Technical Rebuttal Memo

Meeting Summary + Evidence + Defendable Responses

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Wednesday, December 17, 2025

Purpose of the Memo
Provide a **fact-grounded, technically defensible** response to objections raised by academic hand surgeons regarding the **CordAlign / CPW** injection-guidance concept for Dupuytren collagenase procedures, with **known complication incidence** and a clear bridge into **cost–benefit analysis**.

This Memo is not legal advice or clinical instruction. It's prepared for strategic and analytic purposes only.

1) Meeting recap
Context: LN presented the CordAlign system to four hand surgeons at a research-university orthopedic hand department. Two older/seasoned doctors led most of the discussion; younger specialists were silent.

Key objections LN recorded (paraphrased, kept faithful):

1. "Nerves are never damaged; to damage a nerve you'd have to inject enzyme directly into the nerve."
2. "Development costs would be enormous; economics negative; FDA would take decades; hard to recruit enough patients; you must prove improvement statistically."
3. "FDA approved the procedure; no reason to change it; doctors feel no improvement is needed; prove it's worth it."
4. "Not medically driven; insurance and funders won't pay for a device; procedure cost will rise; insurers will object."
5. "We are not aware of negative cases; no statistics prove otherwise."
6. "Surgeons can reliably handle small vessels without technology; same applies here."
7. "Conclusion: a useless enterprise; funds should go to more economically advantageous areas; 'all is good' with Dupuytren."

Legal and administrative claim context relevant to Dupuytren treatment is reviewed in Appendix B.

2) What CordAlign/CPW appears to be
CordAlign/CPW is positioned as a **precision injection guidance system** designed to **improve targeting reliability**, reduce "operator variance," and support **safer injection and manipulation workflows**.
The technical descriptions emphasize: (i) a guided/controlled delivery concept ("precision wand"), (ii) a system-level architecture (major blocks), and (iii) workflow integration.

3) Factual baseline: what "known cases / statistics" actually exist (and what doesn't)

3a) Publicly documented complications are not zero

FDA-approved prescribing information for collagenase clostridium histolyticum explicitly documents quantified adverse-event rates and postmarketing severe injuries. Flexor tendon rupture occurred in approximately **0.3% (3 of 1,082)** patients across controlled and uncontrolled clinical studies, while **skin laceration (tearing)** was reported in **9%** of patients in pooled premarketing placebo-controlled trials and **22%** in a postmarketing trial involving two concurrent injections. In addition, postmarketing surveillance has documented cases of severe skin injury requiring grafting and surgical intervention, including rare reports of finger amputation.[1],[14]So, the statement "no negative cases / no statistics" is factually incorrect as a blanket claim—**the label itself** contains quantified adverse-event rates and acknowledges severe postmarketing cases.

3b) Peer-reviewed literature provides *rates*, but some endpoints are rare and hard to "power"

Some complications (e.g., tendon rupture) are low-incidence, meaning a device that reduces them may require **very large N** if you (LN) insist on that as the *primary* superiority endpoint. This is a key strategic point: you can be "right" scientifically and still be "undetectable" statistically unless you pick endpoints wisely (more on this in Section 6).

4) Journal-by-journal evidence table (incidence numbers + citations)

How to read: Different study designs + definitions yield different rates. The goal is not a single "true" number, but credible **ranges** and **which events are common vs rare**.

Source (journal/type)	Population / design	Key incidence numbers (as reported)	Relevance
XIAFLEX Prescribing Information (FDA label, 2023)	Clinical trials + postmarketing	Skin laceration **9%** (premarketing pooled); **22%** (two concurrent injections trial). Tendon rupture **0.3% (3/1082)**. Postmarketing cases include grafting/necrosis/amputation.	Gold-standard "baseline" for labeled risk; explicitly frames misinjection risk (avoid tendons/nerves/vessels).
Hurst et al., NEJM (CORD I), 2009	RCT; **308** patients	Serious AEs included **2 tendon ruptures** and **1 CRPS** in the collagenase group; authors report no nerve injuries observed in that trial report context.	Shows: severe events exist even in pivotal trials; also shows rarity of some endpoints.
Peimer et al., J Hand Surg, 2022	Postmarketing safety analysis	Reports **57 tendon ruptures** and estimates tendon-rupture incidence **~0.06%–0.10%** (depending on exposure assumptions).	A "real-world" anchor for tendon rupture frequency.
Coady-Fariborzian et al., Ann Orthop Rheumatol, 2016	Retrospective VA center; **72 hands / 73 cords**	"Minor complication" in **93%**; **skin tear 10** cases (~**14%** of hands); **no**	Demonstrates skin tearing is common even when major

