



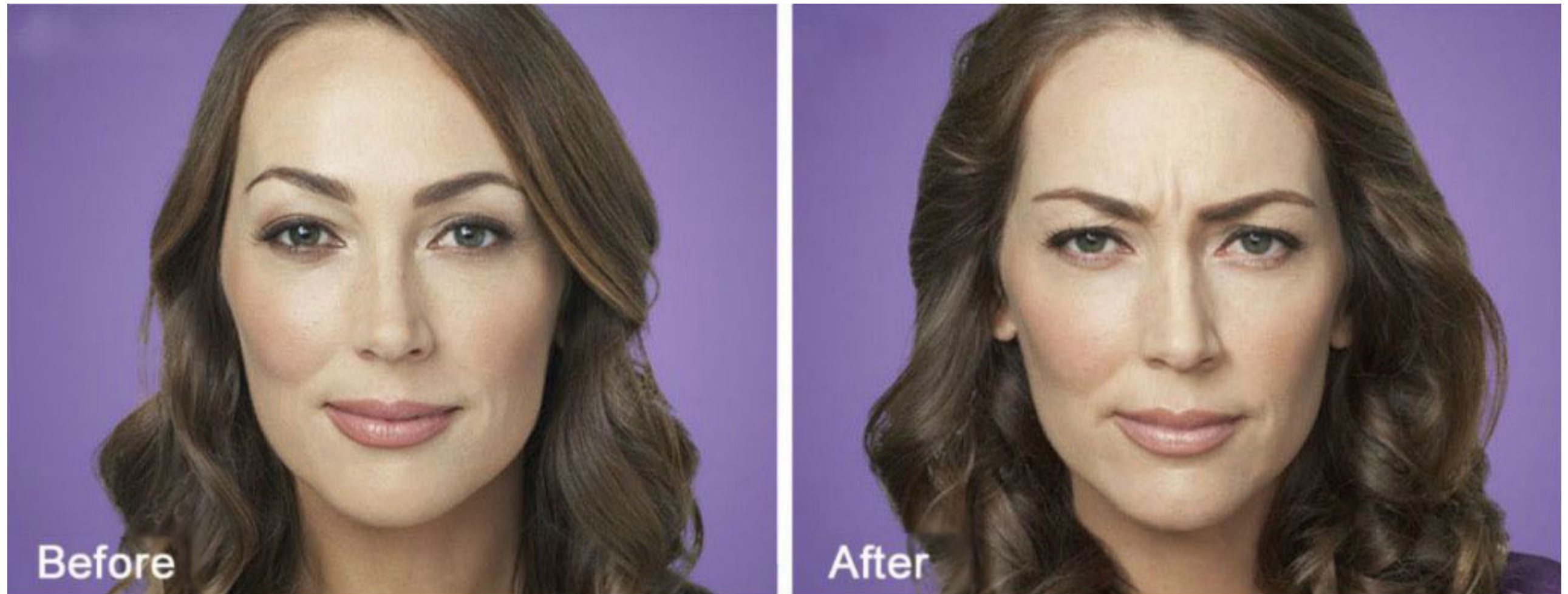
# **Injection vs Incisional treatment of Strabismus**

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# Injection Treatment or Surgery?

- Mechanisms are distinct: injections alter intrinsic muscle properties – stiffness & contractility – whereas surgery affects muscle lengths & actions (pulling vectors).
- Unlike surgery, injection treatment does not damage extraocular biomechanics by effecting compensatory damage or simply leaving scars.
- Injections are not obstructed by pre-existing surgical or other damage.
- Injection is a low-cost office procedure that does not require general anesthesia in cooperative adults, and only brief anesthesia in others, eg, the very young & old.
- Injection may be a good choice to correct post-operative deviations in patients with good potential for binocularity, who wish to avoid re-operation
- Injection may be specifically indicated where previous retinal or glaucoma procedures have left adhesions and fibroses, as when an EOM is incorporated in the capsule surrounding a scleral buckle or glaucoma drainage device





