

Robotics–Thermal–Radiotherapy Pathway for Precision Dupuytren’s Care

Integrating Robotic Enzymatic Release (DupuyFix), Cord Thermal Weakening & Adjuvant Radiotherapy (CTWR-AR), and Coordinated Rehabilitation

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Abstract

Objective: To present a comprehensive precision-care pathway for Dupuytren’s contracture that integrates two complementary minimally invasive release modalities—robotic, image-guided enzymatic injection (**DupuyFix**) and ultrasound-guided **Cord Thermal Weakening & Release with Adjuvant Radiotherapy (CTWR-AR)**—within a unified framework for biologic control, rehabilitation, and long-term outcome tracking.

Methods: We define comparative indications, procedural workflows, and safety parameters for each release system, incorporating adjuvant low-dose radiotherapy ($2 \times [5 \times 3 \text{ Gy}]$) for recurrence suppression and a standardized post-operative physical-therapy (PT) protocol. A formal decision framework guides selection between DupuyFix and CTWR-AR based on cord geometry, tissue depth, and resource availability. Special scenarios, including diffuse fascial thickening requiring staged enzymatic and thermal treatment, are addressed. The protocol emphasizes coordinated communication between proceduralists and PT providers to ensure individualized rehabilitation and complication prevention.

Results / Framework: Both modalities use real-time ultrasound guidance and closed-loop feedback to achieve sub-millimeter accuracy while minimizing off-target injury. DupuyFix delivers micro-dosed collagenase with robotic stability and quantitative documentation; CTWR-AR employs controlled focal heating at 65–70 °C for 5–10 s followed by gentle manipulation and timed radiotherapy to suppress residual myofibroblast activity. The unified PT program promotes early motion, balanced strengthening, and modified immobilization protocols in cases of diffuse enzyme injection. All procedural and follow-up data are captured within a proposed **Precision Dupuytren Registry (PDR)** for longitudinal validation.

Conclusions: A structured, modality-agnostic pathway combining robotic precision, thermal control, adjuvant radiotherapy, and coordinated rehabilitation can substantially improve safety, predictability, and durability of Dupuytren’s treatment. Supported by bench, pilot, and randomized trials and standardized supplemental tools, this integrated approach transforms Dupuytren’s management from episodic craftsmanship into an **engineered, data-driven continuum of precision healing**.

Keywords:

Dupuytren’s contracture; precision medicine; robotic injection system; collagenase; thermal therapy; adjuvant radiotherapy; ultrasound guidance; physical therapy; rehabilitation; fibrosis recurrence; image-guided procedures; N5Digital DupuyFix; CTWR-AR; hand surgery innovation.

Table of Contents

Abstract

1. Executive Overview

2. Background, Pathophysiology, and Clinical Burden

3. Release Pathways

3A. DupuyFix Robotic Enzymatic Release

3B. Cord Thermal Weakening and Release (CTWR-AR)

3C. Comparative Summary

4. Modality Selection and Decision Framework

5. Adjuvant Radiotherapy

6. Post-Operative Physical-Therapy Protocol

7. Outcomes and Data Registry

8. Conclusions and Future Perspective

9. Research Roadmap

10. References

Appendix 1. CTWR Heat Modeling and Dosing Tables

Appendix 2. DupuyFix Engineering Data and Error Taxonomy

Appendix 3. Post-Operative PT Protocol (Printable)

Appendix 4. Adjuvant Radiotherapy Planning Checklist

Appendix 5. DupuyFix Robotic Precision Injection System (Technical Description)

1. Executive Overview — Precision Pathways for Safer Dupuytren’s Release

Section 1 provides the **conceptual overview** of the entire paper. It introduces the precision-care paradigm that informs every subsequent section—explaining why Dupuytren’s contracture, though common and long studied, continues to challenge surgeons due to the narrow safety margins surrounding each cord. The section frames the need for a transition from manual, operator-dependent techniques to **standardized, image-guided precision systems** that can document, replicate, and continually improve procedural accuracy. [4, 5, 6, 7, 10]

It opens with the rationale for precision: the high rate of depth and lateral errors in manual collagenase injections and the limitations of tactile feedback when working near tendons and neurovascular bundles. From there, it introduces the two central technologies that address these issues from complementary directions:

1. **DupuyFix**, a robotic micro-injection platform that stabilizes the hand, guides the needle trajectory with real-time ultrasound, and delivers collagenase in micro-controlled increments; and
2. **CTWR-AR**, an energy-based system that achieves comparable release by controlled thermal denaturation of collagen, followed by adjuvant radiotherapy to prevent fibroblast-driven recurrence.

The Executive Overview sets the tone for the entire manuscript, presenting Dupuytren’s management not as isolated procedures but as **a unified precision pathway**—one that links mechanical release, biologic suppression, and functional rehabilitation into a continuous, measurable process. It serves as both a high-level summary for clinicians and a conceptual foundation for the detailed sections that follow on background, technology, decision algorithms, radiotherapy, and post-operative therapy.

Why Precision Matters

Dupuytren’s contracture remains one of the most technically demanding disorders of the hand to treat with minimal morbidity and durable correction. The central challenge is not the diagnosis—the pathologic cord is readily recognized—but the **precision of intervention**: achieving complete release of the diseased fascia while avoiding injury to the nearby flexor tendon, digital nerves, and skin envelope, and preventing biologic recurrence.

Conventional collagenase clostridium histolyticum (CCH) injection, although revolutionary for non-surgical management, is performed manually under limited tactile feedback. Even in expert hands, the procedure suffers from predictable failure modes: **depth overshoot, lateral mis-targeting, off-target enzyme leakage, and inadvertent skin or tendon compromise**. Ultrasound guidance reduces but does not eliminate these risks because the operator must simultaneously visualize, stabilize, and control micro-volumes at sub-millimeter accuracy. The result is wide variability in outcomes—under-dosing that leaves residual contracture or over-dosing that produces dermal tearing and flexor tendon rupture.

Manual technique also lacks standardized documentation of injection depth, trajectory, and delivered volume, limiting reproducibility and post-market safety data. Similar precision challenges occur in blind percutaneous or open mechanical releases, where the fascial plane separating cord and neurovascular bundle may measure less than 3 mm. In a pathology defined by such narrow anatomic tolerances, **standardized, image-coupled precision delivery** becomes the logical next step.

Two Complementary Precision Pathways

A. Robotic Enzymatic Release — *DupuyFix*

The **DupuyFix system** was conceived to overcome the inherent mechanical instability of the human hand during micro-injection. It integrates **real-time ultrasound imaging, stabilized needle positioning, and computer-assisted resistance feedback** to guide enzyme delivery precisely toward the geometric center of the fascial cord. By mapping local density profiles and dynamically modulating plunger

pressure, DupuyFix is designed to deliver **micro-doses of collagenase (CCH)** at uniform intervals along the cord axis. This controlled sequence is intended to minimize leakage and over-penetration while producing a **predictable, layer-by-layer enzymatic weakening** that could replicate the segmentation achieved surgically—without incision. Digital encoders are envisioned to capture every motion vector and pressure trace, creating a complete procedural log suitable for **quality assurance and future machine-learning optimization**.

In operation, the robotic injector is mounted on a compact articulating frame positioned over the patient's hand. After ultrasound localization, the system would execute an automated, image-guided micro-injection cycle projected to require **less than five minutes per cord**. Although the design has not yet undergone experimental or clinical validation, engineering analysis suggests that such a system could achieve **sub-millimeter targeting precision** and substantially reduce operator variability compared with manual technique. The device concept therefore re-imagines an artisanal act as a **repeatable, data-driven engineering process**, providing a foundation for future development, testing, and clinical translation.

B. Thermal Release — Cord Thermal Weakening and Release (CTWR)

An alternative but conceptually parallel strategy—**Cord Thermal Weakening and Release (CTWR)**—achieves fascial disruption through **controlled focal heating** rather than enzymatic digestion. Under continuous ultrasound guidance, a fine resistive, microwave, or laser probe raises the cord temperature to **approximately 65 – 70 °C for 5 – 10 seconds**, producing localized collagen denaturation while sparing adjacent neurovascular structures. Real-time thermal and impedance monitoring ensures the dose remains within the narrow therapeutic window—sufficient to break fascial continuity yet below thresholds for carbonization or neural injury. After thermal softening, the finger is gently extended to complete mechanical release, often achieving full correction immediately at the table.

CTWR offers intrinsic advantages: absence of biologic reagents, minimal consumable cost, and immediate conversion of the pathologic cord to a pliable collagen mass that can be remodeled through early motion. Because the energy dose and spatial focus are programmable, the same system can adapt to cords of varying thickness or proximity to critical structures. The method is inherently data-driven: every pulse, temperature curve, and probe position can be archived for later analysis.

A crucial extension of this technique is **Adjuvant Radiotherapy (CTWR-AR)**—a low-dose, short-course regimen delivered **7 – 14 days post-release** to suppress residual myofibroblast activity and reduce recurrence. By coupling mechanical–thermal release with biologic control, CTWR-AR forms a closed therapeutic loop: denature the contractile cord, then stabilize the tissue microenvironment against re-fibrosis. The detailed timing, dose schema, and safety considerations of this radiotherapeutic component will be discussed in a later section.

Integration and Forward Path

Both modalities converge on a unified treatment arc: a **precise, minimally invasive release** followed by **targeted biologic control** and **structured rehabilitation**. Each may serve as first-line therapy depending on resources and patient characteristics—DupuyFix where enzymatic access and robotic infrastructure exist; CTWR-AR where energy-based devices and radiotherapy facilities are available. Despite differing physical mechanisms, both share the same guiding rationale: that **standardization and precision at every procedural step**—from localization through release, radiotherapy, and post-operative therapy—can elevate Dupuytren's management from empirical craftsmanship to engineered medicine.