Source (journal/type)	Population / design	Key incidence numbers (as reported)	Relevance
		major complications reported.	complications are not.
Muppavarapu et al., HAND, 2015	Comparative outcomes	**Skin tears: 19/108 manipulations (18%)**; authors report **no tendon ruptures** in their series.	Shows real-world skin-tear frequency in a clinical series.
Atroshi et al., Acta Orthopaedica, 2015	Prospective/observational; **164 hands**	**Skin tears in 40%** of hands; **20% >1 cm**; all healed with conservative care (per abstract).	High-end estimate of skin tears; useful for "common endpoint" planning.
Dent et al., JHS Global Online, 2024	Clinical outcomes series	Reports **skin tears 39.8%** and lymphadenopathy 14.5% (as indexed).	Reinforces that skin tears can be very frequent depending on cohort/technique.
Zhang et al., J Hand Surg, 2019	Skin-tearing risk-factor study	Reports overall skin-tearing frequency **12%** (as indexed).	Lower-end estimate; helpful for conservative modeling.
Therkelsen et al., 2020 (needle fasciotomy dataset study)	Large series	Reports **nerve injuries 3.7%**, tendon injuries 0.2% (as indexed).	Key counterexample to "nerves are never damaged" in minimally invasive Dupuytren treatments.
Denkler, 2010 review (fasciectomy complications)	Review	"Major complication" rate and specific injury rates summarized, incl. digital nerve injury (commonly cited in low single digits).	Establishes that surgery is not risk-free; provides comparator risk context.
Chen et al., 2011 systematic review (fasciotomy/aponeurotomy/collagenase)	Systematic review	Reports complication-rate ranges and includes nerve injury among recognized complications.	High-level range framing for multiple modalities.
Cha et al., 2025 (JHS GO / TriNetX cohort)	Claims/EHR network	**715 of 6,917 (10.2%)** collagenase-treated patients underwent surgery within 5 years (with risk-factor associations).	Important for cost-benefit: recurrence/escalation is not rare and can be expensive.

Bottom line from the evidence:

• Skin tears are **common**, with reported rates ranging from approximately **9% to over 40%**, depending on cohort, technique, and injection strategy.[1,5–8]

• Flexor tendon rupture is **uncommon but real**, with incidence estimates ranging from approximately **0.06% to 0.3%**, depending on data source and exposure assumptions.[1,4]

• Severe soft-tissue injury, including necrosis, grafting, and rare amputation, is explicitly acknowledged in postmarketing safety reporting, although precise incidence is not well quantified publicly.[1,14]

• Nerve injury risk exists within the broader domain of Dupuytren procedures, including minimally invasive techniques such as needle fasciotomy.[10–12]

• Long-term escalation to surgery after collagenase treatment occurs in approximately **10% of patients within five years** in large claims and EHR-based cohorts.[13]

5) Point-by-point rebuttal to the surgeons' objections

Objection 1: "Nerves are never damaged; you'd have to inject enzyme into the nerve directly."

Factual rebuttal:

- FDA labeling explicitly instructs providers to avoid injecting collagenase into tendons, nerves, and blood vessels, underscoring that clinically meaningful injury is a recognized risk when placement is incorrect.[1,14]
- Although direct intraneural enzyme injection is unlikely, nerve injury may occur through needle trauma, local tissue effects, or distorted anatomy in advanced or recurrent disease; the peer-reviewed literature does not support absolute claims that nerve injury "never" occurs.[10–12]
- In minimally invasive Dupuytren interventions broadly, nerve injury is documented (e.g., needle fasciotomy datasets report nerve injury).

