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Evaluation of type II thyroplasty on phonatory physiology in an excised canine larynx model

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Abstract

Objective—Type II thyroplasty is an alternative treatment for spasmodic dysphonia, addressing hyperadduction by incising and lateralizing the thyroid cartilage. We quantified the effect of lateralization width on phonatory physiology using excised canine larynges.

Methods—Normal closure, hyperadduction, and type II thyroplasty (lateralized up to 5mm at 1mm increments with hyperadducted arytenoids) were simulated in excised larynges (N=7). Aerodynamic, acoustic, and videokymographic data were recorded at three subglottal pressures relative to phonation threshold pressure (PTP). One-way repeated measures ANOVA assessed effect of condition on aerodynamic parameters. Random intercepts linear mixed effects models assessed effects of condition and subglottal pressure on acoustic and videokymographic parameters.

Results—PTP differed across conditions ($p<0.001$). Condition affected percent shimmer ($p<0.005$) but not percent jitter. Both pressure ($p<0.03$) and condition ($p<0.001$) affected fundamental frequency. Pressure affected vibratory amplitude ($p<0.05$) and intra-fold phase difference ($p<0.05$). Condition affected phase difference between the vocal folds ($p<0.001$).

Conclusions—Hyperadduction increased PTP and worsened perturbation compared to normal, with near normal physiology restored with 1mm lateralization. Further lateralization deteriorated voice quality and increased PTP. Acoustic and videokymographic results indicate that normal physiologic relationships between subglottal pressure and vibration are preserved at optimal lateralization width, but then degrade with further lateralization. The 1mm optimal width observed here is due to the small canine larynx size. Future human trials would likely demonstrate a greater optimal width, with patient-specific value potentially determined based on larynx size and symptom severity.

Keywords

Type II thyroplasty; laryngology; laryngeal framework surgery; vocal folds; excised canine model

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INTRODUCTION

Spasmodic dysphonia is a focal dystonia that affects speech. Adductor spasmodic dysphonia (ADSD) accounts for about 85% of spasmodic cases and affects laryngeal adductor muscles resulting in adductory vocal fold spasms that cause a strained, strangled voice.^{1,2} Patients' dysfluency affects their ability to communicate. The cause of ADSD is unknown, although it is believed to be a central sensorimotor processing disorder that causes excessive laryngeal adductor muscle activation.^{1,3} ADSD is relatively rare and estimated to affect 1 in 100,000 people in the United States with a female predominance.⁴ However, ADSD is a chronic condition and typically resistant to voice therapy. Treatments for ADSD have focused on symptom relief and the gold standard is botulinum toxin injection. Less frequently used treatments include recurrent laryngeal nerve section and type II thyroplasty.

Botulinum toxin has been used successfully with minimal morbidity though it must be repeated every 3-4 months.^{2,5,6} Despite some symptom relief, a normal voice is rarely achieved⁷ and voice can vary dramatically over the injection cycle. Suboptimal voice is experienced 70% of the time.⁸ Temporary dysphonia, frequent clinic visits, and difficulty selecting the proper dosage and injection site are additional patient barriers. For patients with unsatisfactory results or for whom the frequency of office visits is not feasible, a more permanent solution is warranted.

Recurrent laryngeal permanently weakens the vocal fold adductors and relieves symptoms, but often results in a weak, breathy voice. RLN section can also cause glottal incompetence, which increases risk of dysphagia. Long-term follow up results with patients of denervation-reinnervation procedures resulted in breathiness (30%), swallowing difficulties (32%), and breathing difficulties (21%).⁹ Additionally, the procedure is irreversible so poor outcomes can be permanent. Anecdotally, many patients reported the relief of symptoms and permanence outweighed negative voice outcomes; however, poorer voice outcome than botox, swallowing risks, and high late-recurrence rates have limited widespread use of this procedure as an option for ADSD treatment.^{10,11}

Isshiki et al. reported type II thyroplasty to addresses limitations of both recurrent laryngeal nerve section and botulinum toxin injection.¹² Type II thyroplasty lateralizes the thyroid cartilage lamina to relieve vocal fold compression and reduce the effects of adductor spasticity. Silicone wedges, titanium mesh with Gore-Tex, and titanium bridges have been used to fix and stabilize the thyroid cartilage, with titanium bridges showing greater stability and durability.¹³ A relatively low revision rate of 5.6% has been reported,¹⁴ and VHI-10, aerodynamic, and acoustic results have been evaluated at 1-3 years post-surgery and regularly shown improvements post-operatively.^{13,15-18} Careful surgical technique, the right patient indications, and stable glottal separation were indicated as essential to improving outcomes.¹⁴ Because this procedure offers a more permanent solution to ADSD symptoms than botulinum toxin injection, but is reversible and easily tailored to the patient, it is worth exploring as a routine option for patients that are not satisfied with the results or frequency of botulinum toxin.