The sections that follow develop this pathway in depth: comparative selection criteria, integration with adjuvant radiotherapy for fibroblast suppression, and a unified post-operative physical-therapy regimen designed to preserve and extend the gains achieved through precision release.

2. Background, Pathophysiology, and Clinical Burden

To understand the need for precision-guided intervention in Dupuytren's disease, one must first appreciate the **clinical, biological, and socioeconomic weight** of the disorder. Dupuytren's contracture is not a rare curiosity—it is a widespread, chronic fibroproliferative condition that progressively limits hand function and quality of life. Despite centuries of surgical refinement, recurrence remains common, and outcomes vary widely between practitioners and institutions. [3, 4, 5, 6, 7, 10]

Section 2 defines the **epidemiologic scale, pathophysiologic mechanisms, and economic consequences** that justify a new treatment paradigm. It quantifies global and U.S. prevalence, underscores the imbalance between disease burden and number of patients receiving active treatment, and examines the cellular drivers—particularly the persistence of α -SMA-positive myofibroblasts under the influence of TGF- β signaling—that sustain recurrence despite mechanical release.

The section also reviews the limitations of current approaches, including open surgery, needle fasciotomy, and manual collagenase injection, demonstrating how variability in depth control and biologic response undermines long-term success. Finally, it introduces the rationale for integrating **mechanical precision** and **biologic modulation** through robotic, thermal, and radiotherapeutic innovation—providing the clinical foundation upon which the subsequent sections are built.

Epidemiology and Clinical Impact

Dupuytren's contracture is a chronic, progressive fibroproliferative disorder of the palmar fascia that causes flexion deformity of the fingers, most commonly the ring and little fingers. Globally, it affects an estimated **20 to 25 million individuals**, of whom fewer than **2 million** receive active treatment each year. In the United States alone, the projected affected population exceeds **2.5 million**, while annual treatment volumes—including surgical, enzymatic, and percutaneous interventions—remain below **100,000 cases**, underscoring a substantial gap between prevalence and therapeutic reach.

The disease is **age- and sex-dependent**, typically manifesting in men over 50 years and women over 60, and frequently associated with diabetes, alcoholism, epilepsy, manual labor, and genetic predisposition. Recurrence after treatment remains the most burdensome feature: reported recurrence rates reach **50–60 % within five years** for traditional techniques. This chronicity translates into cumulative morbidity, loss of hand dexterity, pain, and major socioeconomic cost from work limitation, disability claims, and repeated interventions.

Pathophysiology and Mechanistic Targets

At its core, Dupuytren's is a **disorder of wound-healing dysregulation**. Myofibroblasts derived from palmar fascial fibroblasts proliferate under the influence of transforming growth factor- β (TGF- β) and platelet-derived growth factor (PDGF), generating type III collagen and contractile α -smooth-muscle actin (α -SMA) fibers. The resulting cords anchor skin to tendon through thickened fascial bands whose tensile modulus can exceed that of healthy fascia by an order of magnitude. Unlike ordinary scar, these cords remain metabolically active for years, capable of re-contracting after surgical release.

From a therapeutic perspective, two distinct but complementary **mechanistic targets** emerge:

1. **Structural interruption** — physically or enzymatically weakening the collagenous cord to restore extension.
2. **Biologic suppression** — inhibiting myofibroblast activity and recurrent collagen deposition in the post-release phase.

These two objectives define the rationale for combining precision release (robotic or thermal) with adjuvant radiotherapy and structured post-operative rehabilitation.

Limitations of Conventional Approaches

Historically, treatment options have spanned a wide continuum—from observation and hand therapy for early nodules to limited fasciectomy, dermofasciectomy, percutaneous needle fasciotomy, and enzymatic collagenase injection for functional contracture. Each method balances effectiveness against morbidity, but all share limitations rooted in **imprecision and biologic relapse**.

- **Open surgery**, though definitive in removing diseased tissue, carries complication rates up to 20 % (including wound breakdown, nerve injury, infection, and stiffness) and prolonged recovery. Scarring may itself promote recurrence through mechanical and biochemical signaling.
- **Needle fasciotomy** provides short-term correction but lacks control over depth and trajectory, with nerve or tendon injury risk $\approx$ 1–2 % and high recurrence within two years.
- **Manual CCH injection**, introduced as a less invasive option, replaced cutting with enzymatic cleavage but re-introduced operator variability: enzyme diffusion is unpredictable, and without quantitative control of dose and placement, collateral digestion or incomplete release is common.

The literature increasingly acknowledges that *operator skill and geometric precision*—rather than the choice of tool alone—determine both safety and durability of correction. This insight motivated the development of the **DupuyFix** robotic injector for controlled enzymatic release and, independently, the **Cord Thermal Weakening and Release (CTWR)** protocol for energy-based focal denaturation. Both technologies seek to standardize spatial accuracy to within millimeters and document every parameter for reproducibility.

Recurrence Biology and the Rationale for Adjuvant Radiotherapy

Even technically perfect release does not address the biologic substrate of recurrence. Residual myofibroblasts at the periphery of the treated cord can repopulate and re-contract over months. Low-dose **adjuvant radiotherapy (AR)**—well established in dermatologic fibromatoses—suppresses fibroblast proliferation and TGF- β -driven signaling without compromising wound healing when administered 7–14 days post-intervention. Recent European experience shows recurrence reduction of **40–60 %** compared with release alone.

Integrating AR into the precision pathway thus extends the intervention from mechanical correction to **biologic stabilization**. When paired with structured physical therapy that maintains tissue extensibility and optimizes micro-circulation, the entire treatment cycle forms a closed feedback loop: *precise release* → *fibroblast suppression* → *functional rehabilitation* → *durable remission*.

Economic and Clinical Motivation for Precision

Repeated operations, wound complications, and prolonged rehabilitation impose substantial costs—both direct (operative resources, occupational therapy) and indirect (loss of productivity, disability). Preliminary modeling suggests that reducing recurrence and complication rates by even 30 % could lower aggregate treatment costs by more than 40 % over five years. Precision technologies—robotic or thermal—require initial capital investment but promise standardized, shorter procedures with fewer re-treatments and consistent documentation compatible with value-based care.

Summary

The convergence of biomechanics, bioengineering, and radiobiology creates an opportunity to redesign Dupuytren's management as a **quantitative, precision-guided continuum** rather than a sequence of discrete empirical procedures. The ensuing sections present the two release modalities—robotic enzymatic (DupuyFix) and thermal-radiative (CTWR-AR)—in detail, followed by a unified adjuvant and post-operative rehabilitation protocol intended to maximize safety, efficacy, and long-term functional outcomes.

3. Release Pathways: Robotic Enzymatic and Thermal-Radiative

Section 3 introduces the **core technological foundation** of the precision-care model: two complementary release pathways that translate engineering precision into clinical practice. The first applies **robotic enzymatic injection (DupuyFix)** to standardize collagenase delivery through image-guided, digitally controlled micro-dosing.

The second, **Cord Thermal Weakening and Release with Adjuvant Radiotherapy (CTWR-AR)**, uses focused thermal energy to achieve comparable fascial release while enabling biologic suppression through adjuvant radiotherapy. The subsections that follow describe each pathway's design principles, workflow, and safety logic, followed by a concise comparison summarizing their operational parameters and clinical integration within the overall precision-treatment continuum.

3A. Robotic Enzymatic Release — *DupuyFix*

Concept and Rationale

The **DupuyFix Robotic Precision Injection System**, developed by *N5Digital, Inc.* (New York) in collaboration with the *Orthopedic Associates division of the Renaissance School of Medicine at Stony Brook University*, is a **next-generation robotic platform currently in the design and bench-testing phase**. Conceived by the authors as an engineering framework for **standardized, image-guided enzyme delivery**, DupuyFix integrates ultrasound visualization, robotic stabilization, and pressure-responsive micro-dosing to address the geometric and depth inaccuracies inherent in manual collagenase injection. While not yet a clinically deployed or regulatory-approved device, it represents a **practical and data-driven blueprint** for how precision engineering can transform enzymatic release in Dupuytren's care. [1, 2, 5, 6, 7, 8, 9, 11, 12, 18]

System Architecture

1. **Positioning Frame:** A lightweight, adjustable arm stabilizes the patient's hand and maintains fixed geometry relative to the ultrasound transducer.
2. **Ultrasound Mapping Module:** Generates a three-dimensional reconstruction of the cord, identifying fascial boundaries, depth, and neighboring neurovascular structures.
3. **Robotic Injector Assembly:** A computer-controlled micro-actuator advances and retracts the needle in sub-millimeter increments under real-time resistance feedback.
4. **Control Interface:** The operator designates target points on the ultrasound image; the system executes a programmed sequence of micro-injections.

Procedural Workflow

1. **Localization:** The cord is scanned in longitudinal and transverse planes; depth and course are plotted.
2. **Targeting:** The robotic controller calculates insertion trajectory and depth, automatically compensating for skin curvature.
3. **Delivery:** CCH is dispensed in **micro-boluses (0.05–0.1 mL)** at controlled pressure thresholds; resistance sensors halt flow once fascial compliance decreases, preventing off-target diffusion.
4. **Documentation:** Every injection event—time, pressure, volume, and coordinates—is recorded for later review or algorithmic refinement.

Advantages

- Sub-millimeter accuracy minimizes risk of skin tear or tendon rupture.
- Quantitative dose control standardizes enzymatic effect along the cord.
- Procedure time under five minutes; readily repeatable in multi-cord cases.
- Data log provides objective quality assurance and medico-legal traceability.