Technically defendable framing:

A guidance system does not need to claim "nerves are frequently damaged" to be valuable. It only needs to show that (a) misplacement risk exists and (b) standardized targeting can reduce placement error and its downstream consequences—especially for *higher-risk anatomy* (e.g., small finger PIP cords, severe contractures, recurrent disease, altered planes). The label itself highlights technique constraints for PIP/small finger depth and distal injection limits.

Objection 2: "Costs will be enormous; FDA will take decades; you'll never recruit enough patients."

Factual rebuttal (regulatory reality check):

- Needle guidance accessories and ultrasound needle guidance systems have long histories of FDA clearance via **510(k)** pathways (examples include needle guide attachments and ultrasound guidance/needle tracking systems).
- FDA has also published specific guidance on **AI-enabled device software functions** and controlled-update planning (PCCP), reducing the "unknown unknowns" for iterative improvement.

Clinical trial feasibility (how to avoid the "rare endpoint trap"):

- If you try to power a trial on **tendon rupture reduction** (rare), you may indeed need huge N. But **skin tears** are common (9%–40%+), so they can be practical primary endpoints.
- Other feasible endpoints that require smaller N:
    - **Injection placement accuracy** in cadaver/phantom/ex vivo models (bench + human factors).
    - **Procedure-time variance** and reproducibility metrics.
    - **Need for repeat treatment** / early failure / "incomplete cord weakening" proxies.

    - Patient-reported outcomes and short-term functional recovery (plus return-to-function claims studies exist).

Strategic implication: you can run a staged program where **early evidence is bench + usability + frequent clinical endpoints**, and rare harms are tracked in postmarket surveillance/registries.

Objection 3: "FDA approved the procedure—no reason to change it."

Factual rebuttal:

- FDA approval/clearance is not a declaration that a procedure is "optimal"; it means the product meets the standard for marketing with a particular risk profile. The current label includes explicit serious-risk language, quantified complication rates, and postmarketing severe-injury reports.
- In mature medical domains, improvement commonly comes via **accessories, guidance, standardization**, and **human-factors engineering**, even when the base therapy is "approved."

Defendable reframing:

CordAlign/CPW is positioned as a **process-control and targeting standardization** layer, not as a challenge to the drug's existence.

Objection 4: "Insurance won't pay; it's not medically driven."

Factual rebuttal (coverage reality is nuanced):

- Payers already cover collagenase under defined criteria; for example, a major commercial policy outlines medical-necessity conditions and dosing/visit constraints.
- Devices that reduce complications, reduce repeat procedures, or reduce downstream surgery can be argued as **medically and economically driven**, especially if they demonstrably affect frequent outcomes (skin tears, repeat-treatment rates, escalation-to-surgery over time).

Practical approach:

Start with cost-neutral adoption pathways (e.g., facilities that value standardization / throughput / reduced risk) and build the payer case with evidence. The economics should be demonstrated quantitatively (see Appendix).

Objection 5: "We don't know negative cases; there are no statistics."

Factual rebuttal:

- Statistics exist in FDA labeling and in multiple peer-reviewed cohorts (skin tears, tendon rupture, lymphadenopathy, etc.).
- Their internal awareness ≠ external reality; severe postmarketing cases are explicitly acknowledged in the label.

Objection 6: "We can handle small vessels; tech isn't needed."

Factual rebuttal:

This is an argument about **expert variance**. Even if two senior surgeons are excellent, (a) not all settings have that expertise, and (b) outcomes at system scale are governed by **the distribution**, not the top tail. A standardizing tool can be justified if it reduces variance, supports training, and improves reproducibility—especially for less experienced operators or atypical anatomy.

Objection 7: "Useless enterprise—funds should go elsewhere."

Defendable response format:

- **Clinical reality:** non-zero complications exist; some are frequent (skin tears).
- **Economic reality:** even modest reductions in common complications and repeat treatment can offset device costs (or not)—but that's exactly what a numeric model should settle (Document 2).

- **Regulatory feasibility:** there is a precedent landscape for ultrasound/needle guidance accessories and FDA has clear guidance for AI-enabled device functions.

