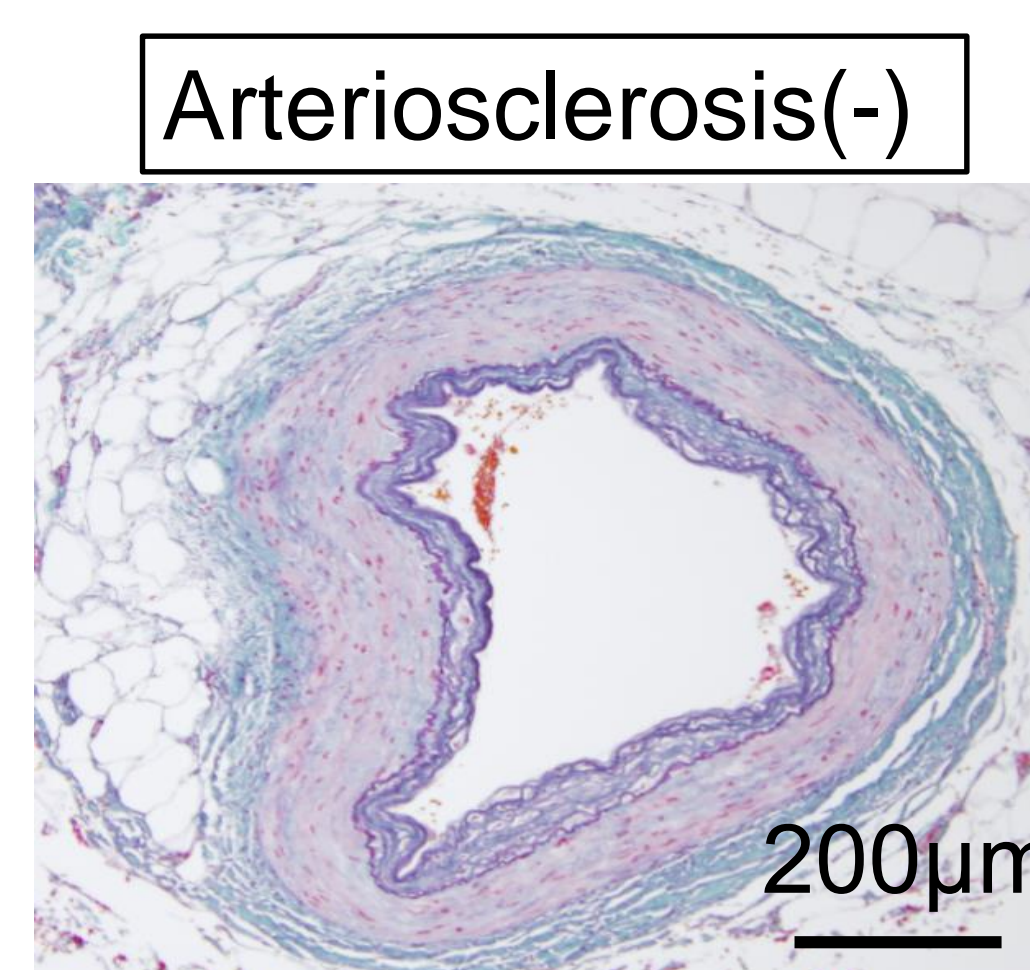
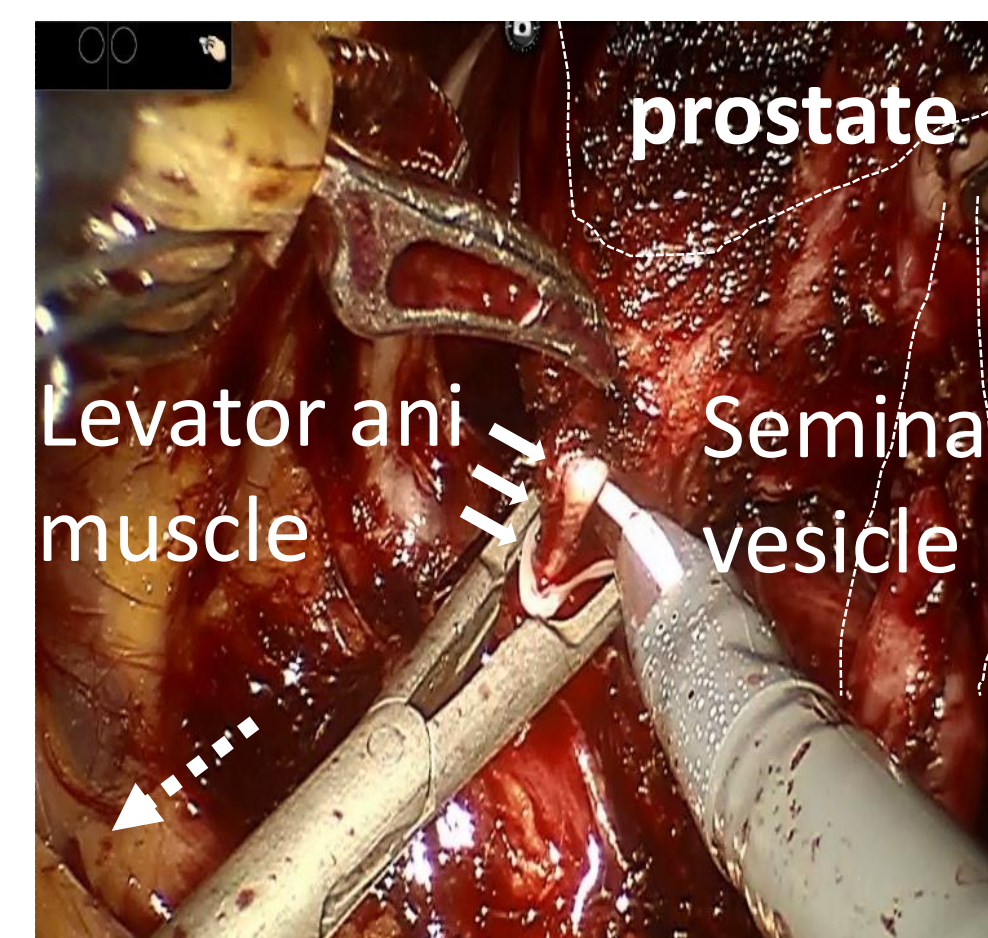
**Materials** 50 subjects who underwent robot-assisted radical prostatectomy (RARP)

