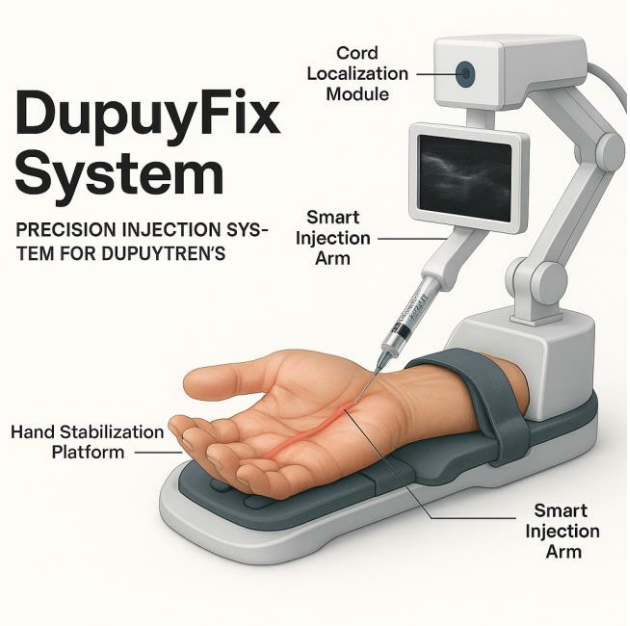


DupuyFix™ – ROBOTIC PRECISION SYSTEM FOR SAFE, TARGETED CORD INJECTION

"A Smart Delivery Platform to Minimize Complications in Collagenase-Based Treatment of Dupuytren's Contracture"

Samantha I Muhlrad, MS, MD
Renaissance School of Medicine
Stony Brook University
Orthopedic Associates
Chief of Hand Surgery
Stony Brook, NY 11794

Lev Neymotin, PhD
N5Digital, Inc., CEO, R&D
Plainview, NY 11803

1 ABSTRACT

Dupuytren's contracture treatment using collagenase injections remains highly dependent on manual skill, which limits precision and predictability. The risks—ranging from skin tears and hematomas to tendon ruptures—are rooted in misplacement of the needle, enzyme leakage, and unpredictable tissue resistance. These outcomes reduce adoption of the collagenase method and frustrate both patients and physicians.

To date, no known commercial or academic systems offer an automated or robotic solution specifically designed for the precision injection of collagenase into Dupuytren's cords. While various improvements in injection technique, imaging guidance, and physician training have been proposed to enhance accuracy and safety, none address the fundamental limitations of manual operation.

The **DupuyFix™** system (patent pending), as proposed here, represents a novel and unique integration of robotic targeting, real-time tissue feedback, and AI-assisted control — filling a critical gap in current clinical practice and research.

DupuyFix™ offers a robotics-guided alternative: a compact system combining hand stabilization, anatomical mapping, and pressure-sensitive drug delivery. Its core benefit lies in eliminating the human error factor from injection-based treatment. This device could become a new standard, reducing training burden and raising safety and precision standards to match other advanced surgical systems.

2 DUPUYTREN'S MEDICAL CONDITION

2.1 Overview of Dupuytren's Disease

Dupuytren's contracture is a chronic, progressive fibrosing disorder of the palmar fascia, characterized by the formation of nodules and cords that lead to permanent flexion deformities of the fingers — most commonly the ring and little fingers. It is thought to result from aberrant fibroblast activity, excessive type III collagen deposition, and myofibroblast-mediated contractile forces within the fascia.

The disease often starts subtly, with a painless thickening or nodule at the base of the finger. As it progresses, fibrous cords extend longitudinally, pulling one or more fingers into flexion. The condition can severely impair hand function, affect grip strength, and diminish quality of life — especially when tasks such as washing, putting hands in pockets, or shaking hands become difficult or impossible.

