Injection vs Incisional treatment of Strabismus

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Eye muscles & motor control

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- EOM Pulleys and Compartments - Sense and Nonsense PDF
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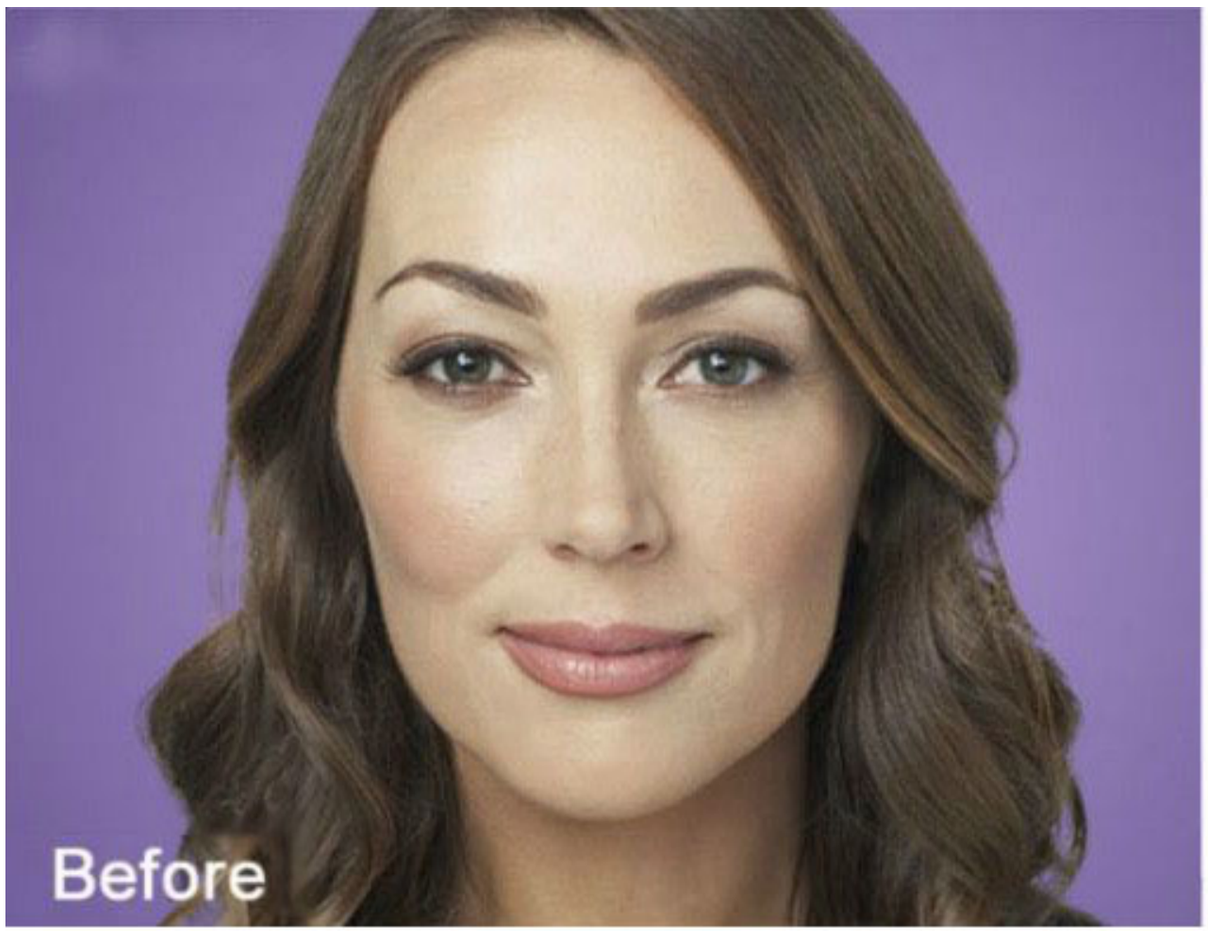

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A silly, smiling bimbo? Or a serious hard-working colleague?
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Injection Treatment or Surgery?