The definition of local arteriosclerosis in the prostatic arteries

Haga N, et al. Prostate, 2018

Removal of the prostatic artery

Elastica-Masson staining



Arteriosclerosis was defined when atheroma occupied more than 50% of the inner cavity in the prostatic artery.

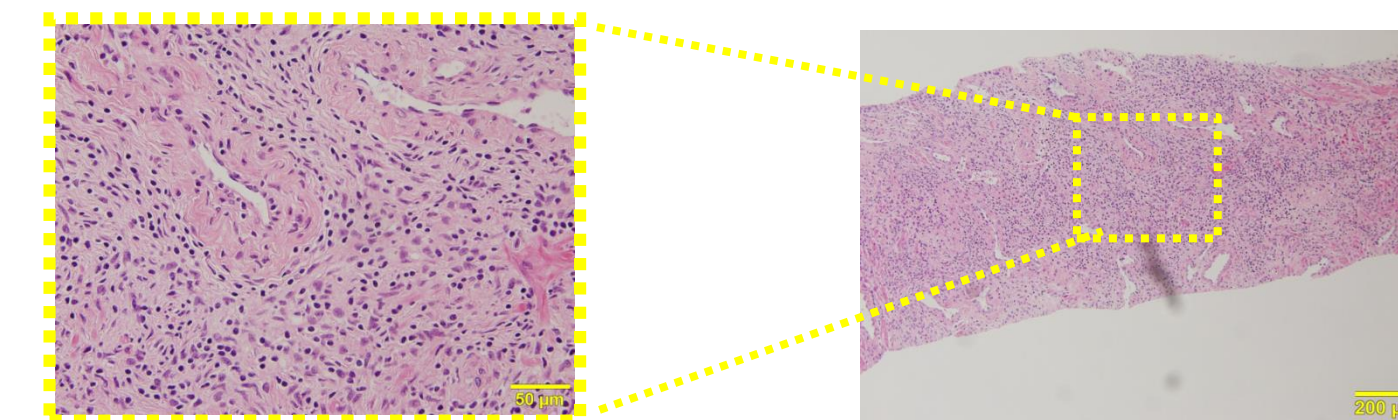
The association between local arteriosclerosis and chronic inflammation