Dupuytren's disease has a strong genetic predisposition, particularly among individuals of Northern European descent, earning it the nickname "Viking's disease." It is more common in men (approximately 7–10 times more likely than women), with onset typically in the fifth or sixth decade of life. Risk factors include diabetes, epilepsy, chronic alcohol use, and manual labor.

Despite its relatively high prevalence — estimated at 3–6% of adults over 45 — many patients go undiagnosed until the disease has reached a functionally limiting stage. This is partly due to the slow progression and absence of pain in the early stages.

2.2 Pathophysiology and Anatomy

The palmar fascia, a complex web of connective tissue, is involved in anchoring and stabilizing the skin of the palm. In Dupuytren's disease, pathological remodeling of this fascia leads to cord-like structures that run longitudinally through the palm and fingers, sometimes displacing or compressing nearby anatomical features:

- **Flexor tendons**, located just beneath the fascia, are essential for finger movement and may be ruptured if mistakenly exposed to enzymatic degradation.
- **Digital nerves** run adjacent to the cords and are at risk of injury during surgical or injection procedures.
- **Blood vessels** within the digital neurovascular bundle may also be affected by trauma or chemical exposure.

3 TREATMENT LANDSCAPE: EXISTING SURGICAL AND NON-SURGICAL OPTIONS

Once contractures impair daily activities or finger extension becomes significantly limited, patients seek therapeutic intervention. Treatment options include:

3.1 SURGICAL-A: Open Surgery (Fasciectomy or Dermofasciectomy)

- The traditional gold standard for advanced disease.
- Involves direct excision of the pathological cord and surrounding fascia.
- In cases of recurrent or aggressive disease, skin grafting may be needed (dermofasciectomy).
- Advantages: complete visualization and cord removal.
- Disadvantages:
    - Invasive
    - Requires anesthesia and surgical facility
    - High recurrence (up to 39%)
    - Risk of neurovascular injury, infection, hematoma, and prolonged rehabilitation

3.2 SURGICAL-B: Percutaneous Needle Fasciotomy (PNF)

- A minimally invasive method where a needle is used to cut the cord percutaneously.
- Advantages:
    - Office-based
    - Low downtime
- Disadvantages:
    - Blind technique
    - Incomplete release in some cases
    - Higher recurrence rates than surgery (up to 85%)

3.3 NON-SURGICAL: Manual Enzymatic Injection

(Collagenase Clostridium Histolyticum Injection, Xiaflex®)

- The only FDA-approved enzymatic therapy for Dupuytren's contracture.
- Involves injecting a purified bacterial enzyme directly into the cord.
- Over 24–72 hours, the enzyme selectively dissolves collagen, weakening the cord for manual manipulation.
- Advantages:
    - Minimally invasive
    - No anesthesia or incisions required
    - Performed in-office
    - Faster return to normal activity
- Disadvantages:
    - Variable effectiveness
    - Requires high operator skill to avoid complications
    - Not effective for all cord types (e.g., spiral cords, cords near joint capsules)
    - High risk of adverse events due to poor targeting or enzyme leakage, including: (a) skin tears (reported in up to 20–30% of clinical trials), (b) flexor tendon rupture, (c) nerve damage, and (d) edema, hematoma, or inflammation. This is exacerbated by the fact that enzyme action is not target specific: collagenase breaks down **type I and III collagen**, which are found in Dupuytren's cords, dermis of the skin, and Blood vessel walls.

- High risk of skin tears, tendon injuries, or nerve damage during Manipulation, the manual cord rupture procedure, especially if the enzyme has diffused into surrounding tissues or if unspent collagenase is released during finger extension.

4 FROM RISK TO PRECISION: RETHINKING COLLAGENASE DELIVERY IN DUPUYTREN'S CONTRACTURE

The current method for delivering collagenase injections in Dupuytren's contracture is a manual procedure that depends heavily on the physician's anatomical knowledge, palpation skills, and real-time tactile feedback. While this approach can be effective, it is fundamentally imprecise, especially in complex cases involving elderly, obese, or surgically altered hands.