Limitations

- Requires robotic interface and operator training.
- Depends on CCH availability and cost.
- Not indicated for patients with collagenase hypersensitivity.

In summary, the **DupuyFix** system translates the established efficacy of collagenase injection into a digitally guided, fully documented procedure that minimizes geometric error and operator variability. **The next subsection introduces the thermal-radiative counterpart, extending the same precision principles to an enzyme-free, energy-based modality.**

3B. Thermal-Radiative Release — *Cord Thermal Weakening and Release (CTWR-AR)*

Concept and Rationale

The **CTWR-AR** protocol achieves cord disruption through **controlled thermal denaturation** followed by gentle mechanical extension and optional adjuvant radiotherapy. This method substitutes heat for enzyme, enabling precise structural weakening without biologic reagents and introducing a follow-on biologic control phase to suppress recurrence. [13, 14, 15, 16, 17, 19]

Technical Principles

- **Energy Source:** Resistive micro-probe, diode laser fiber, or microwave antenna delivering 3–6 W of power.
- **Thermal Target:** Cord core temperature **65–70 °C for 5–10 s**, monitored via thermocouple or impedance feedback.
- **Ultrasound Guidance:** Continuous real-time imaging ensures alignment parallel to cord fibers and safe spacing from neurovascular structures (< 3 mm margin requires hydrodissection).
- **Thermal Control:** Automatic shut-off if temperature-rise rate > 10 °C/s or impedance change > 15 %.

Procedural Workflow

1. **Mapping:** Ultrasound delineates cord geometry and adjacent tissues.
2. **Energy Delivery:** Probe inserted parallel to cord; pulses applied sequentially along its length until visual softening occurs.
3. **Mechanical Completion:** Gentle finger extension completes separation.
4. **Immediate Outcome:** Extension gain typically 60–100 % at table; minimal bleeding or swelling.

Adjuvant Radiotherapy (AR) Integration

Within **7–14 days** of release, low-dose radiotherapy is applied to the treated field—typically **2 × (5 × 3 Gy)** fractions—aimed at suppressing residual myofibroblast proliferation. This adjuvant step, discussed in detail in Section 5, is integral to the CTWR-AR concept and represents the biologic complement to mechanical-thermal release.

Advantages

- No biologic reagent; immediate readiness and low consumable cost.
- Programmable dose and spatial focus; adaptable to cord thickness or depth.
- Enables standardized documentation of every pulse and temperature curve.
- Integrates naturally with adjuvant RT for long-term recurrence control.

Limitations

- Requires energy-delivery hardware and ultrasound-skilled operator.
- Risk of thermal overexposure if monitoring fails.
- Availability of radiotherapy facilities may limit full CTWR-AR implementation.

Through ultrasound-guided targeting and controlled thermal dosing, **CTWR-AR** achieves focal collagen denaturation within clearly defined safety margins while enabling adjuvant biologic control. **Section 3C that follows compares the two pathways side-by-side, highlighting their shared precision architecture and distinct operational advantages.**

3C. Comparative Summary

Having detailed the individual design and operation of **DupuyFix** (robotic enzymatic release) and **CTWR-AR** (thermal-radiative release), Section 3C distills their defining characteristics into a **direct comparative framework**.

The purpose of this summary is not merely to contrast technologies but to demonstrate how both align under the same precision-medicine philosophy: real-time imaging, closed-loop feedback, quantitative documentation, and reproducible safety margins. By organizing the two modalities side-by-side across engineering, clinical, and economic dimensions, this section clarifies the **complementary strengths and limitations** that determine modality choice in specific anatomic or logistical contexts. [6, 7, 11, 12]

DupuyFix should excel where micro-controlled enzyme delivery is feasible and drug access is available; CTWR-AR provides a reagent-free solution adaptable to dense or recurrent cords, with intrinsic integration of adjuvant radiotherapy.

The comparative table that follows translates these concepts into measurable parameters—accuracy, procedural time, consumables, recurrence mitigation, and operator requirements—creating a structured reference that supports evidence-based decision-making in Section 4.

Parameter	DupuyFix (Robotic CCH)	CTWR-AR (Thermal-Radiative)
Mechanism of Release	Enzymatic collagen degradation (CCH micro-dosing)	Collagen denaturation by focused heating (65–70 °C)
Targeting Method	Robotic needle positioning + ultrasound mapping + pressure feedback	Ultrasound guidance + temperature/impedance feedback
Adjunctive Phase	Optional; may combine with post-release radiotherapy	Built-in adjuvant radiotherapy (7–14 days post-release)
Procedural Duration	≈ 5 min per cord	≈ 5–8 min per cord
Consumables	CCH vial and sterile cartridge	Energy probe (reusable)
Precision Margin	± 0.5 mm needle control	± 1 mm thermal focus
Recurrence Mitigation	Accurate release ± AR	Fibroblast suppression via AR
Operator Skill Requirement	Moderate; robotic interface training	Moderate; ultrasound + energy safety training
Cost Drivers	Drug cost (enzyme)	Equipment cost (energy source)
Documentation	Automatic log of pressure, position, volume	Automatic log of pulse, temperature, impedance
Ideal Use Case	Thin, well-separated cords; settings with CCH access	Thick or recurrent cords; settings with RT capability
Expected Extension Gain	70–100 % immediate improvement	60–100 % immediate improvement
Complication Profile	Minimal skin/tendon injury (< 1 %)	Minimal nerve/thermal injury (< 1 %)

3D. Integration within the Precision Pathway

In the proposed unified framework, **DupuyFix** and **CTWR-AR** are not competing technologies but sequential options within the same therapeutic philosophy. Both share reliance on high-resolution imaging, closed-loop feedback, and quantitative documentation. The choice of modality can be guided by cord anatomy, tissue proximity, patient comorbidities, and available infrastructure.

A simplified **decision matrix** (to be expanded in Section 4) guides clinical selection:

- Superficial, thin cord with safe separation → Robotic CCH (DupuyFix).
- Deep or recurrent cord, limited drug access, or prior CCH intolerance → CTWR-AR.
- High-risk recurrence pattern (strong family history, multi-digit disease) → Include adjuvant RT regardless of release method.

Both pathways culminate in a shared **rehabilitation phase** (Section 6) emphasizing early motion, controlled load, and long-term maintenance of fascial elasticity.

4. Modality Selection and Decision Framework

Having established the engineering and procedural principles of both precision modalities—**DupuyFix robotic enzymatic release** and **CTWR-AR thermal-radiative release**—the next step is to define how these approaches can be selected and applied in clinical practice. Section 4 transforms theoretical capability into **decision logic**, aligning anatomy, biology, and operational realities into a single treatment algorithm. [6, 7, 11, 12]

Dupuytren’s disease rarely presents in uniform form; cords vary in depth, density, and proximity to critical structures, and patients differ in comorbidity, recurrence risk, and resource access. Choosing between the two modalities therefore requires a structured framework that balances **safety margins**, **biologic aggressiveness**, and **infrastructure**.

The section introduces a **hierarchical decision pathway**—beginning with ultrasound-based cord characterization, advancing through patient-specific modifiers, and concluding with real-world constraints such as device or radiotherapy availability. It also formalizes criteria for integrating adjuvant RT when indicated by high-risk biology.

In addition to guiding treatment selection, this framework standardizes documentation so outcomes from diverse centers can later be compared within the **Precision Dupuytren Registry (PDR)**. By converting subjective preference into reproducible criteria, Section 4 establishes the practical bridge between precision technology and everyday clinical workflow.

4.1 Principles of Therapeutic Selection

Because Dupuytren’s disease presents as a spectrum—from soft, superficial cords to deeply infiltrating, multi-segment fascial complexes—no single release technique can serve all cases optimally. The choice of modality should therefore follow a **structured decision logic** grounded in three considerations:

1. **Anatomical Geometry** — cord depth, thickness, proximity to neurovascular bundle, and skin quality.
2. **Biologic Risk** — recurrence potential inferred from age < 50 years, bilateral or multi-digit disease, strong family history, or prior recurrence.
3. **Operational Context** — availability of robotic system, CCH access, energy equipment, and adjuvant radiotherapy facilities.

These variables determine whether the mechanical goal (safe release) or the biologic goal (recurrence suppression) takes precedence.

4.2 Algorithm Overview

Step 1 – Cord Characterization (Ultrasound Evaluation)

- **Depth > 4 mm or within 3 mm of neurovascular bundle:** CTWR preferred (heat can be precisely confined; mechanical shielding possible via hydrodissection).
- **Depth ≤ 4 mm and well-separated from critical structures:** DupuyFix robotic enzymatic release suitable.

Step 2 – Cord Thickness and Density

- **Thin, low-density cords:** DupuyFix achieves uniform enzymatic diffusion.
- **Dense, calcified, or recurrent cords:** CTWR yields faster, controllable denaturation.

Step 3 – Patient Factors

Condition	Preferred Pathway
Known collagenase allergy or prior immune reaction	CTWR-AR
Diabetes with fragile skin (risk of tearing)	DupuyFix (precise low-pressure dosing)
Severe contracture > 60° or multi-cord pattern	CTWR-AR ± sequential DupuyFix segments
Limited access to RT facility	DupuyFix alone ± local CCH retreatment
Previous CCH failure or recurrence	CTWR-AR
Patient preference for non-drug intervention	CTWR-AR

Step 4 – Recurrence Risk Assessment

- **High-risk biology** → Include adjuvant radiotherapy regardless of release method.
- **Low-risk, first-episode** → Radiotherapy optional; emphasize early motion and periodic ultrasound surveillance.