Prostatic inflammatory score

Vignozzi, L. et al.: Prostate, 2013

Inflammatory grade	Inflammatory extent	Anatomical location
Mild	1	Focal
Moderate	2	Multifocal
Severe	3	Diffuse
	1	Stromal
	2	Periglandular
	3	Glandular

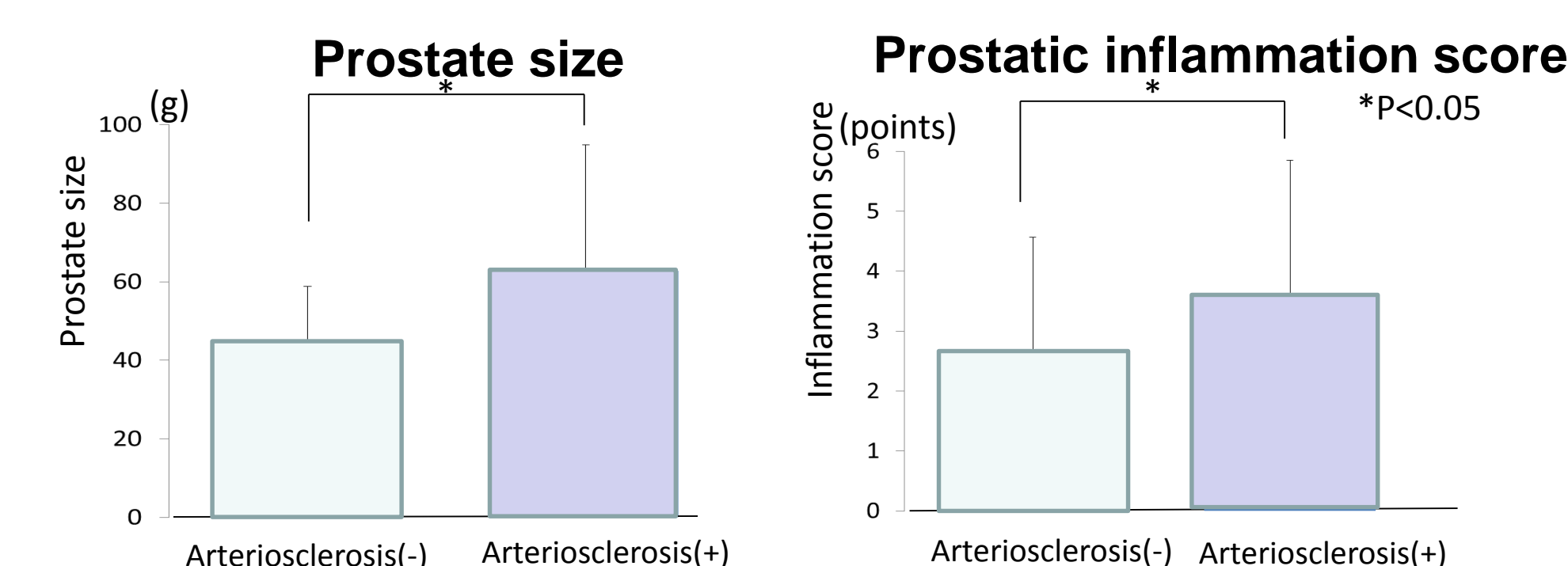
Inflammatory score was calculated by the sum of three different histological inflammatory parameters. Higher score indicated more severe inflammation.