# Injectons in Children

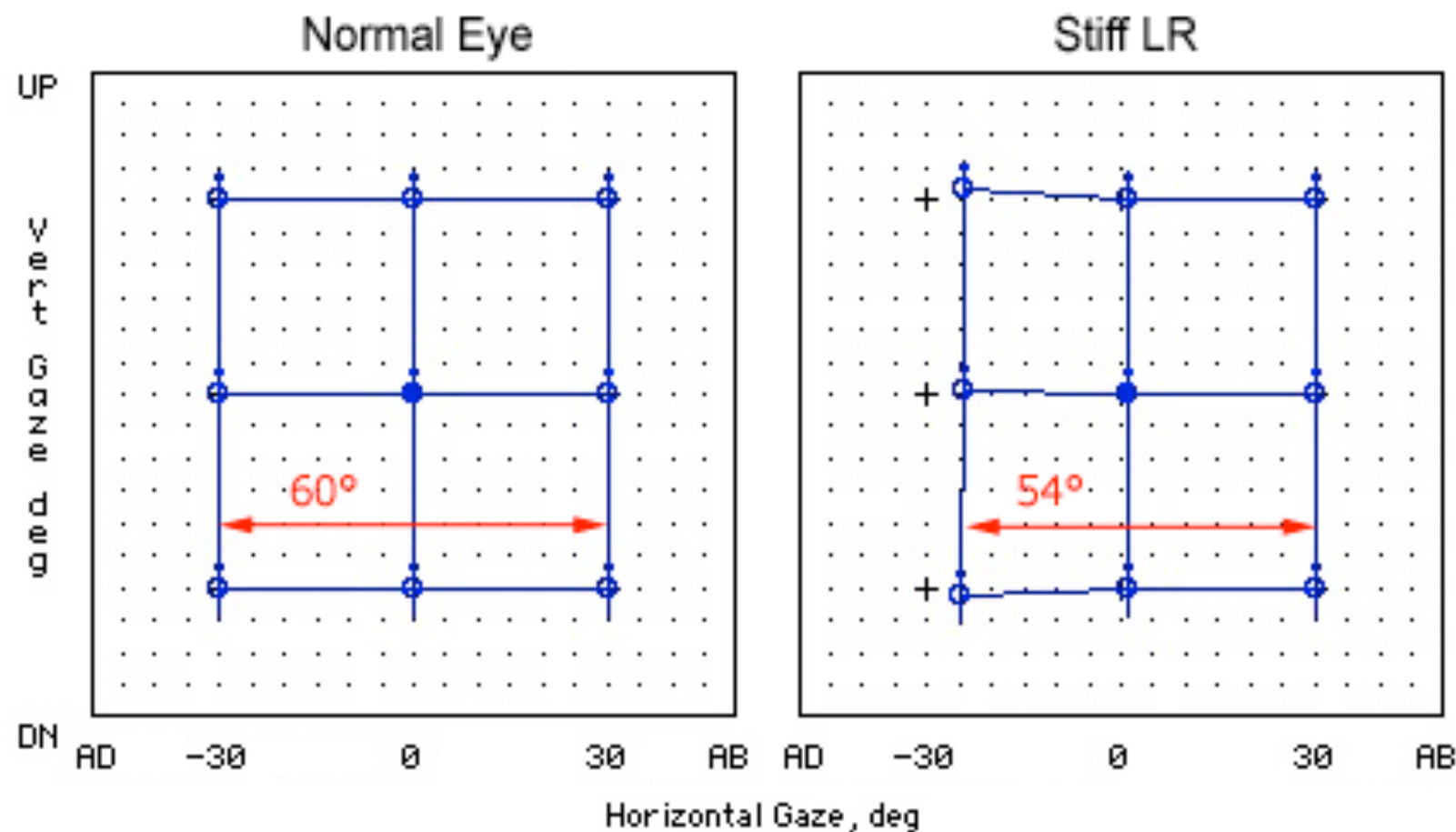
- Small, voluntarily-controlled muscles can be identified for injection in alert cooperative patients with voluntary movements and EMG recording.
- When not possible, eg, under general anesthesia, electrical stimulation can produce movements that help identify muscles.
- Young children can thereby be injected under brief general anesthesia.
- We developed a device to produce a train of monophasic 0.2-10.0 mA constant-current, 0.5 ms wide, negative square-wave pulses at frequencies up to 250 Hz





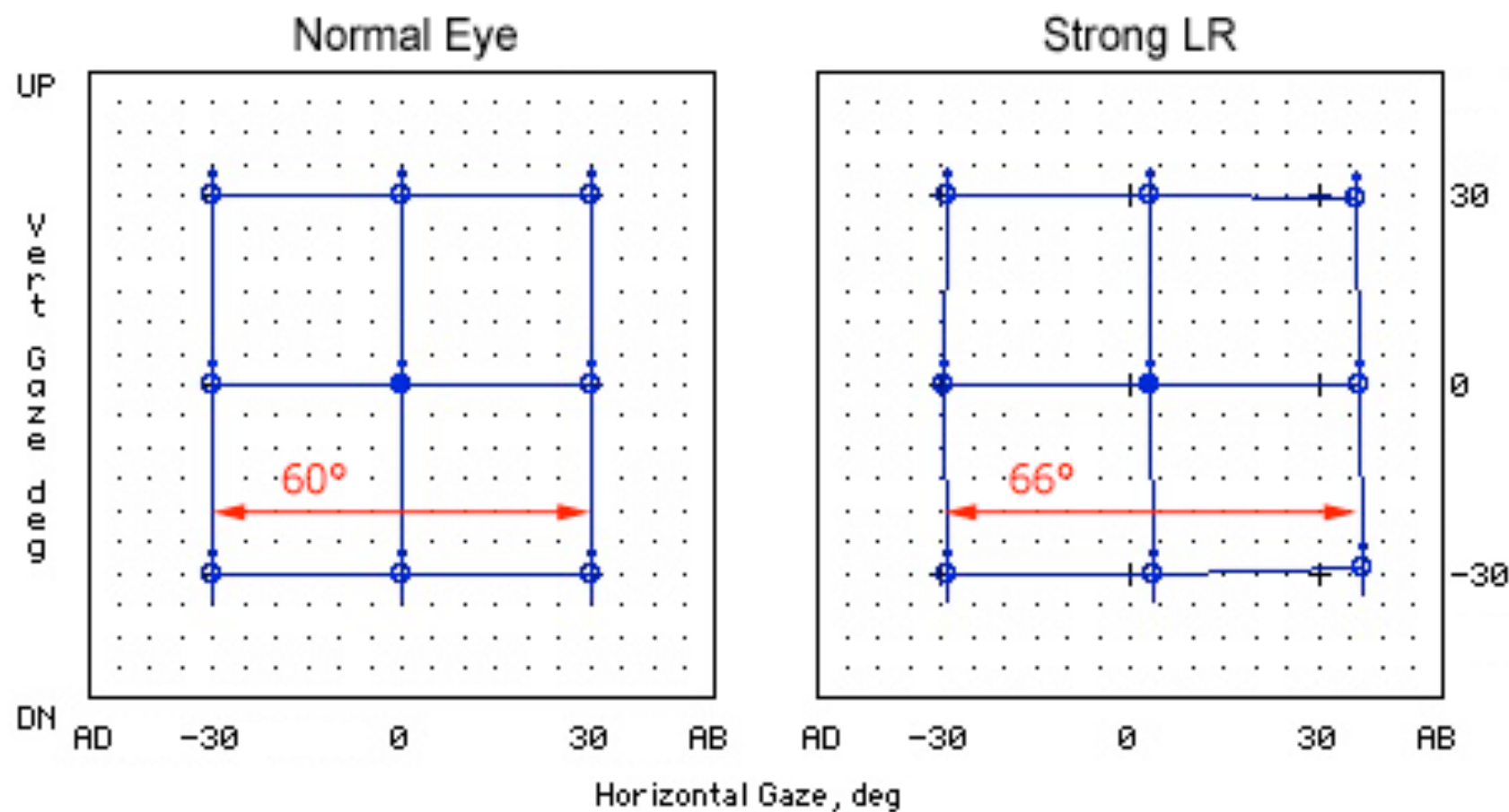
# Stiffness is an Intrinsic EOM Property