- Mechanisms are distinct: injections alter intrinsic muscle properties – stiffness & contractility – whereas surgery affects muscle lengths & directions of action.
- Unlike surgery, injection treatment does not damage extraocular biomechanics with compensatory damage or by 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

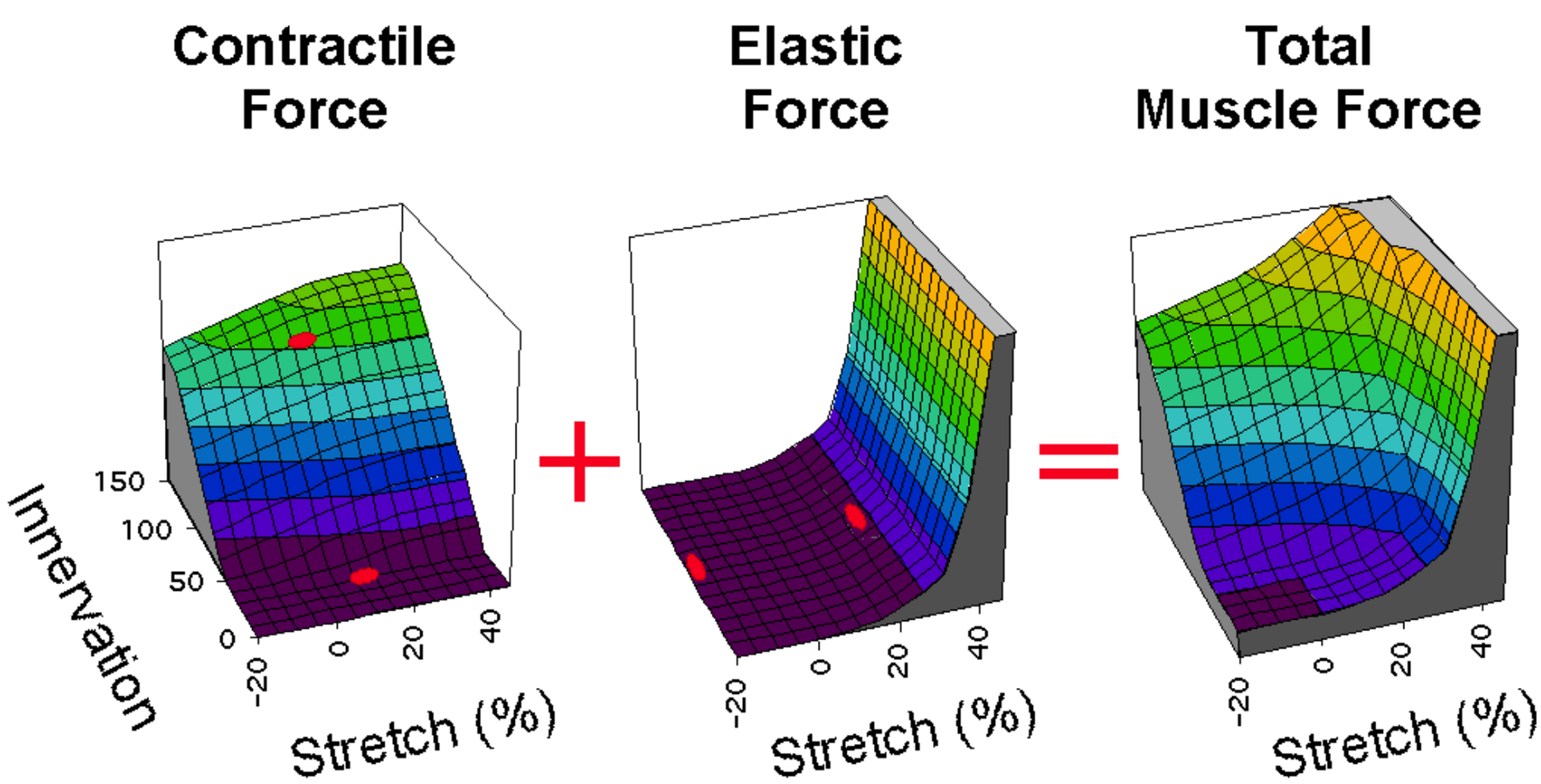
Injections in Children

1. Small, voluntarily-controlled muscles can be identified for injection in alert, cooperative patients with voluntary movements and EMG recording.
2. When such recording is not possible, eg, under general anesthesia, electrical stimulation can produce characteristic movements that help identify muscles.
3. Young children can thereby be injected under brief general anesthesia.
4. 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 & Contractility are Intrinsic EOM Tissue Properties, Not Directly Affected by Surgical Manipulation