As a result, outcomes are highly variable, and the therapy remains underutilized despite its potential. The risks include:

- Skin tears, from enzyme diffusion into the dermis
- Bruising and hematomas, due to vascular wall degradation
- Pain and inflammation, from exposure of surrounding soft tissue
- Tendon rupture, a rare but serious complication

These adverse effects most often result from inaccurate needle placement, uncontrolled enzyme spread, or over-injection into non-target areas. APPENDIX 1 presents the standard multi-step manual procedure, illustrating numerous opportunities for error during the process.

This mismatch between the pharmacologic precision of collagenase and the mechanical imprecision of its delivery represents the central obstacle in current practice.

DupuyFix™ offers a transformative solution. It introduces a standardized, image-guided, and feedback-controlled platform that automates the most critical elements of the injection process. By stabilizing the hand, precisely locating the cord, and delivering enzyme at an optimal rate and depth, DupuyFix™ dramatically minimizes operator error, protects surrounding anatomical structures, and maximizes treatment safety and consistency.

In doing so, it bridges the gap between therapeutic promise and real-world performance—paving the way for a safer, more predictable, and more widely adopted collagenase-based therapy.

4.1 Injection Error Dynamics in Manual Collagenase Delivery

Enzymatic injection has revolutionized outpatient treatment of Dupuytren's contracture. However, its broader adoption is constrained by inconsistent results and medicolegal concerns stemming from manual delivery and its associated risks.

4.2 Major Features and Limitations

Manual injection of collagenase exhibits high variability in needle placement—both in lateral and depth dimensions. The most frequent error is **depth overshoot**, which can result in enzyme reaching the flexor tendons or surrounding neurovascular structures.

Given the cord's small diameter (~3 mm), and difficulty in visualizing the needle tip position,

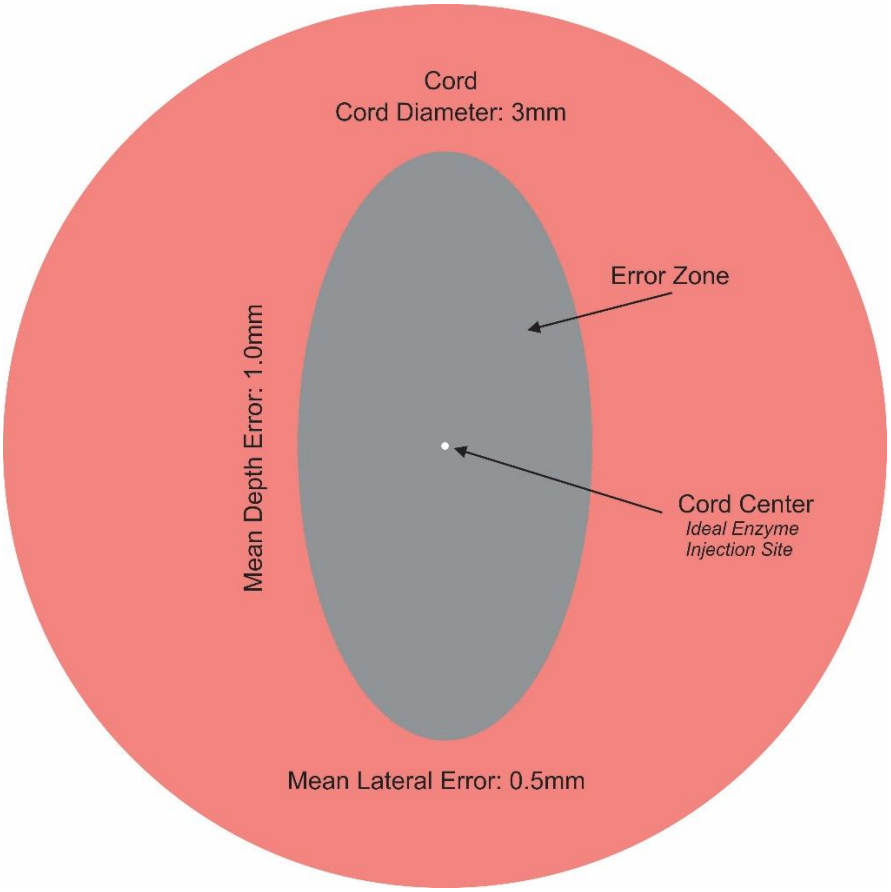
error zones tend to form vertically elongated ellipses with a 2:1 depth-to-lateral error ratio.