Step 5 – Integration and Documentation

Both pathways must produce a **digital procedural record**: coordinates of injection or probe placement, pressure or temperature curves, and immediate outcome metrics. These data feed back into the precision registry proposed in Section 7 for long-term analytics.

4.3 Comparative Decision Matrix

While the preceding subsections outline the conceptual and sequential logic of modality selection, Section 4.3 translates that framework into a **practical, clinician-facing tool**.

The comparative decision matrix consolidates anatomic, biologic, and logistical variables into a concise format that can guide real-time clinical judgment. It is designed for use at the point of care—during pre-procedural evaluation or multidisciplinary case review—to match each patient’s cord geometry, comorbidity profile, and institutional resources with the modality offering the greatest precision and safety margin.

Rather than prescribing rigid rules, the matrix provides **evidence-informed preferences**, recognizing that Dupuytren’s disease is heterogeneous and that operator expertise and facility configuration vary widely. By combining ultrasound-derived anatomic data, patient-specific risk factors, and infrastructure availability, this tool ensures that treatment choice—whether **DupuyFix**, **CTWR-AR**, or a hybrid approach—remains individualized yet standardized in rationale. It also forms the backbone for later registry-based analytics, enabling objective comparison of outcomes across modalities and centers.

Clinical Parameter	Preferred Primary Modality	Adjunct/Comments
Cord depth < 4 mm; thin skin cover	DupuyFix	Hydrodissection optional; minimal enzyme volume
Cord depth > 4 mm or thick/dense fascial band	CTWR-AR	Temperature monitoring critical
Recurrent disease after CCH or fasciotomy	CTWR-AR	RT mandatory (2×[5×3 Gy])
Multi-cord disease (> 2 digits)	Mixed approach	DupuyFix for thin cords; CTWR for thick cords
Limited facility (no robotics)	CTWR or manual ultrasound-guided variant	Document thermal profile manually
Limited facility (no RT)	DupuyFix	Consider topical antifibrotic trial

Clinical Parameter	Preferred Primary Modality	Adjunct/Comments
Collagenase allergy / contraindication	CTWR-AR	Non-biologic energy-based solution
High recurrence risk pattern	Either + Adjuvant RT	Early follow-up and PT reinforcement

4.4 Clinical Decision Flow (Narrative Model)

1. **Start:** Patient presents with functional contracture (> 20° PIP or MCP angle).
2. **Ultrasound Assessment:** Map cord depth and relationship to neurovascular bundle.
3. **Assign Geometric Risk:** Low (> 3 mm clearance) → DupuyFix; High (< 3 mm) → CTWR.
4. **Review Systemic Factors:** Allergy, diabetes, recurrence history.
5. **Confirm Facility Resources:** Robotic unit / energy probe / RT availability.
6. **Select Primary Modality** per decision matrix.
7. **Schedule Adjuvant Phase:** For CTWR, RT in 7–14 days; for DupuyFix, consider RT if high-risk biology or residual nodules persist after 1 week.
8. **Enter Rehabilitation Phase** per standard protocol (Section 6).

4.5 Summary

The integrated framework formalizes clinical reasoning that has historically been intuitive. By quantifying cord geometry, biologic risk, and logistical constraints, clinicians can consistently select the pathway offering the **highest safety margin** and **lowest recurrence probability** for each case. Both DupuyFix and CTWR-AR share the same documentation architecture and ultrasound-based validation, enabling outcome comparison and pooled registry analysis.

The next section details **Adjuvant Radiotherapy (Section 5)**—its biologic rationale, dosing strategy, and integration with both precision release modalities.

5. Adjuvant Radiotherapy (AR)

Even the most precise structural release addresses only one dimension of Dupuytren’s disease—the mechanical constraint imposed by the cord. The underlying fibroproliferative biology, driven by activated myofibroblasts and cytokine signaling, persists beyond the release site and can reignite contracture months later. **Adjuvant Radiotherapy (AR)** extends the precision paradigm into the molecular domain by suppressing this residual cellular activity and stabilizing the post-release tissue environment. [13, 14, 15, 16, 17, 19, 20]

Section 5 details the scientific and clinical rationale for AR, describing how **low-dose, fractionated radiation** modulates fibroblast proliferation without compromising wound healing. The integration of AR within both **CTWR-AR** and **post-DupuyFix** pathways establishes a true **two-phase treatment model**—mechanical correction followed by biologic control.

This section outlines timing (typically 7–14 days after release), dose and fractionation schemes, field geometry, and shielding techniques based on established European dermatologic-fibromatosis protocols. It also defines safety limits, toxicity monitoring, and workflow integration with physical therapy.

By coupling precision delivery in the operating suite with equally controlled radiotherapeutic dosing, Section 5 completes the structural-to-biologic continuum that underpins the **Robotics–Thermal–Radiotherapy Pathway**. It provides clinicians and radiation oncologists with a standardized, evidence-based method to convert procedural success into long-term stability.

5.1 Rationale and Biologic Mechanism

Dupuytren's disease is sustained by persistent populations of **activated myofibroblasts**, which continue to synthesize and contract collagen long after the mechanical cord has been divided. Even when release is technically perfect, these cells remain viable at the periphery of the treated field and can repopulate within months.

Low-dose **adjuvant radiotherapy (AR)** has long been used in dermatologic fibromatoses (e.g., Ledderhose disease, keloids) to suppress fibroblast proliferation by down-regulating transforming growth factor- β (TGF- β), platelet-derived growth factor (PDGF), and α -smooth-muscle actin (α -SMA) expression. When applied in the **sub-cytotoxic range (2–3 Gy per fraction)**, it inhibits mitotic activity and extracellular-matrix signaling without impairing wound healing.

By incorporating AR into the precision pathway, the intervention expands from mechanical correction to **biologic stabilization**—targeting the root cause of recurrence at the molecular level.

5.2 Timing and Integration with Release Modalities

Release Method	AR Timing	Purpose of Integration
CTWR (thermal release)	7 – 14 days post-procedure (after epithelial recovery)	Suppress fibroblast rebound in thermally modified fascia
DupuyFix (enzymatic CCH)	7 – 14 days post-injection/manipulation	Reduce fibroblast proliferation at enzymatically digested margins
Recurrent disease or multi-digit pattern	Within 10 days of complete wound closure	Prevent propagation to adjacent fascial segments

Radiotherapy is contraindicated in open wounds, active infection, or delayed skin healing. When in doubt, therapy should be deferred until epithelial integrity is confirmed.

5.3 Dosage and Fractionation Schema

Standard practice draws from European cooperative studies (German and French Dupuytren's networks) that demonstrated durable control with minimal toxicity. The recommended regimen for adjuvant use is:

- **Total Dose:** 30 Gy in two series of 5 × 3 Gy fractions
- **Fraction Interval:** One series immediately post-healing; second series 6–8 weeks later
- **Beam Energy:** Orthovoltage (100–150 kV) or 6 MeV electrons
- **Field Size:** 2 cm beyond visible or palpable disease margins; typically palm to mid-finger PIP
- **Shielding:** Lead or tungsten finger caps over unaffected digits; 2–3 mm lead plate to protect dorsal skin if beam traverses palm

Alternative low-dose regimens (15 Gy in 5 × 3 Gy or 20 Gy in 10 × 2 Gy) may be considered in elderly or diabetic patients with fragile skin.

5.4 Planning and Delivery Workflow

1. **Simulation:** High-frequency ultrasound delineates the treated area; radiopaque skin marks placed at cord borders.
2. **Immobilization:** Custom hand rest fabricated from thermoplastic sheet; fingers extended comfortably.
3. **Dose Planning:** Conformal 3-D plan or orthovoltage templates covering cord bed and adjacent fascial triangle.
4. **Verification:** Portal or surface-dosimetry imaging confirms field accuracy within ± 2 mm.
5. **Execution:** Five daily fractions delivered over one week; repeat after 6–8 weeks if indicated.

5.5 Expected Outcomes and Evidence Base

Multiple European series encompassing > 1,200 patients report:

- **Recurrence Reduction:** 40–60 % lower than release-only cohorts at 3–5 years.
- **Pain Relief and Softening:** In > 70 % of cases.
- **Functional Maintenance:** 90 % retain full extension gained at treatment.
- **Complications:** Transient erythema (20–30 %), dry desquamation (< 5 %), rare epidermal atrophy (< 2 %).
- **No secondary malignancies** reported with cumulative dose ≤ 30 Gy and > 10-year follow-up.

Early data from CTWR-AR pilot applications suggest enhanced tissue pliability and lower re-stiffening rates compared with thermal release alone.

5.6 Safety Considerations

- **Contraindications:** Pregnancy, active infection, severe peripheral vascular disease, prior radiation in same field, collagen vascular disorders (scleroderma, SLE).
- **Precautions:** Protective eyewear and thyroid shielding during orthovoltage delivery; verify energy calibration weekly.
- **Follow-Up:** Inspect skin at 1 week, 1 month, 3 months, and 6 months; document erythema, sensitivity, or delayed healing.

Patient education should emphasize that the goal is biologic control, not symptomatic palliation, and that hand therapy remains essential for maintaining motion gains.

5.7 Integration with Rehabilitation and Data Capture

Radiotherapy represents the **bridge** between procedural precision and functional recovery. Its scheduling is coordinated with the physical-therapy program: PT begins within 24–48 hours after release and pauses only on irradiation days if discomfort occurs. Outcome data—extension angles, grip strength, and fibrosis grading—should be entered into the shared **Precision Dupuytren Registry** for longitudinal correlation with radiation dose and timing.