- Elastic Force (g) = Stiffness (g/mm) X Stretch (mm).
- Stiffening a muscle decreases eye rotation out of the muscle's field of action.
- Stiffening a muscle decreases range of gaze.



# Contractility is an Intrinsic EOM Property

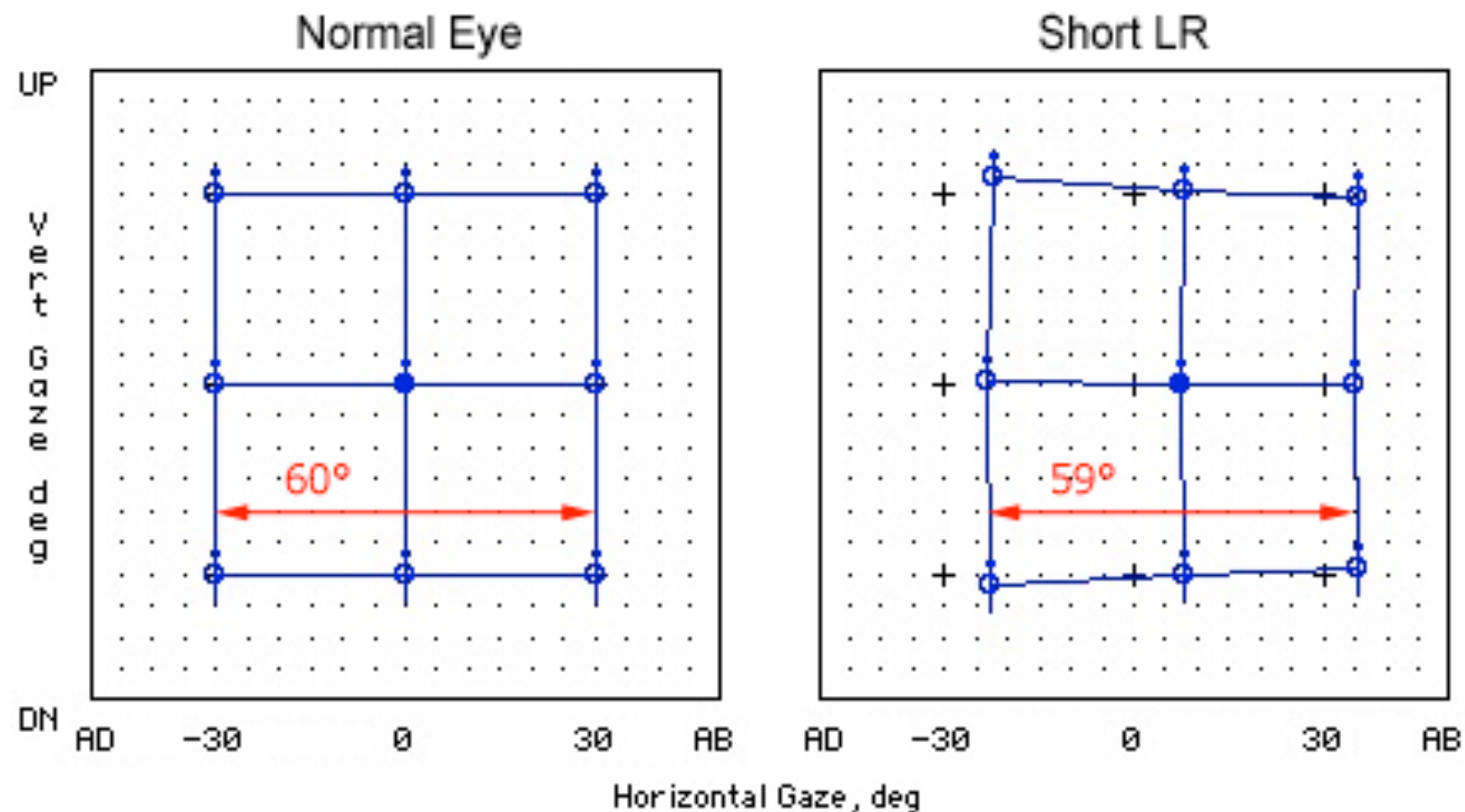
- Contractile Force is a function of innervation, but also depends on Stretch (sliding filament model).
- Strengthening a muscle increases eye rotation in the muscle's field of action.
- Strengthening a muscle increases range of gaze.