Complicating this further is the inconsistency in tissue resistance across patients, making tactile feedback an unreliable guide.

Even experienced clinicians report challenges in ensuring accurate needle tip placement within the narrow 3 mm-wide cord. Errors generally fall into two categories:

- **Depth-related errors,** where undershooting leads to insufficient enzyme activity near the dermis, while overshooting risks damaging the flexor tendon.
- **Lateral errors,** where the injection may miss the cord entirely or affect nearby nerves or vessels.

Because the needle's depth cannot be visually confirmed once inserted, **depth errors are both more prevalent and more severe** than lateral errors. On average, the magnitude of vertical misplacement is roughly **twice** that of lateral deviation. Consequently, tissues **above and below** the cord are more frequently injured, as detailed in the accompanying Summary Table.



Cross-Sectional Error Zone Geometry in Manual Injection

Table: Depth vs. Lateral Errors – A Comparative Overview

Error Type	Cause	Most Affected Tissue	Frequency (Est.)	Severity
Depth overshoot	Enzyme leaks below cord	Flexor tendon	~40%	High
Lateral misfire	Needle too far from center	Skin/nerve/vessel	~25%	Moderate
Enzyme track	Leak along needle exit path	Dermis	~20%	Low-Moderate

Based on anatomical relationships, injection mechanics, and clinical reporting, depth errors are generally more frequent than lateral errors during collagenase injection for Dupuytren's contracture. That's primarily because:

- The vertical (depth) path is longer and harder to judge accurately.
- There's no direct visual feedback once the needle enters.
- Most injections are done manually, without imaging, relying on tactile resistance.

The following table summarizes the estimated frequency, primary cause (depth or lateral error), and severity of complications linked to manual collagenase injection.

Summary Table: Dupuytren's Injection Errors – Prevalence, Cause & Severity

#	Complication / Negative Effect	Est. Frequency*	Main Cause	Severity**	Notes
1	**Skin tearing**	15–30%	Depth (shallow)	Mild–Moderate	Enzyme leaks upward; worsened by tension during cord manipulation
2	**Bruising / hematoma**	10–20%	Depth (shallow) + Lateral	Mild	Often near injection site; resolves without intervention
3	**Pain / inflammation at tendon sheath**	5–10%	Depth (overshoot)	Moderate	Can cause finger pain or stiffness if collagenase affects tendon bed
4	**Swelling / edema**	5–10%	Depth (shallow or deep)	Mild	Often reactive, from enzyme exposure to soft tissue
5	**Temporary numbness or tingling**	1–3%	Lateral	Moderate	Digital nerve irritation (usually resolves)
6	**Skin necrosis / ulceration**	<1%	Depth (shallow) + repeated tension	Severe	Rare; linked to poor wound care or high-dose injections

#	Complication / Negative Effect	Est. Frequency*	Main Cause	Severity**	Notes
7	**Tendon rupture**	<0.5%	Depth (overshoot)	Severe	Very rare; typically, from direct injection into tendon sheath
8	**Digital artery injury**	<0.5%	Lateral	Moderate–Severe	Rare; more likely in small hands or thin fingers

4.3 Key Observations

- The most frequent complications stem from depth errors, particularly when enzyme spreads too superficially (into the dermis) or too deeply (into tendon sheath).
- Although less frequent, lateral errors can lead to serious outcomes when they involve digital nerves or arteries.
- Most published studies do not explicitly distinguish between lateral and depth-related errors; the table reflects inferred causality based on anatomical pathways and clinical injection mechanics.
- Frequency estimates are based on complication rates reported in real-world use of collagenase (Xiaflex).