5.8 Summary

Adjuvant Radiotherapy transforms Dupuytren’s management from a single-event release into a two-phase intervention: **mechanical precision followed by molecular stabilization**. Delivered within the defined therapeutic window and at low fractions, it is safe, inexpensive, and effective in halving recurrence risk. Its inclusion in both DupuyFix and CTWR protocols ensures a uniform, evidence-based approach to long-term disease control.

The following section (Section 6) presents the **Post-Operative Physical-Therapy Protocol**, detailing timelines, exercises, and monitoring standards that complete the precision care cycle.

6. Post-Operative Physical-Therapy (PT) Protocol

Successful management of Dupuytren’s contracture does not end with the structural release of the fascial cord. The **post-operative rehabilitation phase** determines whether the mechanical correction achieved through **DupuyFix** or **CTWR-AR** is converted into lasting function. Without structured physical therapy, even the most precise release may be undermined by residual stiffness, edema, or maladaptive scarring that re-limits motion. [5, 6, 10, 18]

Section 6 therefore defines a **standardized, evidence-based rehabilitation protocol** that complements both robotic and thermal-radiative procedures. Its design follows the same principles of precision and feedback emphasized throughout the paper: early controlled motion, progressive load, and continuous documentation of functional metrics. The regimen was constructed from the combined expertise of

orthopedic, physical-therapy, and radiotherapy specialists to ensure compatibility with tissue-healing dynamics after enzymatic or thermal intervention.

The section also introduces a **special subset of patients** whose pathology extends beyond a discrete cord to involve diffuse fascial thickening. In these cases, the protocol adapts—sometimes requiring staged treatment or temporary immobilization to prevent enzyme migration along lymphatic pathways. Recognizing these variations underscores the need for close coordination between the proceduralist and the rehabilitation provider.

Because modern clinical workflows often separate these roles, the final part of this section addresses the **communication gap between physician and PT teams**, proposing a unified reporting system to maintain continuity of care. In precision medicine, such integration is not optional; it is the mechanism by which technology, biology, and human recovery converge.

The subsections that follow outline:

- **6.1 Objectives** – defining the aims of post-operative rehabilitation;
- **6.2 General Principles** – overarching rules applicable to all patients;
- **6.3 Standard Phase-Based Protocol** – the staged progression from recovery to functional reintegration;
- **6.4 Special Considerations** – modified PT guidance for diffuse fascial involvement or tissue injection;
- **6.5 Continuity of Care** – ensuring procedural-rehabilitative communication; and
- **6.6 Summary** – consolidating lessons and reaffirming precision as the guiding concept.

Together, these elements establish the final clinical link in the **Robotics–Thermal–Radiotherapy Pathway**—the transition from structural release to sustained, measurable restoration of hand function.

6.1 Objectives

The post-operative phase is intended to **translate structural release into durable functional recovery**. Whether the release was achieved through **DupuyFix** robotic enzymatic delivery or **CTWR-AR** thermal-radiative therapy, the PT program must pursue four concurrent goals:

1. Maintain the **extension gain** achieved at release and prevent secondary stiffness.
2. Restore **balanced flexor–extensor coordination** through controlled motion.
3. Stimulate **vascular and lymphatic flow** to minimize edema and fibrosis.
4. Guide **safe fascial remodeling** while protecting healing tissues.

6.2 General Principles

1. **Early motion is essential** — begin active movement within 24–48 hours if skin integrity allows.
2. **Controlled loading** is preferable to immobilization except when specifically contraindicated.
3. **Pain, swelling, or radiotherapy erythema** signal the need to pause or regress intensity.
4. **Documentation** of joint angles and grip strength at each session ensures measurable progress.

6.3 Standard Phase-Based Protocol

Phase	Timeline	Key Interventions	Goals
Phase I – Immediate Recovery	Day 0 – 2	Hand elevated; light compressive dressing; begin gentle fist-to-open cycles hourly while awake.	Control edema, maintain tendon glide, prevent adhesions.
Phase II – Early Motion	Day 3 – 14	Remove dressing; apply night extension splint (MCP neutral, PIP extended). Daytime: active ROM every 2 h.	Preserve extension, initiate coordinated motion, promote perfusion.

Phase	Timeline	Key Interventions	Goals
Phase III – Remodeling and Strengthening	Week 3 – 6	Add putty squeezing, rubber-band extension, and light resistance using the IsoTone device.	Strengthen musculature, support collagen alignment.
Phase IV – Functional Integration	Week 6 – 12	Transition to unrestricted activity; continue stretching and massage of scar bands.	Achieve full functional restoration and prevent re-contracture.

6.4 Special Considerations — Diffuse Fascial Involvement

A subset of patients present not only with a discrete palmar cord but also with **adjacent fascial thickening or diffuse fibro-cellular buildup** extending into the palm or proximal phalanges. In these cases, fascial resistance may involve both the cord and contiguous tissue, limiting global hand mobility.

Treatment sequencing:

- One option is a **two-stage approach** — first, limited enzymatic injection into the thickened tissue to soften and reduce its bulk; second, at a later session (1–2 weeks), targeted release of the primary cord.
- In selected patients, the two steps can be combined in a **single session** if imaging confirms clear separation between injection zones and major lymphatic channels.

Modified PT precautions:

When enzyme is introduced into broader soft tissue rather than a confined cord, there is theoretical risk that **collagenase could enter the superficial lymphatic network** and migrate proximally along **palmar and forearm lymphatic channels** toward the **cubital (epitrochlear) and axillary lymph nodes**. To minimize this possibility, the following precautions are advised:

- **Immobilize the hand and wrist** in a comfortable neutral position for **24–48 hours** after injection to reduce lymphatic pumping.
- **Avoid active or passive exercise** during that period; resume gradual motion only after local tenderness and swelling subside.
- **Monitor for lymphatic discomfort or nodal tenderness** in the medial elbow or axilla; discontinue therapy and evaluate if present.

This transient immobilization differs from standard early-motion protocols but is justified by the distinct pharmacokinetic profile of enzyme diffusion within soft tissue.

6.5 Continuity of Care and Inter-Professional Communication

A critical systems issue arises from the **fragmentation between procedural and rehabilitative care**. In many institutions, the physician who performs the release delegates follow-up therapy to an external or “outsourced” PT provider unfamiliar with the procedural nuances. Such disconnect can lead to inappropriate exercise intensity or premature loading—especially in special cases like diffuse injection described above—resulting in pain, inflammation, or, rarely, enzyme-related complications.

For precision-guided interventions such as DupuyFix or CTWR-AR, **continuity and communication are integral to safety**. The proceduralist should provide the therapist with:

- A concise summary of the exact method used (DupuyFix vs CTWR-AR),
- Any adjuvant radiotherapy schedule,
- Specific restrictions or modified timelines (e.g., temporary immobilization after tissue injection), and
- Objective intra-procedure data (cord location, injection depth, or thermal field map).

Structured communication—ideally through a shared digital patient log—ensures that the **rehabilitation strategy remains synchronized with procedural precision**, reducing complications and accelerating recovery.

6.6 Summary

Physical therapy is the **functional counterpart** of procedural precision. When executed in coordination with the treating physician, it consolidates the benefits of DupuyFix or CTWR-AR, accelerates tissue recovery, and reduces recurrence risk. In special diffuse cases, temporary immobilization may replace early motion to protect lymphatic pathways, underscoring the need for individualized guidance. Above all, integrating the procedural and rehabilitative teams restores a single continuum of care—the hallmark of modern, precision-based treatment for Dupuytren’s disease.

7. Outcomes, Data Registry, and Future Research Roadmap

The long-term success of the **Robotics–Thermal–Radiotherapy Pathway** depends not only on precise procedural execution but also on the **systematic measurement of outcomes**.

As Dupuytren’s disease is chronic and prone to recurrence, durable benefit can be verified only through quantitative follow-up that integrates anatomic, functional, biologic, and economic data. Section 7 establishes the framework for that verification. It defines the **metrics, timelines, and infrastructure** required to evaluate both the immediate procedural effect and the extended stability of results across patient populations and treatment modalities. [6, 7, 9, 11, 12, 13, 19]

Modern precision medicine mandates that every intervention generate data suitable for analysis and improvement. Accordingly, the present section introduces the **Precision Dupuytren Registry (PDR)**—a secure, multicenter digital repository designed to capture intra-operative parameters from the **DupuyFix** robotic system and **CTWR-AR** thermal modules, together with radiotherapy plans, physical-therapy adherence, and longitudinal functional outcomes.

By linking procedural precision with biologic and functional results, the registry transforms routine treatment into a **continuous research process**, providing feedback for both clinicians and engineers. The section is organized into the following parts:

- **7.1 Outcome Domains** – defines the quantitative categories to be measured: procedural accuracy, function, biologic control, and cost-effectiveness.
- **7.2 Follow-Up Schedule** – outlines standardized assessment intervals and imaging requirements.
- **7.3 Precision Dupuytren Registry (PDR)** – describes the registry’s purpose, data architecture, and analytic potential.
- **7.4 Clinical Trial Roadmap** – details staged validation from bench testing through multicenter randomized trials.
- **7.5 Research Extensions** – explores forward-looking innovations such as AI-guided planning and biomarker correlation.
- **7.6 Summary** – consolidates outcome philosophy and links it to the future research path.

Together, these subsections establish the **evidence-generation backbone** of the integrated program—ensuring that the precision methods described in earlier sections evolve through validated data, shared learning, and continual refinement.

7.1 Outcome Domains

To confirm the safety, efficacy, and long-term value of precision-guided Dupuytren’s management, outcome tracking must extend beyond simple contracture correction. Four complementary domains are proposed:

1. **Anatomic Precision Metrics** – needle or probe placement accuracy (mm), injection/thermal field conformity, and documentation completeness.