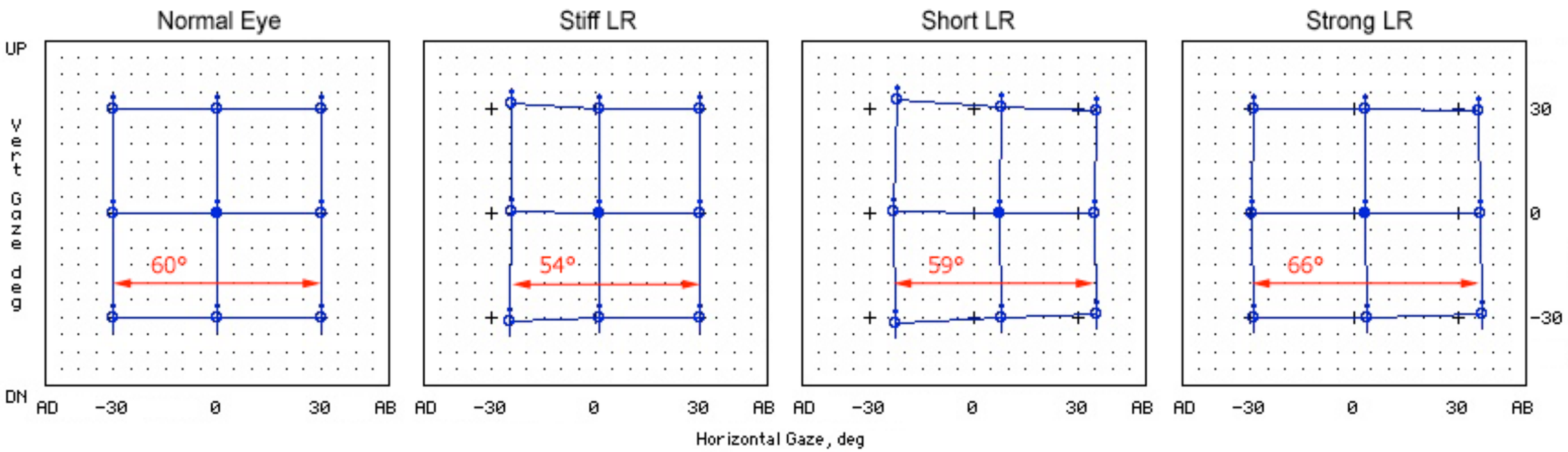
Muscle Force has two components:

1. Contractile Force depends mostly on innervation, but also on Stretch (sliding filament model).
2. Elastic Force is a function of Stretch only.
3. Their sum is the total force exerted by the muscle.



3 Different Manipulations, All Called “Strengthening”

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



Bupivacaine Mechanisms

1. Bupivacaine stimulates a muscle chemically, a bit like how overloading stimulates it mechanically - both damage sarcolemma & release growth factors.

FIG. 7. Electron micrographs of rat muscle fibers 2 hr after bupivacaine injection. *Top:* Z-band lysis has occurred. *Bottom:* The myofibrils have separated into "envelopes" at the former sites of the Z-bands. Calibration bar: above 2.5 μ, below 3.5 μ.

(from Bradley 1980)

   - Bupivacaine releases excessive Ca^{++} → hypercontraction → sarcolemmal damage
   - Ca^{++}-activated protease cuts α-actin, separating sarcomeres at Z-lines.
   - High Ca++ poisons mitochondria, damaging or destroying the cell.

2. Growth factors activate satellite cells, which either:
   - Add nuclei to <u>repair</u> damaged fibers, which tend to retain added nuclei, becoming larger and <u>contractilely stronger</u>, or
   - Destroy & <u>replace</u> badly damaged fibers.

3. Some additional fibrous tissue (from inflammation?) increases muscle stiffness.
   - Length of the rebuilt muscle is affected by eye position during rebuilding, which Dr Scott manipulated with a small dose of Botox in the antagonist, allowing the BUP-injected muscle to rebuild at reduced length.

Two Strategies for Increasing Contractility?