4.4 Notes

- Frequencies reflect outcomes in skilled hands (hand surgeons or experienced injectors).
- Complication rates tend to rise with:
  - Severe contractures
  - Repeat injections
  - Patients with tight subcutaneous tissue or thin skin
- Use of ultrasound or image guidance can significantly reduce injection errors and associated risks.

5 DupuyFix™ SYSTEM ARCHITECTURE: COMPONENTS, FUNCTIONS, AND CLINICAL BENEFITS

5.1 Hand Stabilization Module

- Ergonomically molded hand rest to support palm and fingers in a relaxed but immobilized position.
- Adjustable finger straps or custom-fit pads reduce movement during targeting and injection.
- Transparent, open design around the injection zone provides clear access for the injector arm.
- Enables rapid repositioning between injection sites without needing re-stabilization.
  Purpose: *Ensures precise, repeatable positioning and eliminates hand movement during targeting and multi-point injection sequences.*

5.2 Imaging & Cord Localization System

- Integrated high-resolution ultrasound probe with real-time visualization of cord structure, depth, and surrounding anatomy.
- AI-guided interpretation produces a 3D overlay map highlighting safe injection zones.
- Optional upgrade: Optical Coherence Tomography (OCT) for ultra-fine image fidelity in difficult cases.

- Supports automated planning for multiple rapid injections along the cord, pre-programmed based on the cord's specific geometry and stiffness profile.
- Non-invasive analysis enables longitudinal monitoring of cord condition and response over time.

5.3 Precision-Guided Injection Arm

- Robotic injector mounted on a multi-axis rail ensures accurate needle positioning based on imaging data.
- Calculates and adjusts needle path, angle, and depth to reach the cord's geometric center while avoiding tendons, nerves, and vessels.
- Capable of executing multiple rapid injections along the cord in a single session, reducing total procedure time.
- Manual override available for physician-controlled guidance when desired.

5.4 Adaptive Enzyme Delivery Unit

- Digitally driven syringe plunger system.
- Injection rate and pressure dynamically adjust based on real-time tissue resistance feedback using integrated force sensors.
- Eliminates need to manually recharge the syringe—enabling uninterrupted, multi-point injection with minimal human intervention.
- By reducing procedure complexity and operator dependency, more frequent, lower-dose injection sessions can be scheduled, decreasing risks associated with abrupt manual cord rupture.
- A post-injection seal protocol minimizes leakage of enzyme into surrounding tissues via the needle track.

5.5 Note on Enzyme Neutralization and Risk Mitigation

Currently, there is no clinically approved antidote or neutralizing agent that can be safely injected to deactivate collagenase (e.g., Xiaflex) once administered. While in vitro studies have demonstrated that collagenase activity can be inhibited by agents such as EDTA (a metal chelator), TIMP proteins (tissue inhibitors of metalloproteinases), or pH modulation, these methods are either unsafe for direct injection or not yet developed for clinical use.

Therefore, the most effective way to minimize enzymatic damage to surrounding tissues remains the precise, targeted delivery of collagenase into the cord with minimal diffusion. The DupuyFix™ system addresses this need through real-time imaging, tissue resistance feedback, and controlled multi-point microinjection — significantly reducing the risk of off-target exposure and the complications associated with enzyme leakage.

6. DupuyFix™: UNLOCKING BENEFITS, FEATURES, AND STRATEGIC GROWTH

6.1 Clinical Benefits

- Predictable, standardized results independent of practitioner experience.
- Delivers near error-free injections with dramatically reduced complication rates.
- Shortened learning curve and increased treatment confidence for new providers.
- Dynamic imaging and automated logs boost transparency and patient trust.
- Full record of injection volume, pressure, and location stored for each patient.
- Enables personalized treatment protocols based on cord shape, stiffness, and prior response.