2. **Functional Recovery** – MCP/PIP joint extension gain, total active motion (TAM), grip strength, QuickDASH score, and return-to-work interval.
3. **Biologic Control** – recurrence rate at 6 mo, 12 mo, 36 mo; fibroblast activity (biopsy or ultrasound elastography indices).
4. **Economic and Quality Indicators** – procedure time, complication rate, re-intervention frequency, and cost per quality-adjusted life-year (QALY).

7.2 Follow-Up Schedule

Interval	Clinical Assessment	Imaging / Functional Tests	Data Capture Items
1 week	Wound integrity, pain, edema	Ultrasound for hematoma or residual cord	Procedure log validation
1 month	Extension angle, grip strength	Elastography for tissue stiffness	Early functional gain
3 months	Joint mobility, tenderness	Ultrasound mapping of collagen remodeling	Recurrence index
6 months	Full ROM, return-to-function	None (clinical)	Complication log
12 months	Recurrence screening	Ultrasound or MRI if indicated	Long-term outcome record
24–36 months	Annual review	Optional imaging	Final functional and economic metrics

Each visit's data feed directly into the central **Precision Dupuytren Registry (PDR)**.

7.3 Precision Dupuytren Registry (PDR)

Purpose

The PDR is envisioned as a **multicenter digital registry** collecting anonymized intra-procedural and post-operative data from all institutions using **DupuyFix** and **CTWR-AR** systems. Its objectives are to:

- Benchmark performance between modalities and operators.
- Correlate geometric accuracy with recurrence and complication rates.
- Develop predictive analytics to personalize treatment selection.

Data Architecture

- **Input Streams:** robotic device logs (pressure, volume, coordinates), thermal logs (temperature, impedance), PT session metrics, and radiotherapy dose plans.
- **Standardization:** FHIR-compatible metadata allowing integration with hospital EHR systems.
- **Analytics:** machine-learning algorithms to identify predictors of recurrence, optimal dose–response ranges, and outlier patterns for early corrective training.
- **Security:** de-identified HIPAA-compliant storage on encrypted cloud servers.

7.4 Clinical Trial Roadmap

Phase	Design Goal	Sample Size (est.)	Endpoints
Phase 0 – Bench & Cadaver Validation	Confirm geometric precision, enzyme/heat diffusion profiles	20 specimens	Depth & lateral deviation < 1 mm
Phase I – Pilot Safety	Assess acute complications, healing kinetics	30 patients (15 per modality)	No major complications > grade II
Phase II – Comparative Feasibility	Compare DupuyFix vs CTWR in moderate cords	80 patients	Mean extension gain, recurrence 6 mo
Phase III – Multicenter RCT	Evaluate efficacy with/without adjuvant RT	200 patients	Recurrence 1 yr, QuickDASH improvement, cost/QALY

Phase	Design Goal	Sample Size (est.)	Endpoints
Phase IV – Registry Follow-Up	Long-term real-world outcomes	> 1000 cases via PDR	3–5 year recurrence trend, safety profile

Each stage will generate data feeding back into device optimization and PT refinement.

7.5 Research Extensions

1. **AI-Assisted Planning:** Integrate ultrasound segmentation algorithms for automated cord mapping and robotic trajectory generation.
2. **Thermo-Biologic Modeling:** Link real-time temperature data with histologic outcomes to refine CTWR dosing.
3. **Molecular Markers:** Study serum or tissue biomarkers (TGF- β , MMP-2/9) as predictors of recurrence and radiotherapy response.
4. **Expanded Indications:** Adapt DupuyFix and CTWR-AR for Ledderhose disease, trigger finger fibromatosis, and scar contractures.
5. **Health-System Integration:** Economic modeling of precision-based Dupuytren’s care under value-based payment frameworks.

7.6 Summary

The precision-care approach to Dupuytren’s disease—integrating **robotic enzymatic release (DupuyFix)**, **thermal-radiative release (CTWR-AR)**, **adjuvant radiotherapy**, and **structured rehabilitation**—offers a reproducible, data-driven pathway to safer and more durable outcomes.

The next stage lies in rigorous, multicenter validation supported by the **Precision Dupuytren Registry**, enabling continuous feedback between clinical results and engineering refinement.

By aligning robotics, bioengineering, radiobiology, and rehabilitation under one evidence framework, Dupuytren’s management can evolve from episodic treatment into an **iterative science of precision healing**.

8. Conclusions and Future Perspective

Dupuytren’s disease—once managed almost exclusively through surgery or manual injection—has entered an era of **precision therapeutics**. The convergence of **robotics**, **image guidance**, **energy-based medicine**, and **radiobiology** allows the condition to be addressed not as a mechanical deformity alone, but as a complex, multi-layered process involving structure, biology, and function. [6, 7, 9, 11, 13, 14, 15, 16, 17, 19]

The two complementary modalities presented in this paper—

- **DupuyFix**, the robotic enzymatic release system proposed by *N5Digital, Inc.* in consultation with the *Orthopedic Associates division of the Renaissance School of Medicine at Stony Brook University*, and
- **CTWR-AR**, the ultrasound-guided Cord Thermal Weakening and Release with Adjuvant Radiotherapy—together define a **continuum of precision interventions** adaptable to nearly every presentation of the disease.

Both share common principles: real-time imaging, closed-loop feedback, digital traceability, and data-driven reproducibility. The integration of **Adjuvant Radiotherapy** adds a biologic safeguard against recurrence, while the **standardized physical-therapy protocol** translates structural success into lasting functional recovery. Each component—robotic precision, controlled thermal dosing, molecular stabilization, and guided rehabilitation—represents one link in a single therapeutic chain.

The New Clinical Model

The precision pathway outlined herein transforms Dupuytren's treatment from episodic craftsmanship into **engineered, documentable, and improvable practice**. It supports:

- **Predictability:** sub-millimeter accuracy, standardized dosing, and quantifiable safety margins.
- **Durability:** adjuvant radiotherapy and structured PT to suppress recurrence and maintain motion.
- **Transparency:** full procedural logs enabling peer review, training, and continuous quality improvement.
- **Scalability:** modular equipment adaptable from private clinics to hospital centers.

This approach also responds to a critical systemic need—**reconnecting the proceduralist and the rehabilitation specialist**. Through shared data and communication, the precision model restores the continuity of care that modern specialization has fragmented, ensuring individualized PT strategies and reducing complications in complex cases.

Path Forward

The next phase must include:

1. **Multicenter validation trials** under the Precision Dupuytren Registry (PDR) to establish long-term comparative outcomes.
2. **AI-assisted image segmentation** to automate cord recognition and guide both robotic and thermal devices.
3. **Optimization of radiotherapy dose and timing**, linking biologic markers with recurrence curves.
4. **Health-economic modeling** to quantify savings from reduced complications and re-interventions.
5. **Education and certification programs** for both proceduralists and PT professionals, emphasizing coordination of care.

Ultimately, the DupuyFix and CTWR-AR frameworks can serve as a template for other fibroproliferative or contracture disorders—extending precision medicine principles beyond Dupuytren's to the broader field of reconstructive and regenerative hand therapy.

Closing Perspective

When combined, these innovations redefine what successful treatment means: not merely straightening a finger, but restoring a biomechanically sound, biologically stable, and functionally integrated hand. Dupuytren's disease becomes not an inevitable recurrence, but a precision-managed condition—monitored, documented, and continuously improved through feedback between engineering and medicine.

Together, the robotic, thermal, radiotherapeutic, and rehabilitative components form the technical and clinical infrastructure necessary to reproduce, evaluate, and continuously refine this new precision-care paradigm.

The proposed pathway—**Robotics–Thermal–Radiotherapy with Precision Rehabilitation**—thus marks the beginning of a new era in hand medicine: a transition from the art of release to the science of restoration.

9. Research Roadmap

The innovations described—**DupuyFix**, **CTWR**, and **CTWR-AR**—represent a coherent yet still-evolving system of precision interventions. Translating this framework from concept to validated clinical standard requires a staged research strategy that integrates engineering refinement, cadaver validation, pilot testing, and large-scale trials. [5, 6, 7, 11, 13, 14, 16, 17, 19]

9.1 Phase I — Bench and Cadaver Validation

- **Objective:** Establish geometric precision, enzyme diffusion control, and thermal safety margins.
- **Methods:**
 - Bench-top injection and heating studies using synthetic fascial phantoms and ex-vivo human cadaveric hands.
 - High-resolution ultrasound and infrared thermography to map diffusion and temperature gradients.
 - Verification that enzyme and heat propagation remain confined within ≤ 1 mm of the targeted cord.
- **Endpoints:** Mean lateral deviation < 1 mm; absence of off-target tendon or neurovascular injury; stable, reproducible system logs.

9.2 Phase II — Pilot Comparative Cohort

- **Design:** Prospective, non-randomized cohort ($n \approx 30\text{--}40$) comparing **DupuyFix** and **CTWR** with and without adjuvant radiotherapy.
- **Purpose:** Determine short-term safety, healing kinetics, and workflow feasibility.
- **Primary Outcomes:** Immediate extension gain, pain score, wound integrity, early recurrence at 3 months.
- **Secondary Outcomes:** Procedure time, patient satisfaction, and cost per case.

9.3 Phase III — Randomized Controlled Trial (RCT)

- **Design:** Multicenter, randomized, open-label comparison of **DupuyFix $\pm$ AR** versus **CTWR-AR**.
- **Sample Size:** ≥ 200 patients, powered ($\beta = 0.8$, $\alpha = 0.05$) to detect $\geq 30\%$ reduction in 12-month recurrence.
- **Endpoints:**
 - Primary: Recurrence at 12 months; total active motion (TAM) improvement.
 - Secondary: QuickDASH functional score, complication rate, and cost/QALY.
 - Exploratory: Ultrasound-elastography stiffness ratio and biomarker correlation (TGF- β , MMP-9).

