In vivo degradation of hyaluronic acid (HA)-based fillers by exogenous hyaluronidases

Raj Chopra, MD, FACS;[1] Derek Jones, MD;[2] Christopher K. Hee, PhD;[3]

Garrett T. Shumate, BS;[3] Darin J. Messina, PhD[3]

[1]Department of Surgery, David Geffen School of Medicine at UCLA, Los Angeles, CA, USA;

[2]Division of Dermatology, University of California at Los Angeles, Los Angeles, CA, USA;

[3]Allergan plc, Irvine, CA, USA

Purpose: One advantage of HA-based fillers is their reversibility. Although this has been demonstrated *in vitro* primarily with lab-grade hyaluronidase, there is a perception that some fillers may be more difficult to degrade *in vivo*. The purpose of this study was to evaluate *in situ* the ability of two commercially-available hyaluronidases to degrade HA fillers with different physicochemical properties.

Methods and Materials: Sprague Dawley rats were injected subcutaneously with two HA fillers, VYC-20L [20 mg/mL] or HYC-24L+ [24 mg/mL], to create a projecting bolus. Four days post-injection, recombinant human hyaluronidase (HX) or ovine hyaluronidase (VIT) were administered at varying dose levels (5U/0.1mL bolus, 10U/0.1mL bolus, and 30U/0.1mL bolus). 3D images were captured to quantify the loss of projection at six time points over 72 hours. Histology was performed to confirm degradation at 2 weeks post-administration.

Results: For both HA fillers, complete loss of projection was achieved with the highest dose of HX and VIT. More projection (*i.e.* less degradation) was detected with the lower doses of HX and VIT. No significant differences in the resulting projection were observed when comparing

the effect of HX to VIT (at any dose level) or the degradation response of VYC-20L or HYC-24L+ to either hyaluronidase. The histology showed significant loss of filler material at 2 weeks, with minimal amounts of filler observed.

Conclusion: The *in vivo* susceptibility of HA fillers to hyaluronidase-induced degradation has not been investigated previously. This novel animal model evaluated the susceptibility of fillers with different physicochemical properties to commercially-available hyaluronidases. Using an animal model allowed degradation to be evaluated while incorporating variables introduced by the biological environment (e.g. clearance, competing substrates for hyaluronidase). The results showed that the projection detected by 3D imaging was able to be reduced to non-detectable levels for both fillers. A dose-dependent response was observed, suggesting that the amount of degradation can be varied. Additionally, the same degree of degradation was observed for both commercially-available hyaluronidases and, despite differences in physicochemical properties, the same degree of degradation was achieved for both VYC-20L and HYC-24L+. These outcomes confirm that enzymatic degradation of HA by exogenous hyaluronidase is not hindered by the physicochemical properties of the fillers when evaluated *in vivo*.