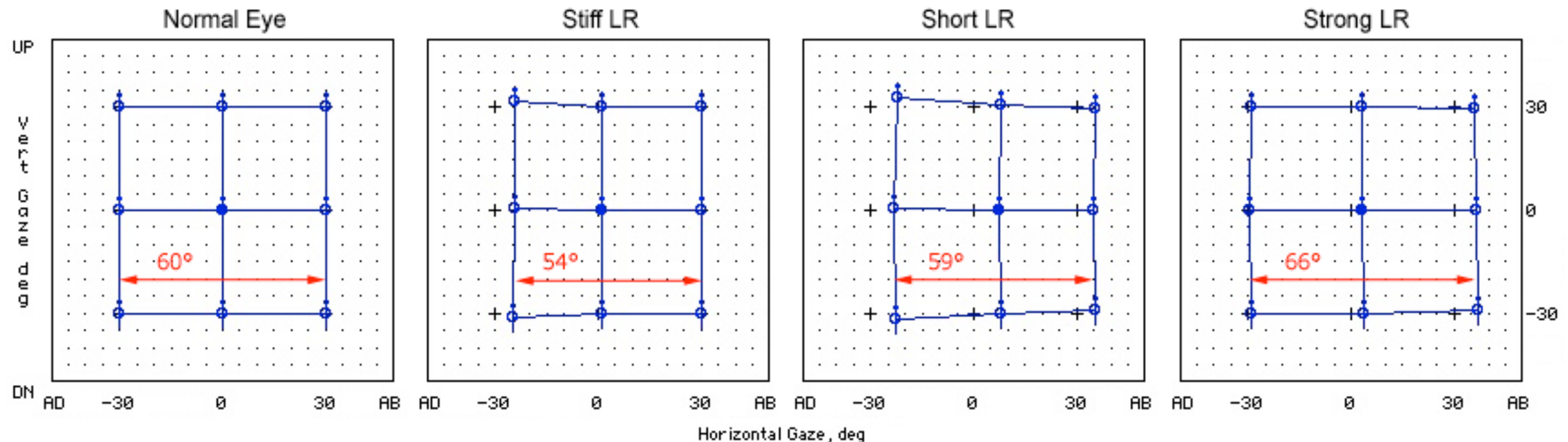
# Muscles can be Surgically Shortened

- Shortening a muscle shifts the alignment pattern towards the shortened muscle.
- Shortening a muscle decreases range of gaze if muscle (in addition to tendon) is removed.



# 3 Different Properties, All Called “Strengthening”

- Increasing Contractility, increasing stiffness & shortening an LR all treat esotropia, eg, but they are not equivalent.
- Only increasing contractility can increase range of gaze.
- Only stiffening can preferentially restrict movement out of a muscle’s field of action.





# Modes of Strabismus Management

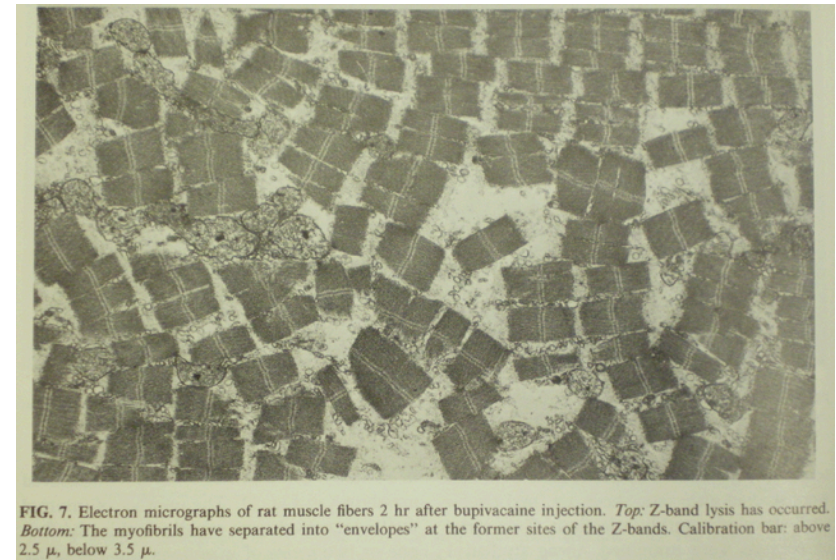
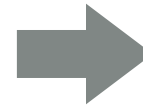
		Surgery	Botox®	BUP (+ Botox)
Stiffness	Increase			✓
	Decrease			
Length*	Shorten	✓	(in antagonist) ✓	✓
	Lengthen		✓	✓
Strength	Increase			✓
	Decrease		(temporary) ✓	
Alter Action Vector		✓		
Increase Range of Gaze				✓
Office Procedure			✓	✓

\* Length of contractile tissue



# Bupivacaine Mechanisms

- Overloading stimulates muscles mechanically. Bupivacaine stimulates them chemically.
- BUP releases excessive  $\text{Ca}^{++}$ .
- $\text{Ca}^{++}$ -activated protease cuts  $\alpha$ -actin, separating sarcomeres at Z-lines.
- High  $\text{Ca}^{++}$  poisons mitochondria, damaging or destroying the cell.
- Growth factors activate satellite cells (muscle stem cells).
- Satellite cells replace destroyed myofibers, or add nuclei to repair damaged myofibers.
- Repaired fibers tend to retain added nuclei, resulting in a larger, contractilely stronger fiber.
- Some additional fibrous tissue (consequent to inflammation?) increases muscle stiffness.
- Length of the rebuilt muscle appears determined by eye position during rebuilding, which we can manipulate with a small dose of Botox in the antagonist, allowing the BUP-injected muscle to rebuild at reduced length.
- BUP + Botox produces about twice the correction achieved with BUP alone.