Type II thyroplasty is a technically challenging operation due to the delicate structures underneath the thyroid cartilage that must be left intact for a good outcome.¹⁹ Optimal thyroid cartilage lateralization is subjectively determined while the patient is under local anesthetic. While patient input on fluency and perceptual assessment are important in determining optimal lateralization, objective intraoperative voice assessment could standardize the procedure and improve outcomes. Acoustic and aerodynamic parameters can objectively assess voice quality and efficiency. Acoustic parameters indicate symmetry and aerodynamic parameters reflect vocal effort. Greater subglottal pressure and laryngeal resistance (R_L) have been measured in patients with ADSD.²⁰ Phonation threshold pressure (PTP) is the minimum pressure necessary to sustain phonation. The relationship between PTP and R_L makes it a good parameter for objectively measuring relief of vocal compression during type II thyroplasty.

We used an excised canine model to evaluate the relationship between vibratory parameters (aerodynamic, acoustic, videokymographic) and glottal compression with subsequent thyroid lateralization. Excised canine models have been used to simulate human voice disorders due to its similar vibratory properties²¹ and allow precise control of vocal fold position to simulate glottal compression and midline lateralization. We evaluate the effects of these simulated conditions on aerodynamic, acoustic, and kymographic parameters. Well-correlated parameters may potentially be useful intraoperatively to determine the optimal separation for each patient.

METHODS

We modeled hyperadduction as a surrogate for spasmodic dysphonia and type II thyroplasty midline lateralization in an excised canine model.

Larynges

Larynges were obtained from canines sacrificed for purposes unrelated to this study (N=7). The larynges were dissected from the neck and the supraglottic structures, including the epiglottis and false vocal folds, were removed to visualize the true vocal folds.

Excised bench apparatus

The excised bench apparatus was developed by Jiang et al.²¹ Briefly, the larynges are mounted and secured above a pseudolung. Micropositioners manipulate the arytenoid cartilages and medialize the vocal folds. Two sutures were placed on either side of the thyroid cartilage midline and extended to elongate the vocal folds 10% (Figure 1). Air is passed through two humidifiers in series (Fisher & Paykel Healthcare Inc., Laguna Hills, California) and forced through the pseudolung to initiate and sustain vocal fold vibration. Pressure and flow sensors (MMG005V10WZMA0T1A4 and FMA 1610A, Omega Engineering, Stamford, CT) below the level of the larynx measure subglottal pressure and airflow. A microphone (RTA-M, dbx Professional Products, Sandy, Utah) positioned 10 centimeters from the glottis collects acoustic data. Microphone and pressure and airflow sensor signals are collected via a data acquisition board (USB 6229, National Instruments, Austin, TX) by a custom LabVIEW program (LabVIEW 8.5, National Instruments, Austin,

TX). A high-speed video camera (FastCAM Ultima APX, Photron USA, San Diego, CA) positioned above the larynx collects videos at 4,000 frames per second and video signals are collected by Photron FastCAM viewer 2.8. Saline solution is applied regularly to the vocal folds to maintain hydration throughout the experiments.

Simulation of conditions

Normal vocal fold adduction is simulated by positioning the vocal folds so that they are just approximated. To model ADSD, compression is applied by angling the micropositioners 30 degrees toward the anterior thyroid cartilage and moving them closer to the midline. Compression is increased until the point when the micropositioners can no longer be moved medially.