Inflammatory score = grade (3) + extent (3) + location (3) = 9

## IV. Results

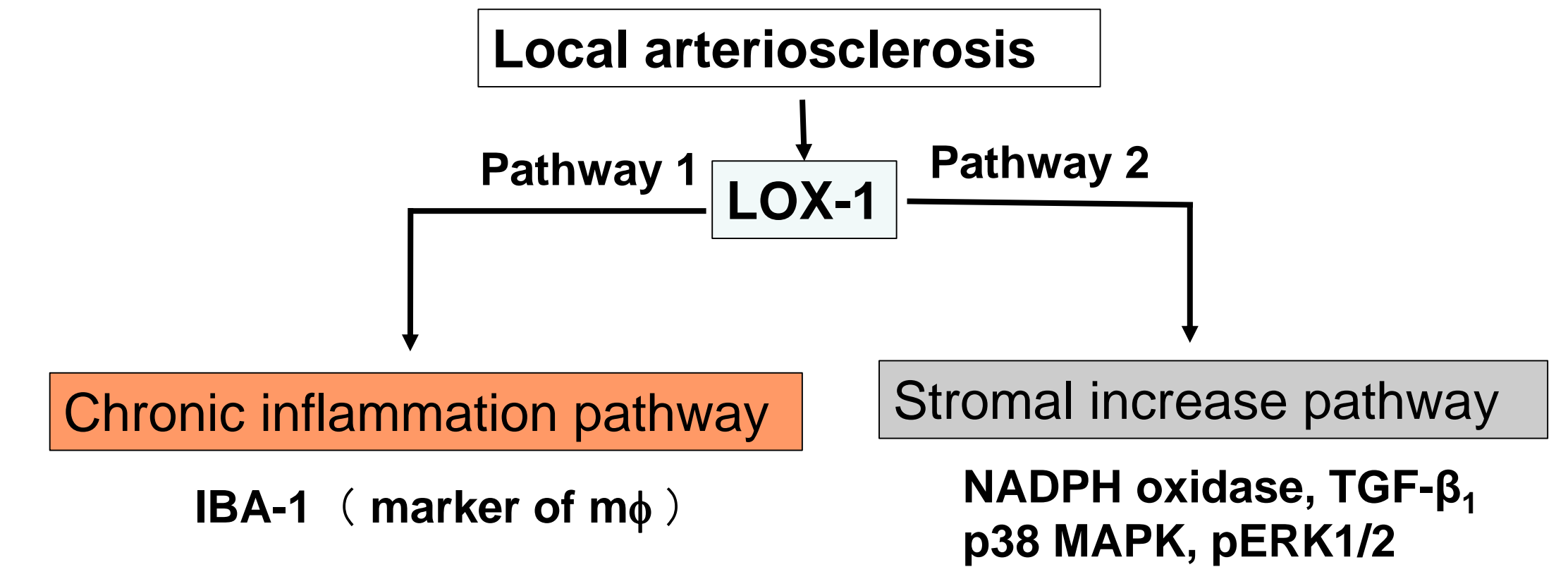
Exam.1 The association between local arteriosclerosis and chronic inflammation



Prostate size was more and prostatic inflammation score were higher in the arteriosclerosis group.