(from Bradley 1980)





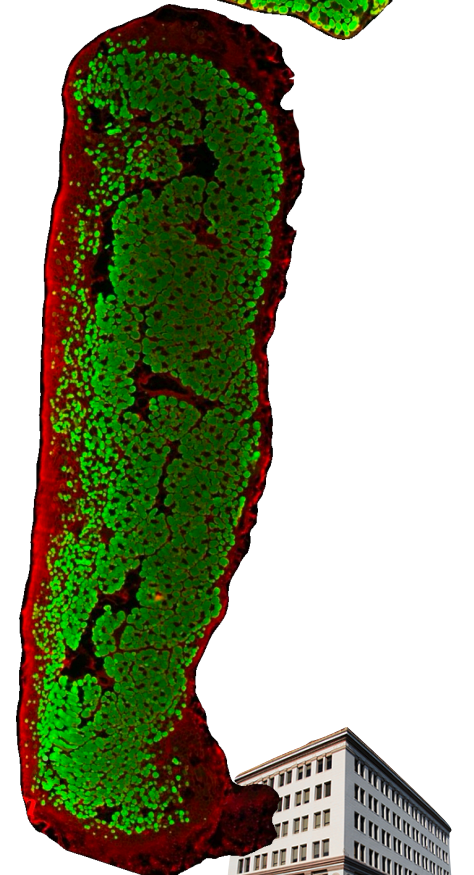
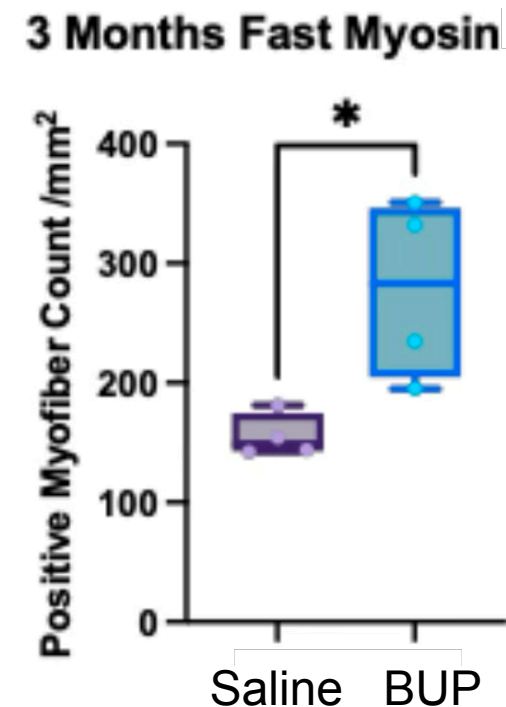
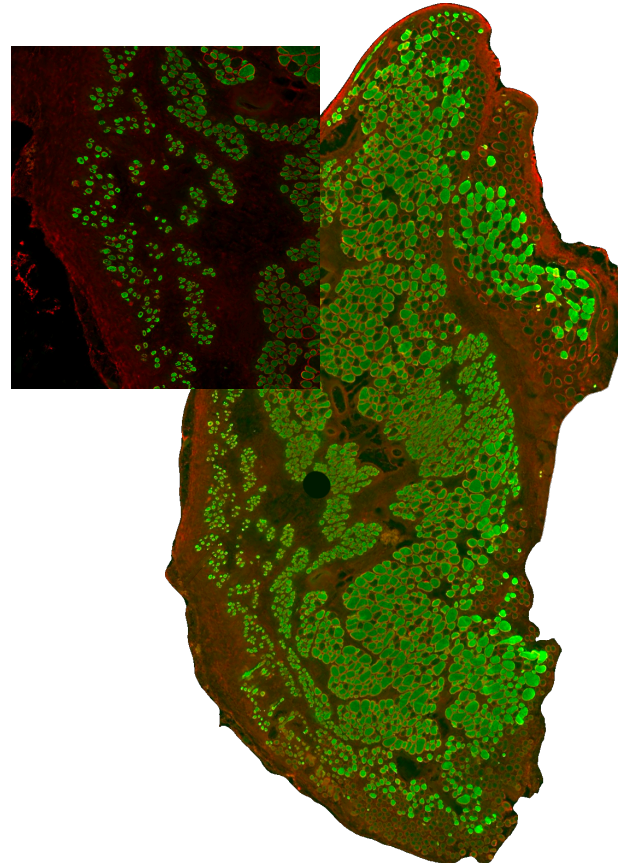
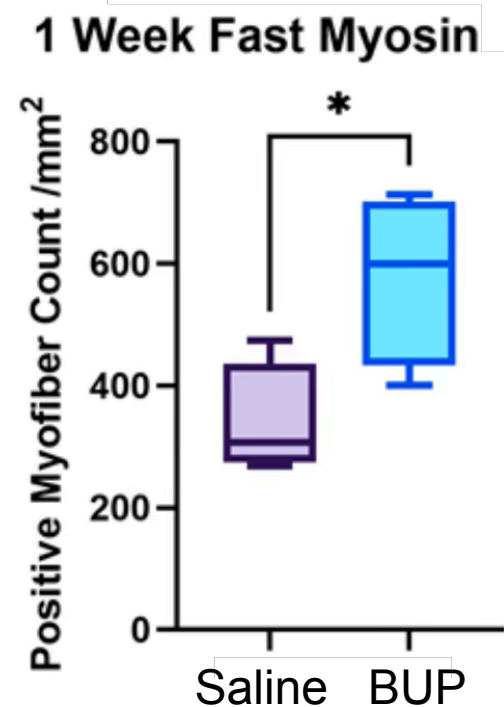
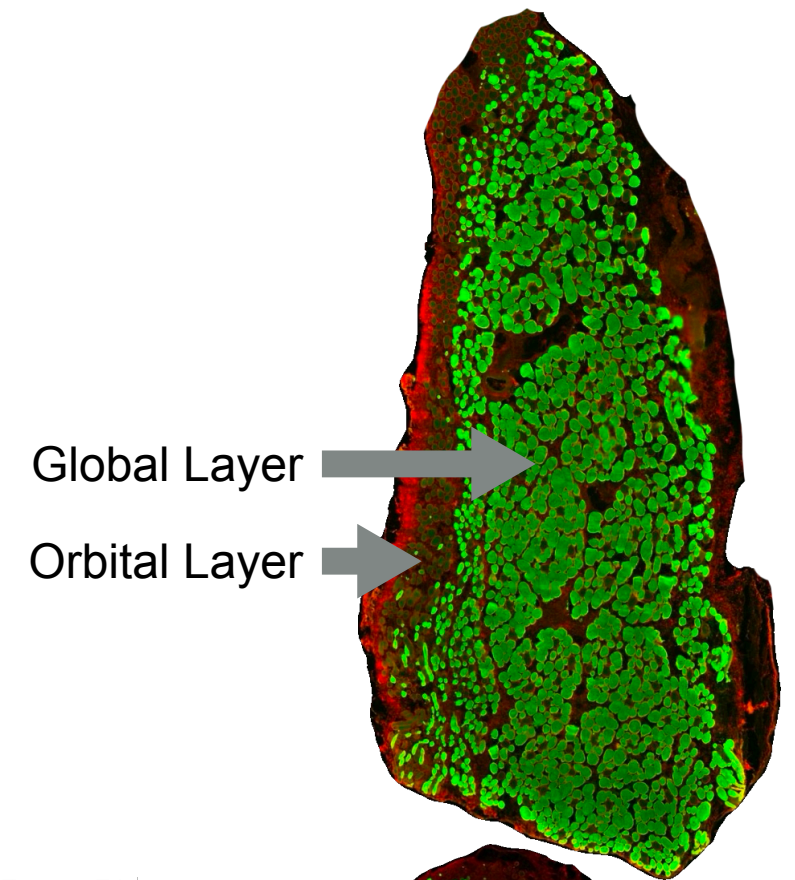
# A Possible Strategy

