A Novel Animal Model for Hyaluronic Acid Filler Longevity

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ABSTRACT

Introduction: Tissue filler injections are among the most commonly performed procedures in Facial Plastic Surgery. No single animal model has emerged as an accepted standard to evaluate tissue filler longevity. To validate a rat model three hyaluronic acid fillers with different known residence times in humans were tested.

Experimental Design: In vivo animal study to compare residence time of three hyaluronic acid fillers to published residence times in humans.

Methods: Two hundred microliter of Restylane (n=10), Captique (n=19), and Juvederm Ultra (n=10) were injected into the dorsal subcutis of each rat. The subcutaneous injection was chosen in the rat secondary to the rat’s dense dermal layer with dermal injections resulting in epidermal and dermal injury. The height, width, and length (Fig 2C-D) of each bleb were measured three times with digital calipers, averaged, and then the skin thickness subtracted to establish the dimensional measurements of each bleb. Ellipsoid volume measurements ([(3/4)(π)(1/2 length)(1/2 width)] were performed at Day 0, Day 1, and every ten days for 1 year or until complete absorption of the filler. Volume ratio and height ratio were calculated by comparing volume and height measurements for each time point to measurements on Day 0. Filler longevity was compared with published residence times of the four tissue fillers in humans. Caliper measurements were validated with MRI volumetric analysis. Statistical analysis was performed using ordinary least squares to determine significance of correlation. The hyaluronic acid filler blub, overlying skin, and underlying subcutaneous tissue were excised and fixed in 4% formalin and embedded in paraffin. Sections were stained with hematoxylin and eosin and analyzed with light microscopy.

RESULTS

Figure 2: A. Persistence pattern in rat model of 4 commercially available hyaluronic acid fillers; B. Filler longevity in the rat subcutis significantly correlates (p < 0.002) with published human residence time of four hyaluronic acid fillers (Fig. 2B).

Concentration: Captique’s residence time was significantly shorter than that of Restylane and Juvederm, which had comparable residence times. While the longevity of the three fillers were not of the same duration in the rat as human residence times, the relative duration of the fillers was comparable therefore demonstrating the rat as a valid animal model to compare various tissue filler materials. The shorter residence time in the rat dermis/subcutaneous space allows for accurate rapid preclinical testing of tissue filler materials.

INTRODUCTION

Due to its minimally invasive nature and relative safety, the use of dermal fillers for the correction of wrinkles and facial contouring has become an increasingly popular procedure. Between 2000 and 2008 the number of dermal filler injections increased by 225%.¹ The demand for dermal fillers is reflected in the steady appearance of new dermal fillers on the market. Since the approval of the first dermal filler in 1981 the FDA has approved more than ten new fillers. The various dermal fillers currently available differ in their composition, concentration, molecular weight, degree of cross-linking, particle size, viscosity, mechanical properties, extrusion properties, reversibility, and, perhaps of greatest concern to patients, longevity. It is therefore not surprising that a major goal in the development of new dermal fillers is to enhance persistence while maintaining biocompatibility. A number of different methods have been used to measure in vivo persistence, which almost always involve volunteer human patients and a subjective visual analog scale assessment.²⁻⁴ MRI and ultrasound have also been used, but these are more costly.⁵ Rabbit ear and porcine animal models have been used to study the persistence of cross-linked collagen and the effects of laser treatment on hyaluronic acid filler implants, respectively.⁶⁻⁷ Rat animal models are smaller, less expensive, and more easily accessible than rabbits or pigs.

DISCUSSION

Hyaluronic acid fillers: Hyaluronic acid (HA) is a naturally occurring polysaccharide found in the extracellular matrix of tissues including the dermis. Its biocompatibility, nonimmunogenecity, natural feel and appearance make HA an ideal facial plastic filler.⁹⁻¹⁰ HA may be crosslinked to stabilize the molecule, thereby decreasing the rate of degradation and increasing its duration of action.

Tissue filler longevity: Various studies report that Juvederm Ultra is estimated to last 9 months,¹¹ Restylane 6 months,¹²,¹³ Prevelle Silk 4.5 months,¹²,¹³ and Hylaform 3 months.¹³ This study directly compares four hyaluronic acid fillers injected into the dorsal rat subcutis. Figure 2D demonstrates the filler location in the subcutaneous space, just deep to the rat’s unique superficial dorsal muscle, the panniculus carnosus.

MRI validation: Volumetric MRI is an accurate and sensitive tool with which to determine the anatomic size and structure of subcutaneous structures.¹⁴ Figure 3 demonstrates a comparison of MRI with our caliper volumetric analysis method to compare various tissue filler materials. The shorter residence time in the rat dermis/subcutaneous space allows for accurate rapid preclinical testing of tissue filler materials.

CONCLUSIONS

Caliper-based rat-subcutis method demonstrates consistent volumetric analysis.

Caliper method correlates with human residence times of hyaluronic acid fillers.

Validated expedited animal model for hyaluronic acid fillers.

Future utility evaluating residence time of other fillers.

REFERENCES

¹³medscape.medscape.com/article/1125066-overview

Supported by a grant from Kythera Pharmaceuticals