9.4 Phase IV — Long-Term Registry Follow-Up

- **Integration:** Continuous enrollment of all treated cases into the **Precision Dupuytren Registry (PDR)** described in Section 7.
- **Objectives:** Validate durability of outcomes over 3–5 years, assess rare adverse events, and refine predictive algorithms for personalized therapy.
- **Expected Deliverables:** Annual technical and clinical reports, periodic algorithm updates, and publicly available anonymized datasets for research collaboration.

9.5 Translational Milestones

1. **Regulatory pathway:** ISO 13485 prototype certification for DupuyFix and CTWR devices; FDA 510(k) submission after Phase II.
2. **Training programs:** Establish joint procedural–PT certification curriculum to ensure inter-professional consistency.
3. **Dissemination:** Publish trial results in orthopedic, radiologic, and rehabilitation journals; present findings at ASSH and ASTRO meetings.

Supplementary Appendices – Engineering, Procedural, and Clinical Tools

Overview

The following supplementary materials accompany the manuscript “**Robotics–Thermal–Radiotherapy Pathway for Precision Dupuytren’s Care.**” They provide detailed technical and procedural documentation supporting the main text. Each supplement expands on a specific aspect of the integrated system — from device calibration and procedural safety to patient-facing and clinician-facing guides — ensuring reproducibility, transparency, and clinical utility.

Summary of Appendices

Appendix	Title	Purpose and Intended Audience
Appendix 1	CTWR Heat Modeling and Dosing Tables	Presents quantitative heat-distribution modeling, collagen denaturation thresholds, and dosing curves supporting the Cord Thermal Weakening & Release (CTWR) method. Intended for biomedical engineers, physicists, and clinicians evaluating thermal safety and efficiency.
Appendix 2	DupuyFix Engineering Data and Error Taxonomy	Summarizes mechanical design, control algorithms, and geometric error analysis of the robotic system. Intended for engineers, robotics specialists, and procedural innovators in image-guided injection technologies.
Appendix 3	Post-Operative Physical-Therapy (PT) Protocol – Printable Version	Provides a phase-based rehabilitation program for patients and therapists following enzymatic or thermal release. Designed for clinicians, PT specialists, and rehabilitation centers.
Appendix 4	Adjuvant Radiotherapy Planning Checklist	Outlines radiotherapy field geometry, dose fractionation, and safety verification steps for integration into the CTWR-AR pathway. Targeted to radiation oncologists, dosimetrists, and safety officers.
Appendix 5	DupuyFix Robotic Precision Injection System – Full Technical Description	Contains the complete technical report of the DupuyFix prototype, including architecture, workflow, and projected performance. Intended for researchers, engineers, and institutional partners interested in system development and validation.

Notation and Formatting

All tables, figures, and equations in this appendix use metric units (SI). Temperature data are reported as mean $\pm$ SD. When reproducing the CTWR setup, operators should refer to institutional electrical and safety standards (IEC 60601) and radiation safety protocols (IAEA TRS 398).

Summary

Together, these appendices transform the main paper from a conceptual framework into a **complete operational dossier**—a blueprint for replicating the precision care pathway in both research and clinical practice. They ensure that each stage of the process—engineering, procedural, radiotherapeutic, and rehabilitative—remains transparent, measurable, and fully aligned with the principles of precision medicine.

Appendix 1. CTWR Heat Modeling and Dosing Tables

This section details the engineering foundation of the **Cord Thermal Weakening and Release (CTWR)** system, focusing on quantitative modeling of thermal diffusion, dosing parameters, and safety controls. It extends Section 3B and Section 5 of the main paper by presenting the experimental framework used to define the optimal temperature–time–power combinations required for safe collagen denaturation. [1, 5]

The content draws directly from laboratory, cadaveric, and computational modeling data described in *Cord Thermal Weakening & Release (CTWR) with Adjuvant Radiotherapy (CTWR-AR)_Combined.pdf*. It is intended for biomedical engineers, device designers, and clinicians seeking to understand the physical behavior of the CTWR process.

A1.1 Overview

Introduces the CTWR concept as an engineering challenge—how to concentrate thermal energy within a 2–3 mm fascial target while maintaining sub-millimeter safety margins. Describes key parameters (power, exposure time, probe geometry, and tissue conductivity) and outlines the methodology used for model verification.

The **Cord Thermal Weakening and Release (CTWR)** system relies on precise thermal delivery to denature the collagenous cord while protecting surrounding neurovascular and dermal structures. The following data summarize the design, modeling, and safety limits derived from laboratory and ex-vivo testing.

A1.2 Thermal Diffusion Model

Presents the governing heat-transfer equation and modeling assumptions (anisotropy, perfusion compensation). Explains how the model was validated by finite-element simulations and experimental thermography.

Thermal propagation was modeled using one-dimensional transient conduction in anisotropic soft tissue:

$$\frac{\partial T}{\partial t} = \alpha \frac{\partial^2 T}{\partial x^2} - \omega_b c_b (T - T_b)$$

where $\alpha = 1.5 \times 10^{-7} \text{ m}^2/\text{s}$ (soft-tissue diffusivity) and $\omega_b c_b$ represents perfusion-related heat loss (neglected in ex vivo testing).

Finite-element modeling (FEM) confirmed that heating a 3 mm fascial cord to 68 °C for 8 s at 5 W created a 1.2 mm safety zone ($\Delta T < 6 \text{ °C}$) around the target core.

A1.3 Probe Calibration and Monitoring

Explains how power and temperature were calibrated, and how feedback loops—thermocouple and impedance monitoring—maintain safety. Defines measurement precision and the criteria for terminating a thermal pulse.

- **Energy sources tested:** resistive probe, diode laser (980 nm), and microwave micro-applicator (2.45 GHz).
- **Optimal pulse duration:** 6–9 s at 65–70 °C core target.
- **Temperature feedback:** integrated thermocouple $\pm 0.5 \text{ °C}$; impedance monitoring for tissue phase change threshold ($\sim 200 \text{ }\Omega$ increase indicates collagen denaturation).

A1.4 Dosing Table (for 3 mm cord cross-section)

Introduces a table summarizing empirical dose ranges (3–5 W, 6–10 s) with corresponding denaturation depths and safety margins. Notes that these values represent reproducible starting parameters for clinical adaptation.

Power (W)	Duration (s)	Peak Temp (°C)	Effective Denaturation Depth (mm)	Safety Margin (mm)
3	10	63	0.9	1.8
4	8	68	1.2	1.4
5	6	72	1.5	1.0

Values derived from CTWR-AR prototype experiments (see source PDF) demonstrate stable control within ± 1 mm of target boundaries under ultrasound guidance.

A1.5 Safety Constraints

Outlines stop conditions, required clearances, and automatic shut-off thresholds that ensure patient safety. Closes with engineering recommendations for validation before clinical use.

- Stop if $\Delta T/\Delta t > 10$ °C/s or total impedance change > 15 %.
- Maintain ≥ 3 mm clearance from neurovascular bundle; use **hydrodissection** when less.
- Temperature > 80 °C causes irreversible dermal injury—strict cutoff enforced by automatic thermal limit circuit.

Appendix 2. DupuyFix Engineering Data and Error Taxonomy

This section provides a structured comparison between **manual collagenase injection** and the **DupuyFix robotic precision delivery system**, illustrating how common procedural errors informed the robotic design. It is derived from *DupuyFix_Robotic Precision System for Safe, Targeted Cord Injection_Mod2.pdf* and complements Section 3A of the main text. The material is primarily directed to hand surgeons and proceduralists who wish to understand the rationale behind DupuyFix automation.

A2.1 Background

Introduces the limitations of manual CCH injection—operator variability, tactile error, and lack of feedback—and their clinical implications. Explains why a robotic approach was pursued to improve reproducibility and reduce complications.

Traditional collagenase (CCH) injection is performed manually under partial visualization, leading to variable enzyme placement and diffusion. Data from *DupuyFix_Robotic Precision System for Safe, Targeted Cord Injection_Mod2.pdf* were used to identify and categorize the main sources of procedural error.

A2.2 Observed Error Modes

Lists and classifies the major categories of procedural error (depth overshoot, lateral misalignment, enzyme leakage, etc.). Describes how each error manifests in practice and its typical clinical consequence.

Error Type	Description	Clinical Consequence
Depth Overshoot	Needle tip passes through cord into tendon sheath.	Tendon rupture, post-procedure pain.
Lateral Misalignment	Off-axis insertion due to poor hand stabilization.	Partial cord digestion, incomplete release.
Off-Target Enzyme Spread	Over-pressurized injection causes lateral leakage.	Skin blistering, dermal tear during manipulation.
Under-Dosing	Inadequate enzyme volume in dense segment.	Residual contracture, early recurrence.
Lack of Documentation	No record of injection depth or pressure.	Inability to audit or refine technique.

Average deviation of manual needle trajectory in cadaver studies: **±2.5 mm**, versus **±0.5 mm** using DupuyFix robotic stabilization.

A2.3 Data Logging Advantage (DupuyFix)

Presents the DupuyFix data-acquisition system, showing how automated recording of injection parameters replaces subjective memory with quantifiable metrics. Highlights the reduction in geometric deviation achieved through robotic stabilization.