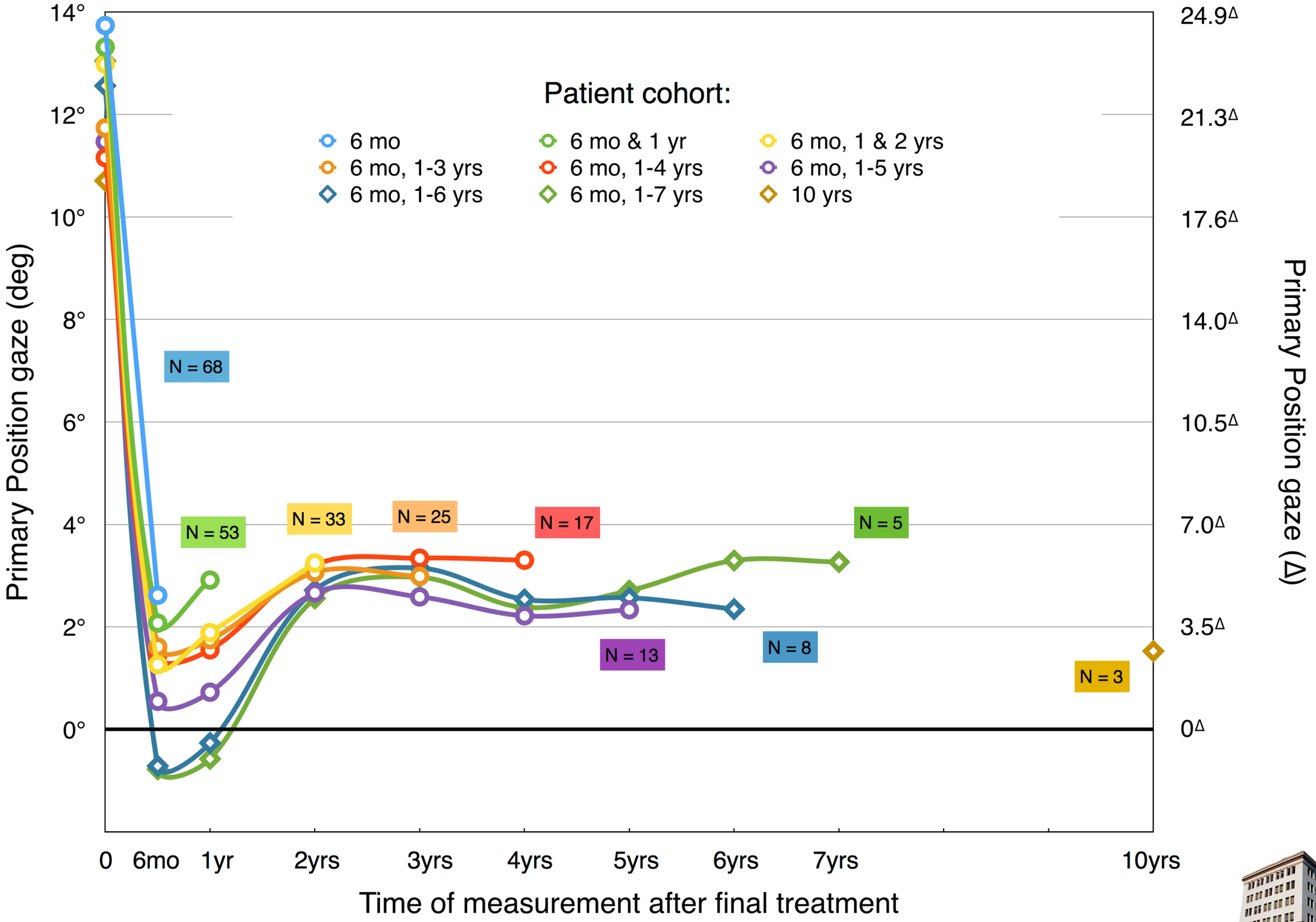
1. <u>High</u> concentrations of bupivacaine cause general myofiber damage, triggering repair, replacement and increased contractility, along with increased stiffness related to inflammation and fibrosis.
2. <u>Lower</u> concentrations might increase contractility without increasing stiffness:
   - Volume, as we know, increases as the cube of length, whereas surface area increases only as the square. Thus small muscle fibers have relatively more surface area to volume compared to large fibers.
   - A fiber's resources for self-repair are related to its <u>volume</u> (eg, the number of protein-synthesizing nuclei).
   - Its vulnerability to external damage, eg, from bupivacaine, is related to its <u>surface area</u>.
   - Small fibers should therefore be more vulnerable to non-reparable destruction.
   - If small fibers destroyed by bupivacaine are replaced by average-sized fibers, the overall distribution of fiber sizes will increase, resulting in a contractilely stronger muscle.