After data collection in the normal and compressed configurations, the larynx is removed from the excised bench to perform simulated type II thyroplasty. As described by Isshiki 2010, precautions are taken to avoid violation of the inner thyroid perichondrium and entrance into the endolarynx. First, a tympanoplasty knife is used to make the midline incision. Second, the upper third of the thyroid cartilage is divided first, followed by the lower third, and lastly the middle third. If separation is restricted, the thyroid cartilage is undermined to release the perichondrium without perforating the tissue. An additional two sutures were placed at the bottom of the thyroid cartilage on either side of the midline. The larynx was then remounted on the excised larynx apparatus. Sutures were extended both forward for elongation and laterally for lateralization (Figure 1). A stage was built to apply tension to the sutures to elongate the vocal folds and separate the thyroid cartilage. After mounting, the PTP was checked to ensure the same glottal configuration was used as in the ADSD condition. The thyroid cartilage was then separated at 1 mm increments from 1 mm to 6 mm or until aphonia or perforation of the inner perichondrium occurred. Figure 2 shows a superior view of each condition. The cartilages were then returned to 1 mm to confirm PTP or estimate any effects of hysteresis throughout data collection.

Experimental variables

Aerodynamic variables include phonation threshold pressure (PTP), phonation threshold flow (PTF), phonation instability pressure (PIP), and phonation instability flow (PIF). PTP and PTF are the minimum pressure and flow required to sustain phonation, and reflect ease of phonation. Laryngeal resistance (R_L) was calculated as PTP/PTF . R_L is also reflective of ease of phonation. PIP and PIF are the pressure and flow and at which the signal becomes unstable or chaotic. The phonatory pressure range (PPR) is the difference between PIP and PTP. The phonatory flow range (PFR) is the difference between PIF and PTF. Larger ranges reflect better vocal function.

Acoustic measurements include fundamental frequency (F0), percent jitter, and percent shimmer. F0 was measured to study the pressure-frequency relationship. Percent jitter is defined as the cycle-to-cycle variation in frequency normalized to fundamental frequency, and percent shimmer is the cycle-to-cycle variation in amplitude normalized to average amplitude. These parameters were calculated using TF32 software (TF32 and Cspeech, Madison, WI) and are good indicators of vocal fold symmetry.

Videokymographic parameters were measured from high-speed videos using a custom MATLAB software (MATLAB R2012b, Mathworks, Natick, MA). Figure 3 shows a kymograph from each condition. Briefly, a pixel line along the glottis at the point of greatest vibratory amplitude is selected and curves are fit to the upper and lower vocal fold lips. The amplitudes of the right and left vocal fold lips were measured. The phase differences between the upper and lower lips of each vocal fold (right intra-fold and left intra-fold phase differences), and the phase differences between the right and left vocal folds (upper inter-fold and lower inter-fold phase differences) were also measured from the curves. These parameters characterize the vibratory motion of the vocal folds.

Statistics

Sigma Plot 13.0 (Systat Software, San Jose, CA) and R 3.0.1 (The R Foundation for Statistical Computing) were used for statistical analyses. A paired t-test was performed to compare PTP at the start and end of data collection. One-way repeated measures analysis of variance (ANOVA) was performed to test for differences in aerodynamic parameters. Tukey's least significant difference (Tukey's LSD) used to correct for pairwise comparisons. Tukey's LSD was calculated at $N=7$, assuming N remained the same for all levels. Since some larynges failed to phonate beyond 3 mm, this assumption breaks down at 4 and 5 mm, so differences seen between these levels should be interpreted cautiously. Random intercepts linear mixed effects models were used to assess the effects of condition and pressure level on acoustic and high-speed video parameters by likelihood ratio tests.

RESULTS

Aerodynamic results

A paired t-test found no significant difference between PTP at the start and end of data collection within each larynx ($t=0.182$, $p=0.862$). Significant differences were found between treatment groups for PTP ($F=18.394$, $df=6$, and PTF ($F=16.358$, $df=6$, $p<0.001$). By Tukey's LSD comparison ($LSD=2.116$), PTP was significantly higher for hyperadduction than normal, and PTP at 1mm was significantly lower than hyperadduction, and 1mm was significantly higher than normal. R_L neared significance ($F=2.117$, $df=6$, $p=0.083$). A trend towards significance was also observed for PIF ($F=2.279$, $df=6$, $p=0.065$) and PFR ($F=2.00$, $df=6$, $p=0.099$), while no significance was found for PIP ($F=1.242$, $df=6$, $p=0.315$) or PPR ($F=1.571$, $df=6$, $p=0.192$). See Figures 4, 5, and 6 for box plots of PTP, PTF, and R_L . A full list of effects evaluated are provided in Table 1, and summary aerodynamic data are provided in Table 2.

