

EP-130

**혈관주위 Hyaluronidase의
혈관투과를 통한 혈관 내
Hyaluronic Acid의 분해기전**

(Transvascular Transport of Perivascular Hyaluronidase Enables Intraluminal Hyaluronic Acid Degradation)



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Purpose: Perivascular hyaluronidase injection is widely used to treat hyaluronic acid (HA) filler-associated vascular occlusion, yet the mechanism by which the enzyme reaches intravascular HA remains unclear. This study aims to provide direct *in vivo* evidence of transvascular delivery and intraluminal degradation of hyaluronic acid (HA) following perivascular hyaluronidase injection.

Methods: A murine hind limb arterial occlusion model was developed using fluorescein-labeled HA. Two-photon intravital microscopy was employed to visualize intravascular HA and Alexa Fluor 594-conjugated hyaluronidase. Hyaluronidase was administered perivascularly at low (1mg/mL) and high (50mg/mL) concentrations. Mean fluorescence intensity (MFI) within the lumen was quantified to evaluate penetration kinetics and the cumulative effects of repeated dosing.

Results: Control observations confirmed stable intravascular HA fluorescence, validating the model. Upon perivascular injection, labeled hyaluronidase accumulated at the vessel wall before traversing into the lumen. High-dose hyaluronidase induced a significant, time-dependent reduction in intraluminal HA fluorescence, whereas low-dose administration showed negligible effects. Repeated injections resulted in a progressive, cumulative decrease in the HA signal, confirming dose-dependent degradation.

Conclusion: This study provide direct intravital imaging evidence that perivascularly administered hyaluronidase can across the arterial wall to degrade intraluminal HA *in vivo*. These findings provide mechanical support for high-dose and repeated administration in the management of HA filler-associated vascular complications and highlight the potential for transvascular delivery of therapeutic macromolecules in vascular pathology.

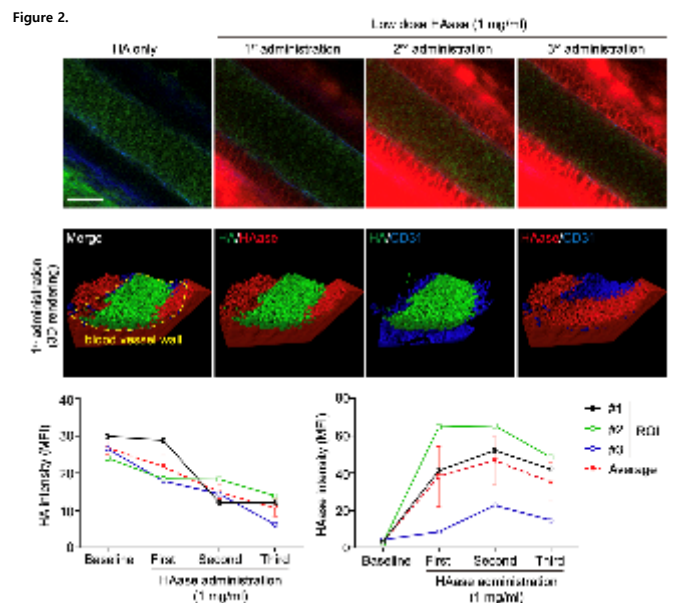
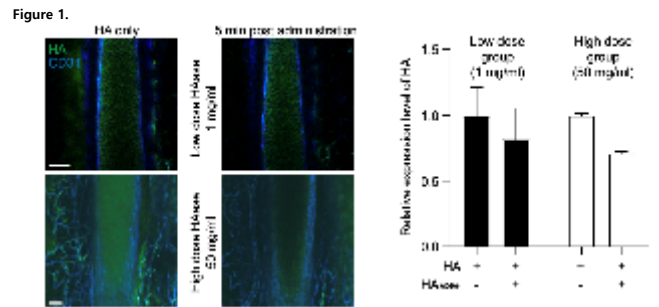


Fig 1. Representative intravital images showing intravascular HA signal in the HA-only group, low-dose HYAL group (1 mg/mL), and high-dose HYAL group (50 mg/mL) at 5 minutes post injection. Quantification of relative HA expression demonstrates significant reduction only in the high-dose group. Data are normalized to HA-only control.

Fig2. Effect of repeated perivascular HYAL injections on intravascular HA degradation. Sequential injections (first, second, and third) resulted in progressive reduction of HA MFI. Quantification demonstrates cumulative decrease in HA signal with repeated dosing. Corresponding HYAL MFI within the vascular lumen increased following each injection, supporting enhanced intraluminal enzyme presence.

Data are presented as mean ± SD. Statistical comparisons were performed using repeated-measures ANOVA with appropriate post hoc testing. Scale bar, 50 μm. Abbreviations: HA, hyaluronic acid; HYAL, hyaluronidase; MFI, mean fluorescence intensity