Modes of Strabismus Management

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

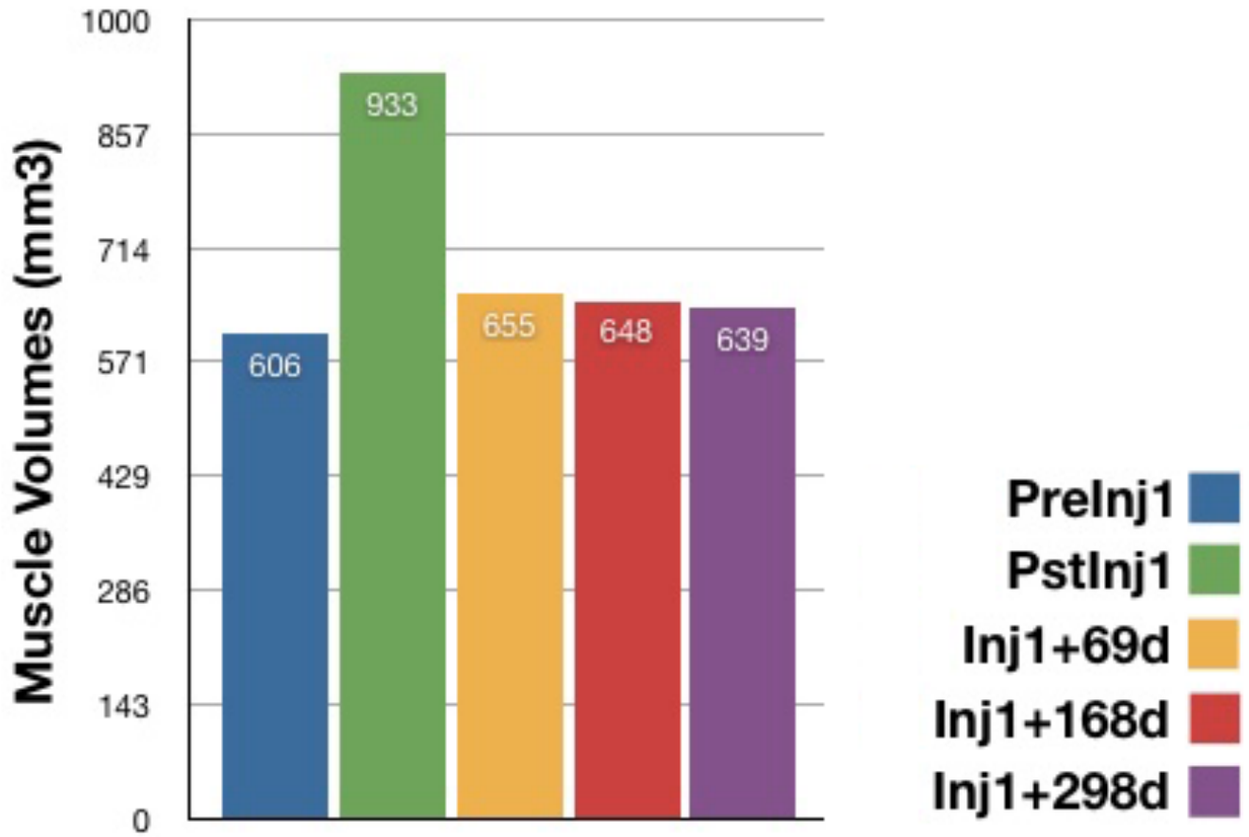
* Length of contractile tissue

Bupivacaine Corrections are Stable

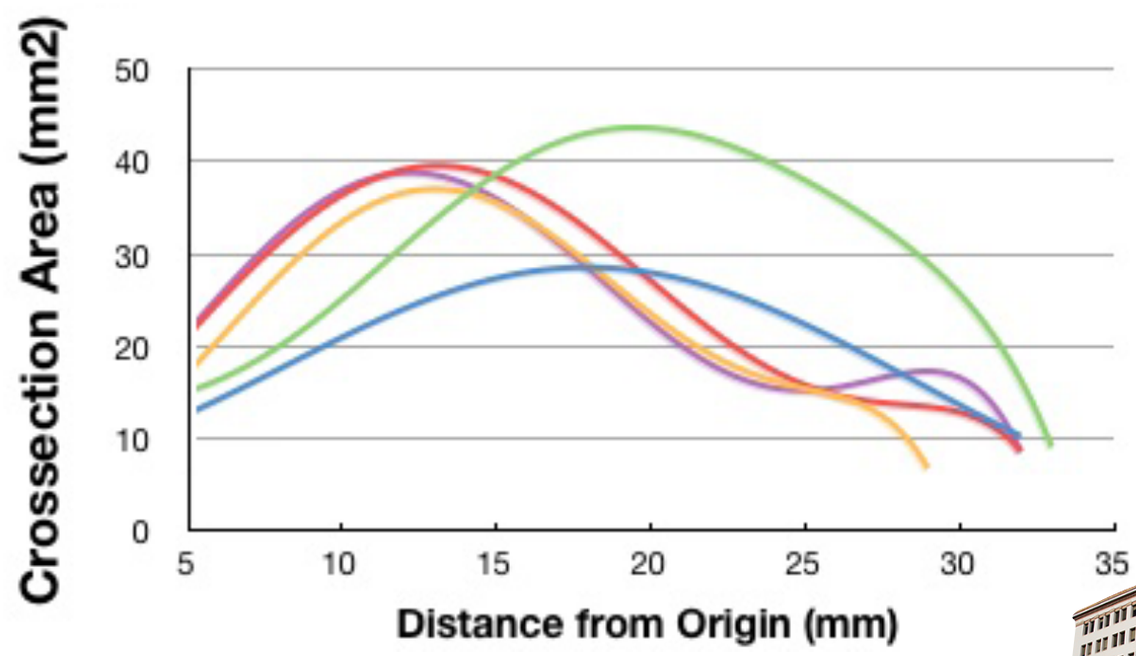


Volumes & Crossectional Areas

- Pre-Injection, post-Injection, and follow-up scans track changes in muscle volume