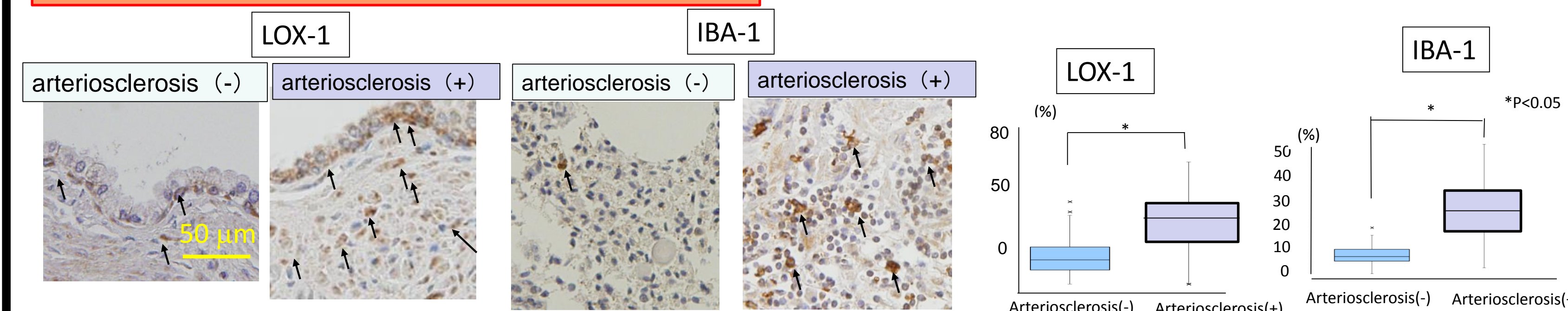
## IV. Results

Exam. 2 : The association between the LOX-1 expression and the generation of BPE



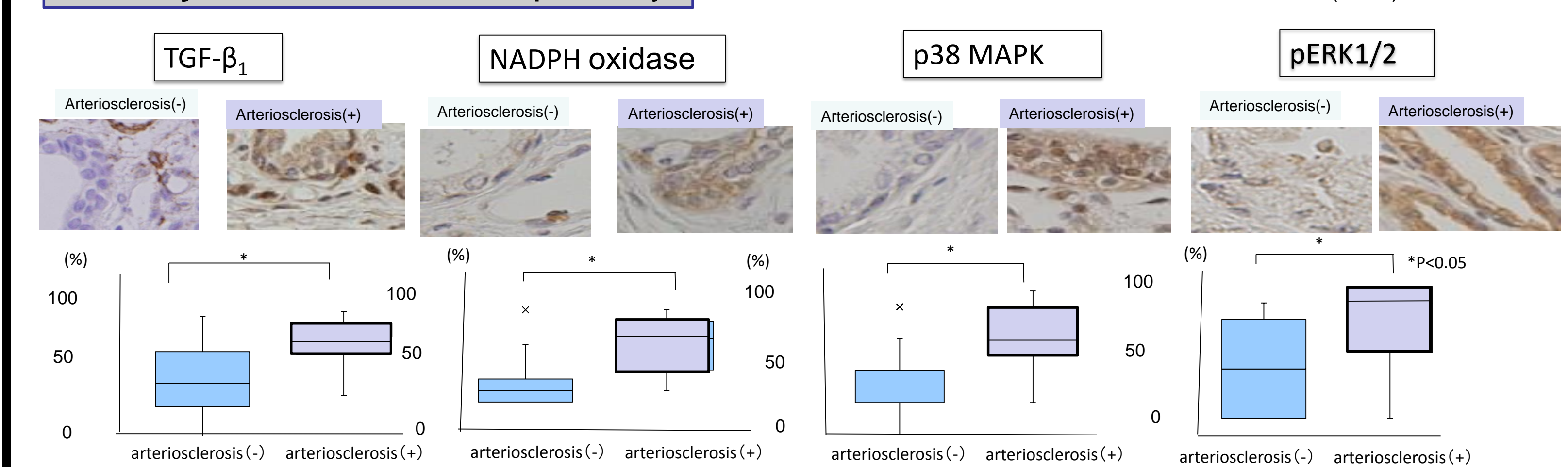
The expression of these markers were compared according to the presence or absence of local arteriosclerosis by immunohistochemistry.

pathway 1 : Chronic inflammation pathway



Significant expression of LOX-1 and IBA-1 were observed in the arteriosclerosis group.