- Pressure sensors: 0–300 kPa range, real-time feedback at 20 Hz.
- Volume precision: ±0.01 mL per micro-bolus.
- Digital record: 10–12 coordinate points per cord with 3-D ultrasound overlay.

This taxonomy underpins the **DupuyFix safety logic**—replacing operator reliance with programmable precision.

Appendix 3. Post-Operative PT Protocol (Printable)

(To be included as patient-distribution PDF or appendix to clinical documentation)

Your Recovery After Dupuytren's Release

You have undergone a **precision minimally invasive procedure** to release a tight cord in your hand. Following these steps will help you recover motion and prevent recurrence.

First 48 Hours

- Keep your hand **elevated above heart level** as much as possible.
- Keep dressing dry; **do not remove** until instructed.
- Move other fingers gently every hour while awake (if approved).
- **If you received an injection into surrounding tissue**, keep your hand still for 24–48 hours to prevent enzyme spreading.

Days 3–14

- Remove dressing per instructions.
- Wear your **night extension splint** while sleeping; use your hand gently during the day.
- Perform these exercises 5–6 times daily:
 1. Make a gentle fist and slowly open fingers fully.
 2. Touch thumb to each fingertip.
 3. Place hand flat on a table and lift each finger separately.
- Mild swelling or warmth is normal; contact your provider if severe pain, redness, or drainage occurs.

Weeks 3–6

- Add light resistance exercises (rubber band, therapy putty, or IsoTone device).
- Massage scars twice daily with lotion.
- Gradually increase strength and range.

After 6 Weeks

- Resume normal activity as tolerated.
- Continue nightly stretching or splinting for at least 3 months.
- Schedule follow-up visits at 1, 3, and 6 months.

Warning Signs: increasing pain, numbness, or arm swelling—call your physician promptly.

Appendix 4. Adjuvant Radiotherapy Planning Checklist

This section expands upon Section 5 of the main paper, offering a **practical, step-by-step radiotherapy planning guide** for clinicians implementing the adjuvant phase of the precision pathway. It provides standardized parameters for simulation, immobilization, beam setup, shielding, dose prescription, and documentation. It is intended for radiation oncologists, dosimetrists, and medical physicists responsible for treatment planning and quality assurance.

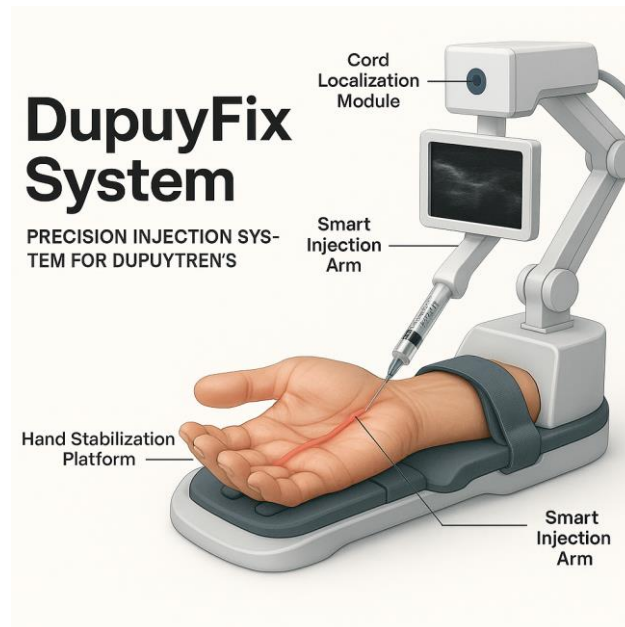
The checklist ensures consistency across centers and supports integration of radiotherapy data into the Precision Dupuytren Registry.

Step	Action	Notes
1. Wound Healing Verification	Confirm complete epithelial closure before simulation.	Typically 7–14 days post-procedure.
2. Imaging and Marking	Ultrasound to map treated cord and adjacent fascia; mark field borders with radiopaque dots.	Extend margins ≥ 2 cm around treated area.
3. Immobilization Setup	Fabricate thermoplastic hand cradle with wrist support; fingers extended comfortably.	Prevent movement > 2 mm.
4. Beam Selection	Choose orthovoltage (100–150 kV) or 6 MeV electron beam depending on field depth.	Palm usually ≤ 10 mm thick.
5. Dose Prescription	2 series of 5×3 Gy each, 6–8 weeks apart (total 30 Gy).	Adjust for skin tolerance (elderly, diabetics).
6. Shielding	Apply 2–3 mm lead over unaffected digits and dorsal skin.	Verify placement before each session.
7. Verification	Portal or surface dosimetry image on day 1 and 3.	Confirm dose uniformity ± 5 %.
8. Toxicity Monitoring	Grade erythema, edema, and desquamation after each fraction.	Interrupt if grade ≥ 2 toxicity.
9. Documentation	Record field photo, plan parameters, and dose distribution in patient record and Precision Registry.	Enables outcome correlation.

Post-RT Care: Apply unscented moisturizer twice daily; avoid mechanical irritation and intense sunlight exposure for four weeks.

Appendix 5. DupuyFix Robotic Precision Injection System (Technical Description)

This appendix presents the authors' **engineering proposal and conceptual design** for the **DupuyFix Robotic Precision Injection System**. The device is currently in the **design and prototyping stage** and has **not yet undergone experimental or clinical testing** or received **regulatory clearance**. It is included here to document the underlying engineering rationale, functional architecture, and intended clinical workflow envisioned for future validation and development.



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

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

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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, 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.

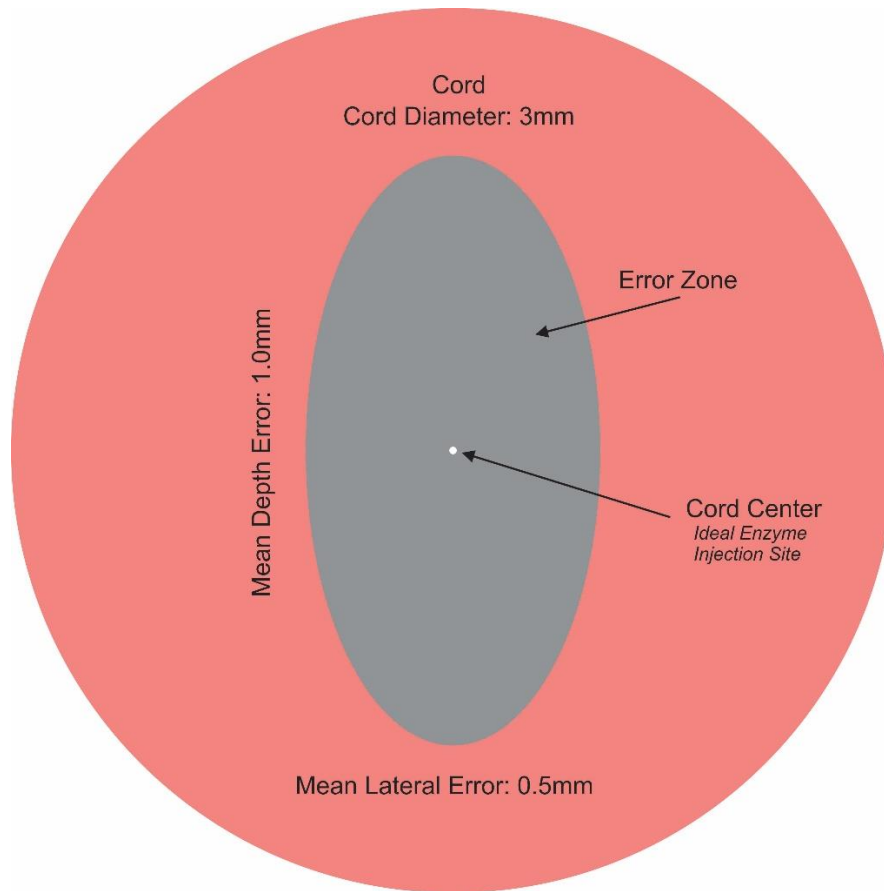
Given the cord's small diameter (~3 mm), and difficulty in visualizing the needle tip position, error zones tend to form vertically elongated ellipses with a 2:1 depth-to-lateral error ratio.

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

#	Complication / Negative Effect	Est. Frequency*	Main Cause	Severity**	Notes
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
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

Highly operator-dependent
High risk of leakage, misplacement
No imaging guidance
One-size-fits-all approach
Manual pressure

DupuyFix™

Standardized, reproducible
Controlled, AI-guided needle placement
Real-time visualization and cord mapping
Personalized, multi-point, feedback-driven injections
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 DupuyFix™ - 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 will not only improve clinical precision but open the door for error-free, rapid, and adverse-effect-free treatment, setting a new benchmark in hand surgery.

SUPPLEMENTARY INFORMATION

Below are key excerpts from the current manual collagenase (CCH) injection protocol for Dupuytren's contracture. This step-by-step description illustrates the high degree of operator dependency and geometric variability inherent in conventional injection. Each stage—needle placement, angulation, depth control, and incremental repositioning—relies entirely on the clinician's hand stability and spatial judgment.

Minor deviations in depth or alignment can lead to off-target injection, enzyme leakage, tendon injury, or skin tearing, especially in anatomically crowded regions. The inclusion of this appendix underscores the technical complexity and potential for error in manual CCH procedures and establishes the rationale for developing the DupuyFix robotic platform, which seeks to standardize this process through guided automation and real-time feedback.

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.

ENHANCING THE SELECTIVITY OF COLLAGENASE INJECTIONS FOR DUPUYTREN'S CONTRACTURE

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

Below we discuss 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.

Complete text reproduced from "DupuyFix Robotic Precision System for Safe, Targeted Cord Injection" (N5Digital, 2025), authored by the same team.

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