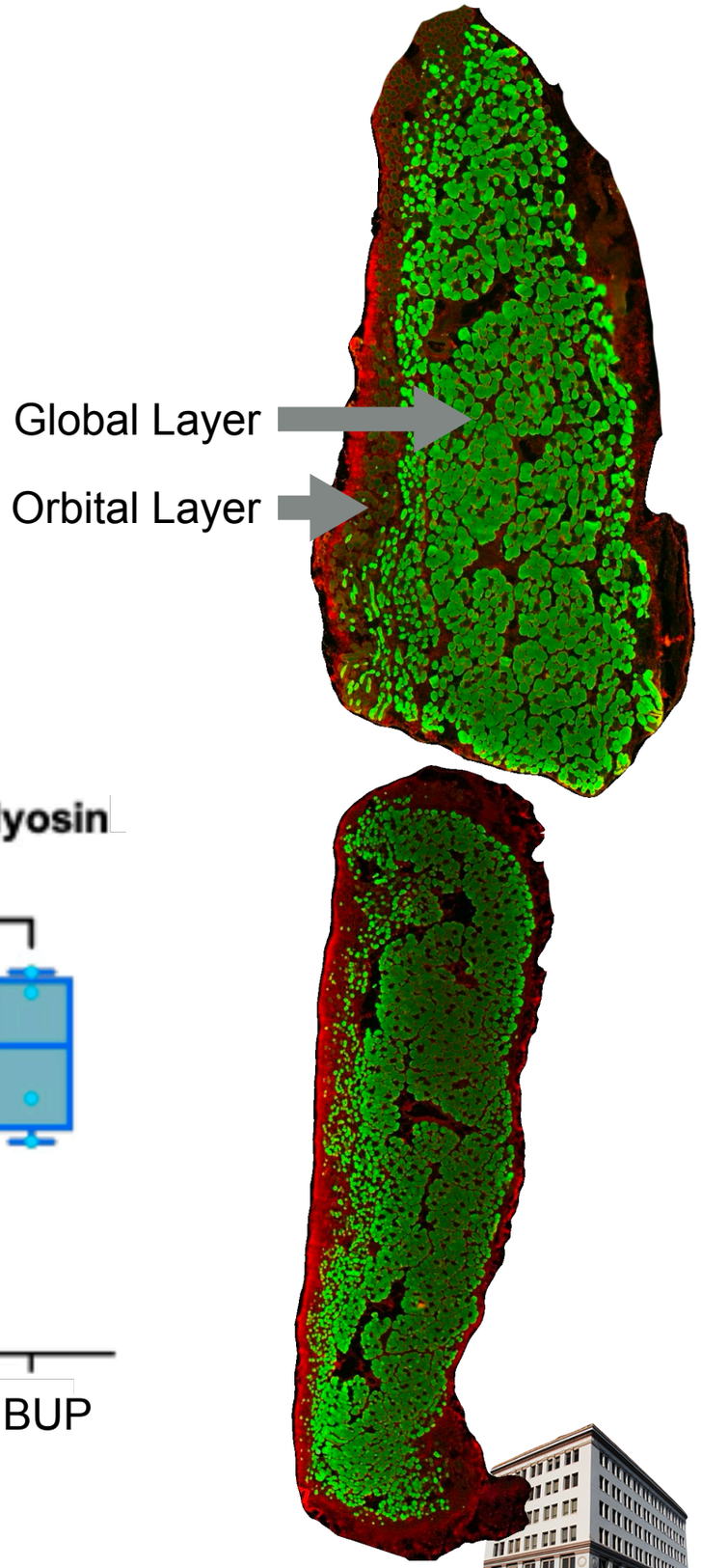


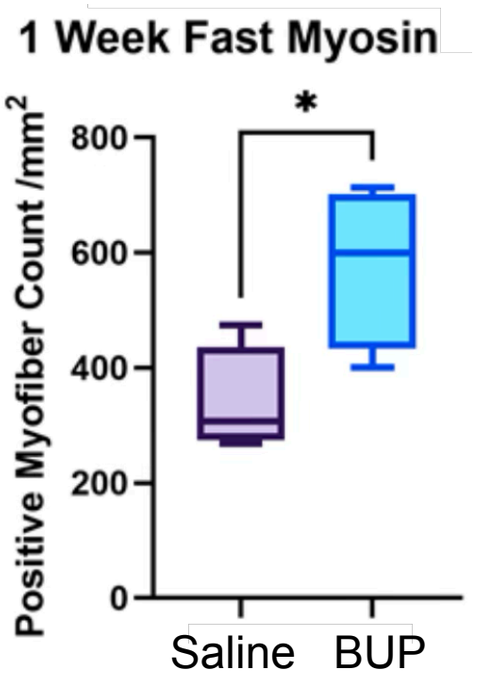
- Crossection analysis shows location of injection bolus (▪), and pattern of regrowth (▪, ▪, ▪)