- A fiber's resources for self-repair are related to its volume (eg, the number of protein-synthesizing nuclei).
- Its vulnerability to external damage, eg, from bupivacaine, is related to its surface area.
- Therefore, small fibers should be more vulnerable to non-reparable destruction.
- If destroyed small fibers are replaced by average-sized fibers, the overall distribution of fiber sizes will increase ...
- ... resulting in a contractile stronger muscle.



# Bupivacaine Increases Fast Myosin in Rabbit

- “**Fast Myosin**” is the protein responsible for rapid, strong muscle contraction.
- It's normally expressed in the global fiber layer, but not in the orbital layer.
- One week after injection of 3% bupivacaine in rabbit SR, **fast myosin** is found in previously destroyed orbital layer areas, and is increased overall.
- This increase is maintained at 3 months.



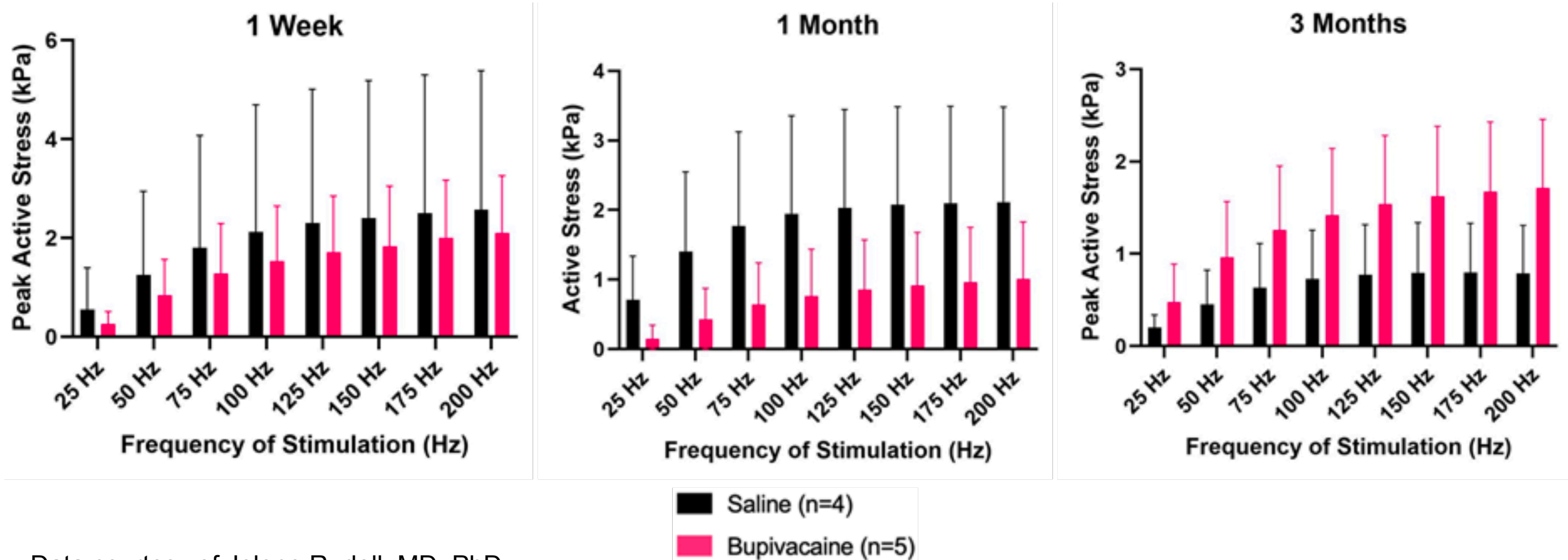
Data courtesy of Jolene Rudell, MD, PhD • Shiley Eye Institute, San Diego