Acoustic results

No significant effects were found for percent jitter, but condition had a significant effect on percent shimmer ($\chi^2=18.808$, $df=6$, $p=0.0045$), and both pressure ($\chi^2=7.3825$, $df=2$, $p=0.02494$) and condition ($\chi^2=30.53$, $df=6$, $p<0.001$) had significant effects on F_0 . No interactions were found between condition and pressure for jitter ($\chi^2=11.414$, $df=12$, $p=0.4938$), shimmer ($\chi^2=7.2499$, $df=12$, $p=0.8407$), or frequency ($\chi^2=10.041$, $df=12$, $p=0.6123$), supporting the validity of the mixed effects models. A full list of effects evaluated can be seen in Table 1.

Videokymographic results

Pressure had a significant effect on left upper ($\chi^2=6.2359$, $df=2$, $p=0.04425$) and lower ($\chi^2=7.5935$, $df=2$, $p=0.02244$) amplitudes, as well as on phase difference within the right ($\chi^2=6.923$, $df=2$, $p=0.031$) and left ($\chi^2=8.4732$, $df=2$, $p=0.014$) vocal folds. Effects of condition were seen on the phase difference in the left vocal fold ($\chi^2=21.574$, $df=6$, $p=0.0014$), inter-fold phase difference for the upper lips ($\chi^2=41.712$, $df=6$, $p<0.001$), and lower lips ($\chi^2=25.771$, $df=6$, $p<0.001$). A full list of effects evaluated can be seen in Table 1.

DISCUSSION

Using an excised canine larynx model allowed evaluation of vocal fold vibration physiology and biomechanics. Increasing hyperadduction in the model to simulate spasmodic dysphonia was successful as measured by increased PTP compared to the normal condition. These results lend support for the validity of this model to study the vibratory physiology of the vocal fold hyperadduction as a surrogate for spasmodic dysphonia.

The primary outcome measures of this study were aerodynamic. Aerodynamic measures reflect the effort required to sustain phonation.²² PTP increased with hyperadduction, but returned to near normal values with type II thyroplasty at 1 mm (Figure 4). This trend supports the use of this procedure to alleviate hypercompression. PTF was reduced with hypercompression but significantly closer to normal with type II thyroplasty (Figure 5). These results indicate that PTP and PTF might be good to measure when determining lateralization distance intra-operatively. Similarly, laryngeal resistance at the phonation threshold (PTP/PTF) was elevated with hypercompression and trended toward normal after type II thyroplasty but did not reach significance (Figure 6). R_L , PIF and PIP were not statistically different across conditions in the one-way repeated measures ANOVA, though significant differences were found using Tukey's LSD (Tables 1 and 2). Trends in the means showed that for PIF, the hyperadduction and 1mm lateralization conditions were lower than normal. PPR and PFR also did not reach significance, though PFR trended towards significance and comparison using Tukey's LSD showed differences (Tables 1 and 2). PPR means indicated that 1mm lateralization was closest, while 5mm lateralization and hyperadduction were farthest, from normal values. It was expected that under hypercompression the phonatory range would be smaller. While patients can accommodate abnormal physiology to achieve a relatively normal voice with an abnormal larynx, they can only sustain those accommodations within a narrow range of pressure and flow values. Therefore, abnormal physiology is reflected in low PIF and PIP values, as well as low PPR and PFR values. In contrast, a larynx after treatment with larger PPR and PFR indicates more normal physiology and a better voice outcome. Within individual larynges, this trend was observed, however the standard deviations were quite high and therefore the observed trend was not significant on one-way repeated-measure ANOVA. Ultimately, however, the phonatory range may not be as important to patients as symptom relief. Many patients are willing to accept what might be considered poor voice outcome (breathiness, small phonatory range, etc.) in order to alleviate their symptoms.¹¹

Acoustic results indicated that type II thyroplasty did not result in adverse changes in signal quality. While condition had an effect on shimmer, this was at the extremes of lateralization.

No differences were seen between normal, hyperadduction, or 1 mm lateralization on pairwise comparison. Additionally, the normal direct relationship between pressure and frequency was preserved.