6.2 Clinical Comparison

Manual Method	DupuyFix™
Highly operator-dependent	Standardized, reproducible
High risk of leakage, misplacement	Controlled, AI-guided needle placement
No imaging guidance	Real-time visualization and cord mapping
One-size-fits-all approach	Personalized, multi-point, feedback-driven injections
Manual pressure	Resistance-guided, auto-calibrated dosage delivery

6.3 Bonus Features

- Pre-set injection protocols based on cord type (central, spiral, natatory).
- Upload capability for pre-op imaging or MRI data.
- Printable patient report with annotated injection map.
- Training mode for simulation-based education of new providers.

6.4 Future Capabilities and Expansion

- EHR integration for automatic documentation.
- Augmented-reality overlay for surgeon training.
- Expandability to other fibrotic or soft tissue conditions (e.g., plantar fibromatosis, keloid therapy).
- Integration with robotic surgical suites.

6.5 Strategic Opportunity

DupuyFix™ fills a major gap in minimally invasive hand treatment:

- Offers the first intelligent injection platform dedicated to Dupuytren's contracture.
- Enables safe, reproducible procedures with massive potential to scale.
- IP-protectable core technology (hardware/software).
- Aligns with commercial interests of medtech giants like Zimmer Biomet, Stryker, or AI-driven surgical startups.

7. SYSTEMIC AND ECONOMIC IMPACT OF DupuyFix™ INTEGRATION INTO CLINICAL PRACTICE

The adoption of DupuyFix™ into routine clinical use represents not just a leap in procedural precision and patient safety, but a broader systemic transformation with implications for healthcare delivery models, economic efficiency, and the professional landscape.

7.1 Systemic Disruption and Shifts in Clinical Practice

As with any transformative medical technology, DupuyFix™ may displace older manual practices and reconfigure the roles of healthcare providers involved in treating Dupuytren's contracture. Currently, an estimated 60,000–80,000 enzyme injection procedures are performed annually in the United States alone, typically by hand surgeons, orthopedists, or specially trained physicians.

The standardized, feedback-controlled nature of DupuyFix™ could reduce the number of highly skilled practitioners needed to perform the procedure. By making the injection process safer, more predictable, and less reliant on manual dexterity or deep anatomical familiarity, the system enables a broader pool of healthcare professionals, such as physician assistants or

trained technicians, to administer the treatment under appropriate supervision. This shift may lessen the burden on specialist time while expanding access to care.

Moreover, the platform reduces the need for extensive training and practice that currently serve as barriers to scaling collagenase injection treatments. While this transformation could be perceived as a threat to traditional practitioners, the reality is more nuanced. DupuyFix™ does not replace medical judgment—it enhances its application. Specialists remain essential for diagnosis, system setup, treatment planning, and management of complex cases. Rather than eliminating roles, it reallocates human expertise to areas where it is most impactful.

7.2 Economic Advantages and Cost Savings

The economic benefits of DupuyFix™ adoption are substantial. Key savings include:

- Reduction in post-treatment complications, which currently range from 20–30% of all manual enzyme injection cases. Fewer skin tears, tendon injuries, or nerve damage translate directly into lower follow-up care costs and less litigation risk.
- Shortened procedure duration, thanks to real-time imaging and automated injection control, reducing the need for prolonged physician or staff involvement. A single-session time saving of even 10–15 minutes across tens of thousands of cases represents a significant labor efficiency gain.
- Fewer repeat procedures. By enabling more complete and accurately placed enzyme injections, DupuyFix™ increases success rates per session, lowering the total cost per cure.
- Reduced need for surgical intervention. A more reliable non-surgical option can reduce the number of patients who progress to surgery, thereby lowering overall system costs.