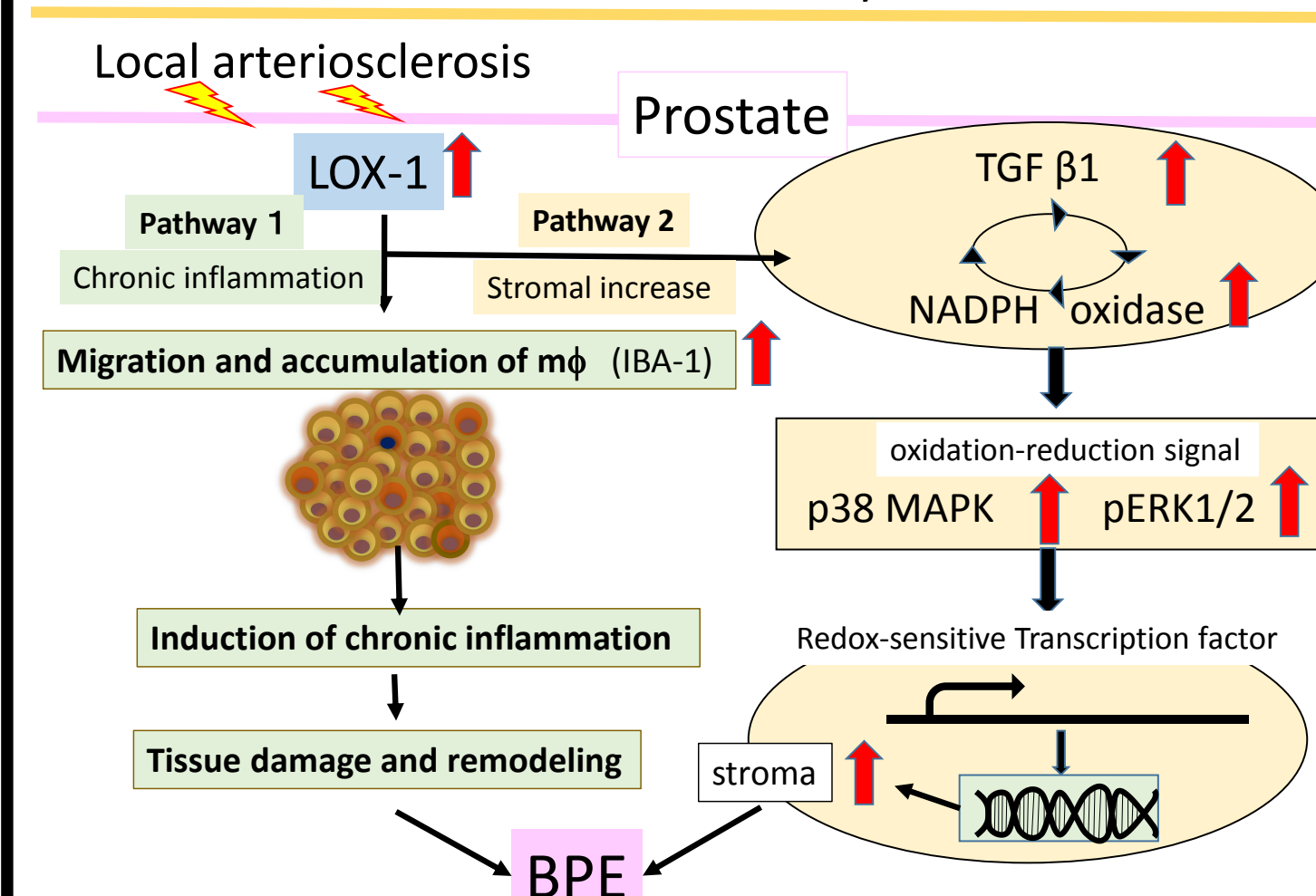
Pathway 2: Stromal increase pathway



Significant expression of TGF-β1, NADPH oxidase, p38 MAPK, and ERK1/2 were observed in the arteriosclerosis group.

## V. Conclusions

Possible mechanism of BPE induced by local arteriosclerosis



Lox-1 is up-regulated by local arteriosclerosis.

Pathway 1

In the chronic inflammation pathway, migration and accumulation of macrophage has occurred, leading the induction of Chronic inflammation. As a result, tissue damage and remodeling has occurred in the prostate, leading to the BPE.

Pathway 2

In the stromal increase pathway, TGFβ1 and NADPH oxidase were activated, leading the activation of oxidation-reduction signal. As a result, stromal increase in the prostate has occurred, leading to the BPE.