Videokymographic results also support the conclusion that signal quality at 1mm of lateralization is similar to normal, suggesting that voice quality would not be significantly adversely affected by type II thyroplasty. Condition did have an effect on inter-fold phase difference, though this was again observed at the extremes of lateralization. Pressure relationships with amplitude and vertical phase difference were maintained.

Overall, the positive pressure and signal quality results observed in this study are encouraging. There are, however, some limitations to the conclusions that can be drawn from an excised canine larynx model. First, canine larynges are smaller than human, so the optimal lateralization distance of 1 mm will not translate directly to the larger human larynx. Generally, patients receive titanium shims ranging in width from 1-6 mm. However, the biomechanical results and functional relationships and results will translate well. Finally, since there is no neurological input to this model, neurological or behavioral changes were not simulated. In spasmodic dysphonia, symptoms are exacerbated by stress and occur during connected speech,² but this study looked only at sustained phonation. Useful conclusions can still be drawn from looking at the physiology and biomechanical responses of the tissue to alleviation of laryngeal compression, but further studies in humans should evaluate the behavioral response to the intervention.

CONCLUSION

Our excised canine model was successful in simulating the physiological effects of hyperadduction on vocal fold vibration. Hyperadduction increased PTP compared to normal, with near normal physiology restored with 1 mm lateralization. Excess lateralization deteriorated voice quality and increased PTP. Acoustic and videokymographic results indicate that normal physiologic relationships between subglottal pressure and vibration are preserved at optimal lateralization width, but then degrade with further lateralization. Future human trials would likely demonstrate a greater optimal width, with patient-specific value potentially determined based on larynx size and symptom severity.

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FIGURE 1.

A photograph of the excised canine larynx set-up. The apparatus used to manipulate the cartilage can be seen in the bottom left of the photo. The arrows indicate the directions of translation that can be applied to the cartilage. Inset in the upper right corner is a close up of a thyroid cartilage lateralized to three millimeters. Sutures in the thyroid cartilage were used to manipulated both elongation and lateralization.

FIGURE 2.

A superior view of the vocal folds at rest under A) Normal compression; B) Hyperadduction; C) Hyperadduction and 1mm lateralization; D) Hyperadduction and 2mm lateralization; E) Hyperadduction and 3mm lateralization; F) Hyperadduction and 4mm lateralization; and G) Hyperadduction and 5mm lateralization.

FIGURE 3.

Kymographs are pictured here. They depict a pixel line along the glottis at the point of greatest vibration amplitude over time. A) Normal compression; B) Hyperadduction; C) Hyperadduction and 1mm lateralization; D) Hyperadduction and 2mm lateralization; E) Hyperadduction and 3mm lateralization; F) Hyperadduction and 4mm lateralization; and G) Hyperadduction and 5mm lateralization.

FIGURE 4.
A box plot of Phonation Threshold Pressure (PTP).

FIGURE 5.
A box plot of Phonation Threshold Flow (PTF).

FIGURE 6.
A box plot of Laryngeal Resistance (R_L).

TABLE 1

Statistical tests and resulting p-values.