While the initial capital investment in the DupuyFix™ system is nontrivial, amortizing the cost over multiple procedures quickly yields net savings—particularly for group practices, ambulatory surgical centers, and hospitals treating large patient volumes.

7.3 Impact on Insurance Payers and Patients

For insurance providers, DupuyFix™ promises a high-value, low-risk intervention. Improved procedural outcomes and fewer complications lead to decreased overall payouts for post-injection care, emergency treatment of complications, and long-term rehabilitation.
Patients benefit directly as well:

- Fewer complications mean less pain, faster recovery, and a reduced need for pain medication, wound care, or follow-up visits.
- Shorter procedure times and safer treatment pathways make the intervention more accessible, even for patients who may have avoided it due to fear of complications.
- Lower out-of-pocket costs, thanks to fewer unanticipated expenses from adverse effects or repeat injections.

7.4 Human Value: Reduction in Pain and Suffering

Beyond clinical and economic metrics, the reduction in patient pain and trauma cannot be overstated. The traditional post-injection "cord rupture" maneuver—often involving a sudden, forceful manipulation of the affected finger—is not only painful but emotionally distressing for many patients. In contrast, the DupuyFix™-enabled protocol allows for gentle, incremental enzymatic weakening and post-treatment stretching that respects patient comfort.

By minimizing tissue trauma, avoiding unspent enzyme leakage, and enabling more tailored multi-point injections, DupuyFix™ provides a more humane, patient-centered pathway for recovery. For many, this may represent the difference between seeking treatment early—before deformity progresses—and delaying intervention due to fear or misinformation.

7.5 Conclusion

In sum, DupuyFix™ enhances—not threatens—the role of medical practitioners by shifting them from manual execution to expert oversight and therapeutic planning. It delivers system-wide economic efficiencies while dramatically improving patient experience and outcomes. As with many other technological advances in medicine, the transition may initially challenge traditional roles, but in the long run, it creates a more efficient, accessible, and compassionate model of care.

8 EXECUTIVE SUMMARY

DupuyFix™ presents a transformative leap in the management of Dupuytren's contracture. By uniting high-resolution imaging, hand stabilization, multi-point injection planning, resistance-guided dosing, and automated enzyme delivery, it overcomes the limitations of manual injection methods. The system not only improves clinical precision but opens the door for error-free, rapid, and adverse-effect-free treatment, setting a new benchmark in hand surgery.

APPENDIX 1: MANUAL INJECTION PROCEDURE FOR DUPUYTREN'S CONTRACTURE (Excerpts)

a) Using a new 1-mL hub less syringe that contains 0.01 -mL graduations with a permanently fixed, 27-gauge 1/2-inch needle, withdraw a volume of reconstituted solution (containing 0.58 mg of XIAFLEX) as follows:
- 0.25 mL for cords affecting a MP joint or
- 0.20 mL for cords affecting a PIP joint.

b) With your non-dominant hand, secure the patient's hand to be treated while simultaneously applying tension to the cord. With your dominant hand, place the needle into the cord, using caution to keep the needle within the cord. Avoid having the needle tip pass completely through the cord to help minimize the potential for injection of XIAFLEX into tissues other than the cord. After needle placement, if there is any concern that the needle is in the flexor tendon, apply a small amount of passive motion at the distal interphalangeal (DIP) joint. If the insertion of the needle into a tendon is suspected or paresthesia is noted by the patient, withdraw the needle and reposition it into the cord.

c) If the needle is in the proper location, there will be some resistance noted during the injection procedure. After confirming that the needle is correctly placed in the cord, inject approximately one-third of the dose.

d) Next, withdraw the needle tip from the cord and reposition it in a slightly more distal location (approximately 2 to 3 mm) to the initial injection in the cord and inject another one-third of the dose.

e) Again, withdraw the needle tip from the cord and reposition it a third time proximal to the initial injection (approximately 2 to 3 mm) and inject the final portion of the dose into the cord.

f) When administering two injections in the same hand during a treatment visit, use a new syringe and separate vial of reconstituted solution for each injection. Repeat steps (a) through (f).