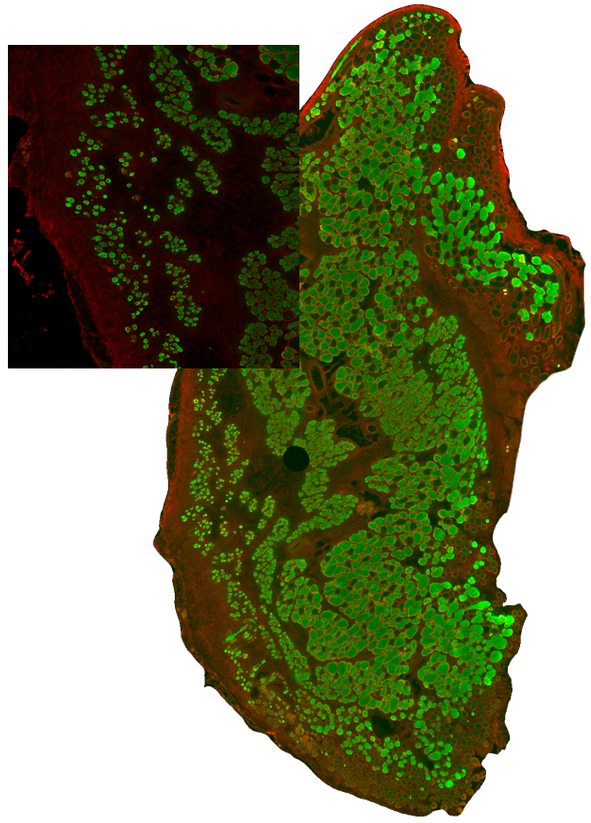


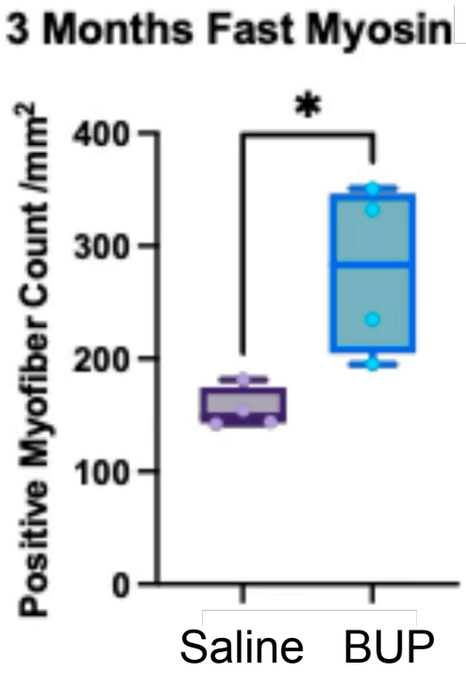
Bupivacaine Increases Fast Myosin in Rabbit

- "**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.