Test	Parameter	Statistic	Df	P-value
One-Way RM AVOVA	PTP	F=18.394	6	<0.001
	PTF	F=16.358	6	<0.001
	PTW	F=21.167	6	<0.001
	LR	F=2.117	6	0.083
	PIP	F=1.136	6	0.368
	PPR	F=1.492	6	0.217
	PIF	F=2.077	6	0.088
	PFR	F=1.970	6	0.104
Random Intercepts Linear Mixed Effects Model- Likelihood Ratio Test—Effect of Condition	Jitter	$\chi^2=4.1263$	6	0.6596
	Shimmer	$\chi^2=18.808$	6	0.0045
	Frequency	$\chi^2=30.53$	6	<0.001
	RU Amplitude	$\chi^2=3.6407$	6	0.7252
	RL Amplitude	$\chi^2=4.7027$	6	0.5825
	LU Amplitude	$\chi^2=10.839$	6	0.09348
	LL Amplitude	$\chi^2=1148$	6	0.07463
	Intra-right PD	$\chi^2=3.009$	6	0.8077
	Intra-left PD	$\chi^2=21.574$	6	0.001446
	Inter-upper PD	$\chi^2=41.712$	6	<0.001
	Inter-lower PD	$\chi^2=25.771$	6	<0.001
Random Intercepts Linear Mixed Effects Model- Likelihood Ratio Test—Effect of Pressure	Jitter	$\chi^2=15351$	2	0.4641
	Shimmer	$\chi^2=2.3477$	2	0.3092
	Frequency	$\chi^2=7.3825$	2	0.02494
	RU Amplitude	$\chi^2=5.2127$	2	0.0738
	RL Amplitude	$\chi^2=5.106$	2	0.07785
	LU Amplitude	$\chi^2=6.2359$	2	0.04425
	LL Amplitude	$\chi^2=7.5935$	2	0.02244
	Intra-right PD	$\chi^2=6.923$	2	0.03138
	Intra-left PD	$\chi^2=8.4732$	2	0.01446
	Inter-upper PD	$\chi^2=2.8671$	2	0.2385
	Inter-lower PD	$\chi^2=13559$	2	0.5077
Random Intercepts Linear Mixed Effects Model- Likelihood Ratio Test—Interaction test	Jitter	$\chi^2=11.414$	12	0.4938
	Shimmer	$\chi^2=7.2499$	12	0.8407
	Frequency	$\chi^2=10.041$	12	0.6123
	RU Amplitude	$\chi^2=3.4451$	12	0.9915
	RL Amplitude	$\chi^2=3.2223$	12	0.9938
	LU Amplitude	$\chi^2=5.8012$	12	0.9258

Test	Parameter	Statistic	Df	P-value
	LL Amplitude	$\chi^2=6.9724$	12	0.8594
	Intra-right PD	$\chi^2=15.431$	12	0.2187
	Intra-left PD	$\chi^2=15.948$	12	0.1936
	Inter-upper PD	$\chi^2=5.3745$	12	0.9443
	Inter-lower PD	$\chi^2=4.4546$	12	0.9738

TABLE 2

Means and standard deviations with Tukey's LSD comparisons. The lines under significance indicate pairs that have mean differences larger than the LSD.

Parameter	Condition	Mean	Standard Dev	Significance
Phonation Threshold Pressure (PTP) LSD=2.116	Normal	11.207	1.709	
	1MM	14.478	4.391	
	2MM	16.486	4.629	
	Hyper	16.782	4.110	
	3MM	22.686	6.344	
	4MM	27.260	10.616	
	5MM	27.663	4.947	
Phonation Threshold Flow (PTF) LSD=3.660	Hyper	9.818	6.011	
	Normal	10.670	5.120	
	1MM	13.308	11.688	
	2MM	19.213	11.509	
	3MM	26.203	12.790	
	4MM	34.616	14.532	
	5MM	45.694	16.682	
Laryngeal Resistance (LR) LSD=0.543	Hyper	2.468	1.822	
	1MM	1.907	1.407	
	Normal	1.697	1.898	
	2MM	1.184	0.795	
	3MM	1.016	0.443	
	4MM	0.884	0.476	
	5MM	0.660	0.235	
Phonation Instability Pressure (PIP) LSD=12.62	Hyper	34.971	11.670	
	3MM	41.373	11.755	
	5MM	45.014	14.453	
	2MM	47.129	23.081	
	Normal	51.182	34.527	
	1MM	55.105	33.480	
	4MM	60.532	25.241	
Phonation Instability Flow (PIF) LSD=10.530	Hyper	24.291	14.441	
	1MM	34.649	11.518	
	3MM	39.359	18.852	
	2MM	41.496	7.997	
	Normal	50.112	35.551	
	4MM	55.896	14.591	
	5MM	57.248	29.203	
Phonatory Pressure Range (PPR) LSD=12.556	5MM	17.351	9.624	
	Hyper	18.188	12.062	
	3MM	18.687	8.001	
	2MM	30.643	23.885	
	4MM	33.272	16.169	
	Normal	39.975	34.301	
	1MM	40.627	32.315	
Phonatory Flow Range (PFR)	5MM	11.554	17.279	
	3MM	13.156	6.569	

LSD=10.858	Hyper	14.473	12.184				
	4MM	21.280	3.789				
	1MM	21.341	11.480				
	2MM	22.283	11.578				
	Normal	39.442	34.273				