g) When administering two injections in the same hand during a treatment visit, begin with the affected finger in the most medial aspect of the hand and continue toward the lateral aspect (e.g., fifth finger to index finger). When administering two injections in a cord affecting two joints in the same finger, begin with the affected joint in the most proximal aspect of the finger and continue toward the distal aspect (e.g., MP to PIP).

h) Wrap the patient's treated hand with soft, bulky, gauze dressing.

i) Instruct the patient to limit motion of the treated finger(s) and to keep the injected hand elevated until bedtime.

j) Instruct the patient not to attempt to disrupt the injected cord(s) by self- manipulation and to return to the healthcare provider's office the next day for follow-up and a finger extension procedure(s), if needed.

k) Discard the unused portion of the reconstituted solution and diluent after injection. Do not store, pool, or use any vials containing unused reconstituted solution or diluent.

APPENDIX 2: ENHANCING THE SELECTIVITY OF COLLAGENASE INJECTIONS FOR DUPUYTREN'S CONTRACTURE

Exploratory Strategies to Minimize Off-Target Tissue Damage During Enzymatic Treatment

This Appendix discusses the **selectivity** of collagenase (used in **Xiaflex**) — a known limitation in Dupuytren's treatment. Collagenase clostridium histolyticum dissolves **type I and III collagen**, which is found not only in the **pathologic cords**, but also in **tendons, ligaments, blood vessels, and even the dermis**. This non-selectivity leads to adverse effects like tendon rupture, skin tears, and nerve damage.

Here are current insights and speculative directions for **enhancing selectivity**:

1. Biochemical Selectivity Enhancement

a. Targeted Collagenase Inhibitors (Adjunct)

- Idea: Co-inject or pre-treat surrounding tissues with reversible collagenase inhibitors (e.g., EDTA, TIMPs) to create a "protection zone."
- Challenge: Ensuring the inhibitors don't diffuse into the target cord area and block the enzyme's action there.
- Status: No approved methods, but under discussion in tissue remodeling research.

b. pH-Dependent Activation

- Modify the enzyme or use a prodrug that is activated only under specific pH conditions.
- Rationale: Fibrotic cords may have different extracellular pH compared to surrounding healthy tissues.
- Status: Experimental.

c. Substrate-Specific Enzyme Engineering

- Re-engineer collagenase to have higher affinity for disordered, densely cross-linked collagen (as in Dupuytren cords).
- Techniques: Site-directed mutagenesis, protein design (AI-guided)
- Status: Theoretical in this context; active in cancer and arthritis enzyme-targeting fields.

2. Physical/External Selectivity Enhancement

a. Ultrasound-Activated Drug Release

- Encapsulate collagenase in microbubbles or liposomes that burst when targeted by high-frequency focused ultrasound at the site.
- Effect: Localized release reduces exposure to unintended tissues.
- Status: In development for chemotherapy delivery; not yet applied to Xiaflex.

b. Magnetic Nanoparticle-Guided Enzyme Delivery

- Attach enzymes to magnetically steerable nanoparticles; inject systemically or locally and guide to the cord using an external magnetic field.
- Status: Early-stage research in drug targeting.

c. Optically Activated Enzyme Release

- Enzyme packaged in light-sensitive carriers that release only when exposed to a specific wavelength directed at the cord site.
- Challenge: Penetration depth in skin is limited for visible/near-infrared light.
- Status: Experimental; not practical yet for hand applications.

3. Practical Future Approach for DupuyFix™

For near-term use in the proposed **DupuyFix™** system, the most practical idea might be: Real-time ultrasound-guided delivery with feedback-controlled micro-dosing, possibly combined with a protective pre-injection of a mild, reversible collagenase inhibitor along the periphery of the cord.

This balances safety and feasibility, while potentially reducing unwanted tissue damage — and it fits naturally with the proposed robotic injection system.