# Contractile Force Is Increased at 3 Months

- Early results of electrical stimulation in rabbit EOM show decreases in force consistent with myodestruction ...
- ... and increases in contractile force after recovery.



Data courtesy of Jolene Rudell, MD, PhD  
Shiley Eye Institute, San Diego

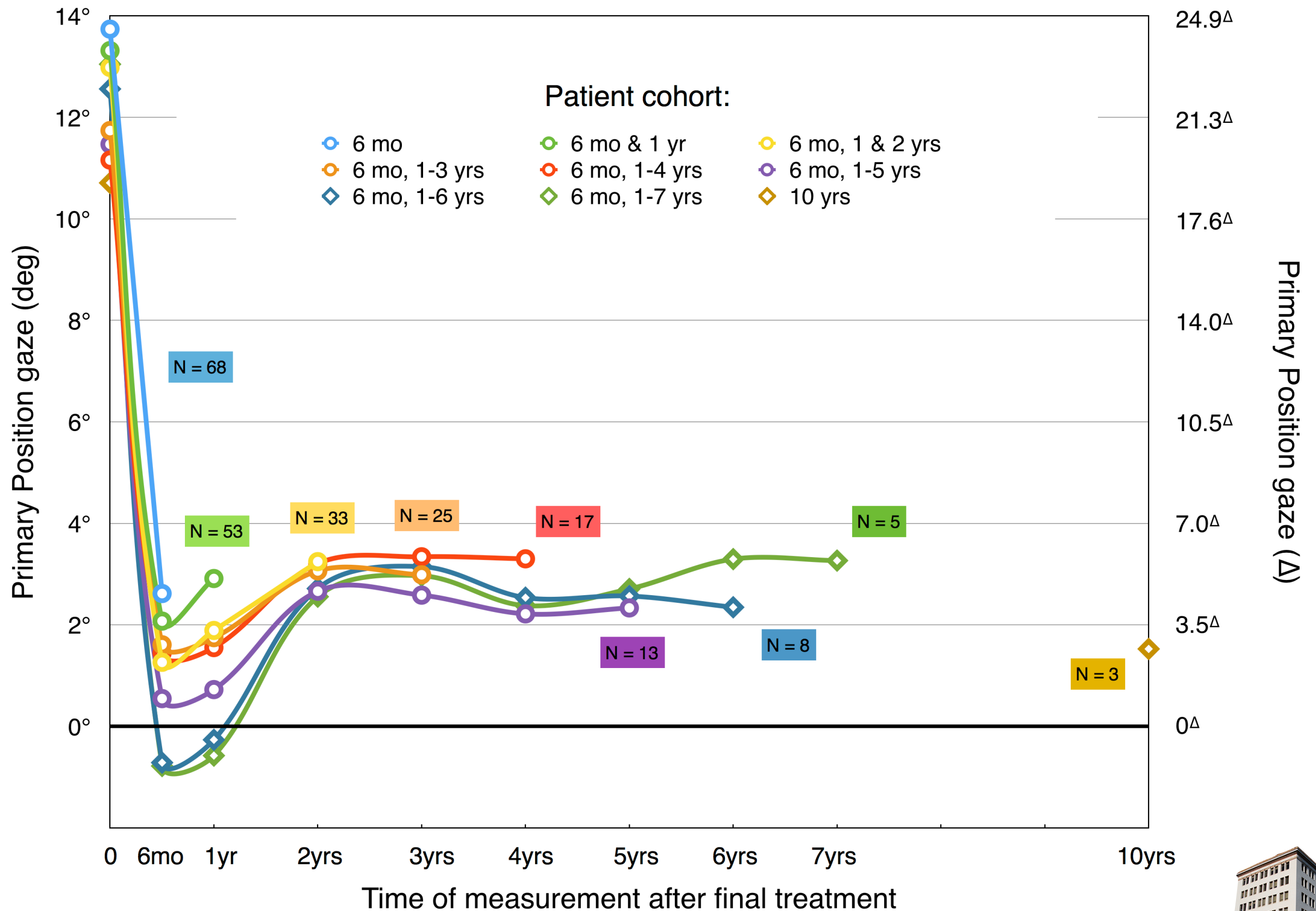


# Current Treatment Doses

Initial Deviation ( $\Delta$ )	Bupivacaine 3%		Toxin (u)	Epi
	Vol (mL)	Conc (%)		
8 - 15	1.5	1.5	0	0
16 - 30	2.5	2.0	2.5	+
> 30	3.0	3.0	5.0	++