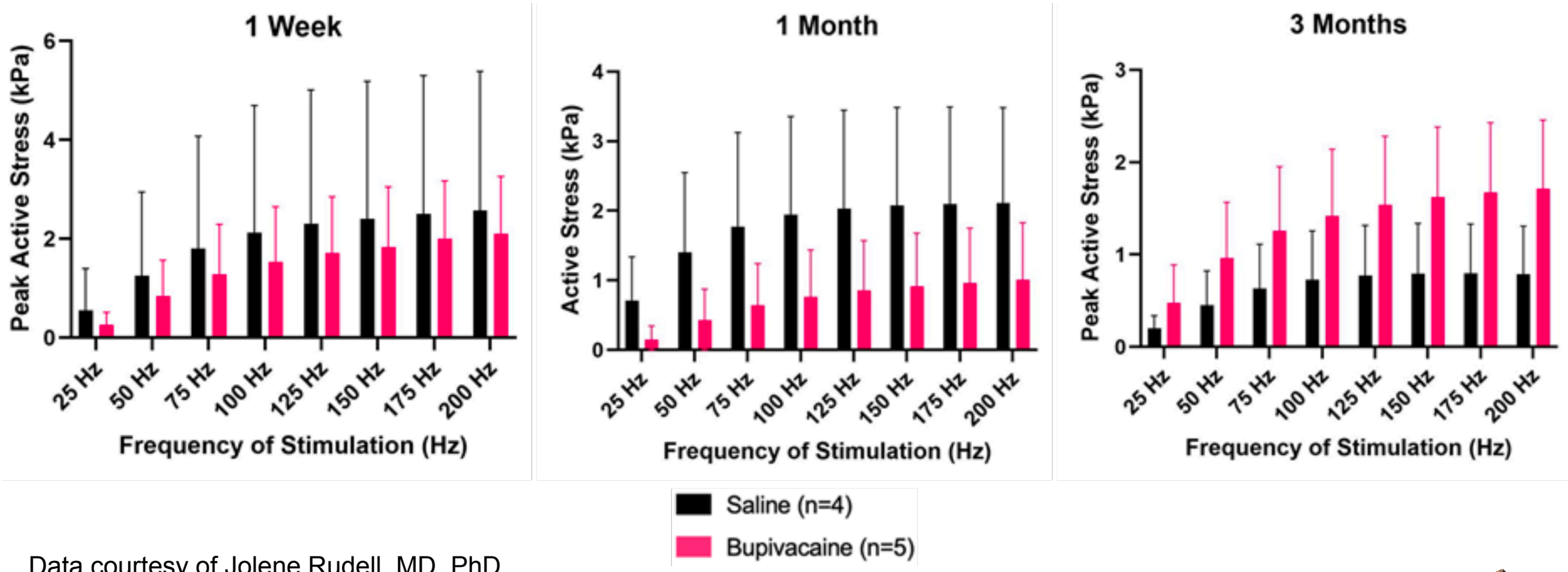




Data courtesy of Jolene Rudell, MD, PhD • Shiley Eye Institute, San Diego

Contractile Force Is Increased at 3 Months

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



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Average Outcomes – Adults, Comitant, N = 74

(Majority had previously been surgical failures)

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

Dosage Recommendations

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

Clinical Take-Home

- Bupivacaine + botulinum toxin injections are safe office procedures giving clinically significant, lasting corrections.
- Bupivacaine + Botox gives about twice the correction of bupivacaine alone.
- “Use Patents” granted to Alan Scott cover manufacture only. No proprietary restrictions on medical use.
- Botox paralysis may move the eye to where motor fusion can take hold and maintain alignment.
- . . . but, in the absence of fusion strabismus tends to recur because sarcomere changes for the new position are not strong and permanent.
- Bupivacaine treated muscles are larger, stronger and stiffer. Correction is long-lasting, apparently permanent.
- Patients with very small deviations (diplopia if over-corrected) are probably better treated surgically.

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