# Bupivacaine Corrections are Stable





# Average Outcomes – Adults, Comitant, N = 74

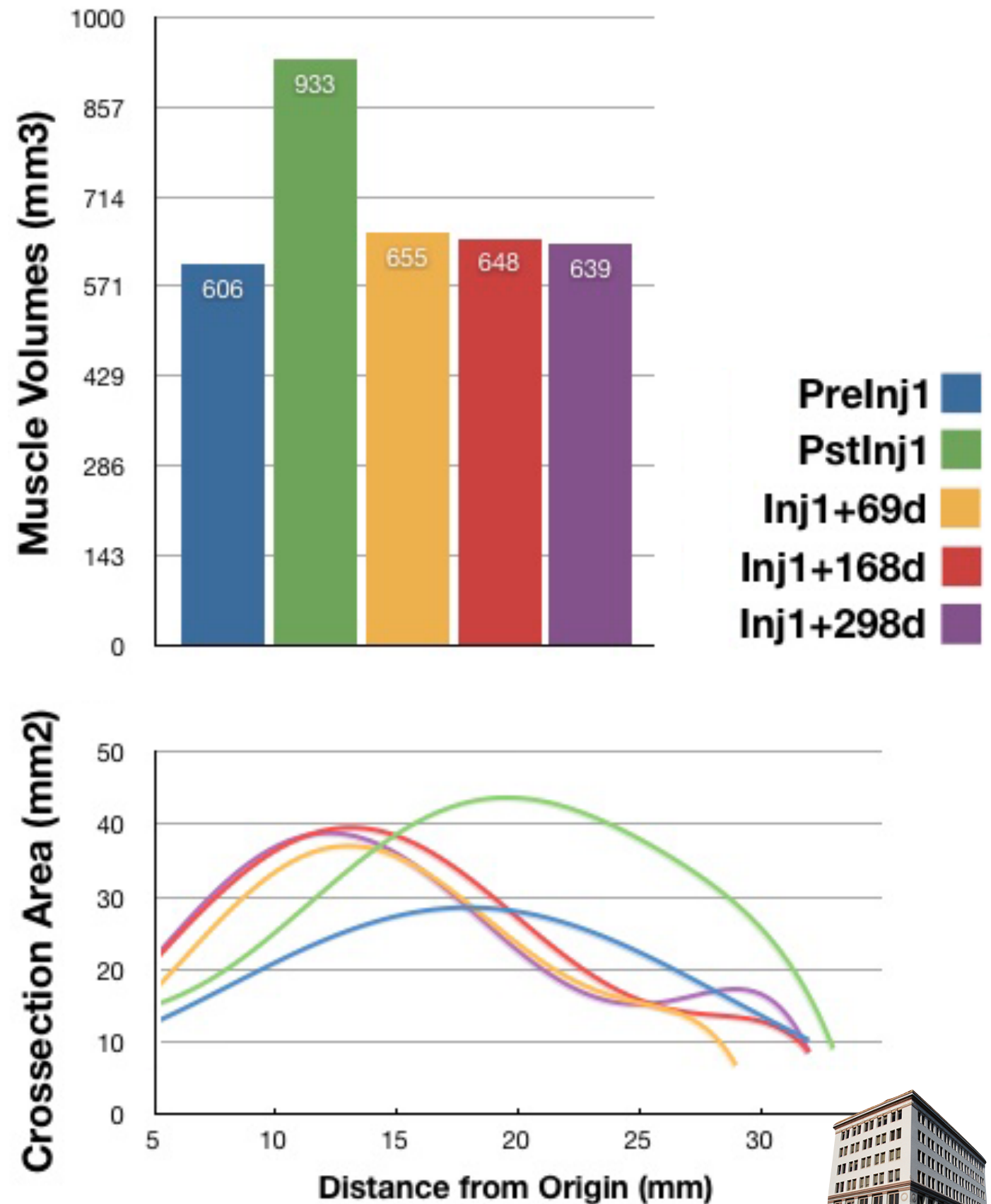
(Majority had previously been surgical failures)

Group	Initial Misalignment	Number of treatments	Alignment Change	Relative Correction	Patients $\leq 10 \Delta$
Small Misalignments $\leq 25\Delta$ n = 44	17.1 $\Delta$	1.9	12.8 $\Delta$	57%	77%
Large Misalignments $> 25\Delta$ n = 30	35.9 $\Delta$	1.7	24.7 $\Delta$	63%	50%



# Volumes & Crosssectional Areas

- Pre-Injection, post-Injection, and follow-up scans track changes in muscle volume
- Crossection analysis shows location of injection bolus (■), and pattern of regrowth (■, ■, ■)



# Dosage Recommendations

Deviation	BUP (Dose depends on deviation)	Botox (Dose depends on restriction)
10 - 20 $\Delta$	1.0-1.5% 1.5-2 mL	0-2 U
20 - 30 $\Delta$	1.5-2.0% 2-3mL	2-4 U
30 $\Delta$ +++	2-3% 2-3 mL	2-6 U





# Clinical Take-Home

- BPX and botulinum toxin injection is a safe office procedure giving clinically significant, lasting corrections.
- Use Patents to Alan Scott cover manufacture. No restrictions on medical use.
- Botox paralysis moves the eye to where motor fusion can take hold and maintain alignment.
- But, in the absence of fusion strabismus often recurs because sarcomere changes for the new position are not strong and permanent.
- BUP treated muscles are larger, shorter, stronger, and stiffer and correction is long-lasting, apparently permanent.
- In the absence of fusion, we need a mechanically effective treatment like this.
- Patients with very small deviations (diplopia if over-corrected) are probably better treated surgically