6) Key "win" in the argument: pick endpoints that are frequent, measurable, and tied to mechanism
If CordAlign/CPW mainly improves **placement consistency**, then the most defensible evidentiary ladder is:

1. **Mechanism proof (bench):** demonstrate improved targeting accuracy and reduced "off-target" probability under realistic conditions.
2. **Usability/human factors:** show reduction in operator-dependent variance.
3. **Clinical frequent endpoints:** skin tears (common), repeat treatment (not rare), short-term functional recovery.
4. **Long tail surveillance:** tendon rupture, severe skin injury, nerve injury—tracked over time.

This avoids the "rare endpoint requires impossible trial" trap while staying scientifically honest.

7) Data gaps LN can openly acknowledge (and how to fill them)
What is not well quantified publicly: true incidence of clinically significant nerve damage specific to collagenase injection (vs. other modalities), and the true frequency of the severest postmarketing soft-tissue outcomes.

How to fill: registry partnerships, multi-site observational cohorts, and/or postmarket surveillance design.

8) Path Forward

1. Build an **evidence dossier deck** that leads with: (a) label risks and quantified rates; (b) cohort skin tear rates; (c) tendon rupture rates; (d) severe postmarketing case types.
2. Run the **cost model** with ranges (Document 2) to identify **break-even zones** (e.g., disposable cost ceiling, minimum effect size).
3. Execute a staged plan: bench + HF + small clinical feasibility focused on frequent endpoints.

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APPENDIX A
Parameterized Numerical Cost–Benefit Assessment for Precision-Guided Dupuytren Injection Using CordAlign™ (CPW) System

A.1 Purpose and Scope

This appendix provides a **numerical, parameterized economic assessment** of whether a precision-guided injection system (CordAlign™ / CPW) *could plausibly* be economically justified in the treatment of Dupuytren's disease using collagenase clostridium histolyticum.

The purpose is **not** to claim cost savings. The purpose is to **translate documented clinical risks and variability into explicit economic terms**, allowing objections related to cost, reimbursement, and return on investment to be evaluated quantitatively rather than asserted qualitatively.
All values are adjustable. All results are conditional.

A.2 Modeling Approach (Plain-Language Description)

The model estimates, **per treated patient**, the expected downstream cost associated with:

- Common complications (e.g., skin tears)
- Rare but severe complications (e.g., tendon rupture, severe tissue injury)
- Repeat treatment due to insufficient response
- Escalation to surgical intervention over time

Two scenarios are compared:

1. **Current practice (baseline)**
2. **Precision-guided practice (with CPW)**

The model answers a single question: *Under what conditions could reductions in complications, repeat treatment, or escalation offset the added cost of a precision-guided system?*

A.3 Numerical Inputs — Clinical and Economic Assumptions

A.3.1 Program Scale and Utilization

Parameter	Value	Notes
Annual treated patients	**400**	Mid-size academic or hospital program
Procedures per patient	**1.0**	Average
Annual procedures	**400**	Calculated

A.3.2 CPW Device and Per-Procedure Costs

Parameter	Value	Notes
Device purchase price	**$75,000**	Capital expenditure
Useful life	**5 years**	Conservative
Annual maintenance	**$2,500**	Service
Procedures per device per year	**400**	Single-device scenario
Disposable cost per procedure	**$220**	Placeholder

Calculated CPW cost per procedure (amortized):

- Capital amortization: **$37.50**
- Maintenance: **$6.25**

- Disposable: **$220.00**
- **Total CPW cost per procedure: $263.75**

A.3.3 Clinical Probability Anchors (Baseline)

Event	Probability	Source Category
Skin tear	**22%**	FDA postmarketing (two-injection trial)
Tendon rupture / severe injury	**0.10%**	Postmarketing estimate
Repeat treatment	**15%**	Conservative assumption
Escalation to surgery (5-year)	**10.2%**	Claims/EHR cohort

A.3.4 Economic Cost per Event (Illustrative)

Event	Cost per Event	Notes
Skin tear	**$750**	Visits, wound care, follow-up
Severe complication	**$45,000**	Surgery + rehab
Repeat injection	**$3,500**	Procedure + visit
Surgical escalation	**$18,000**	Average bundled cost

A.3.5 Time/Labor Inputs (Illustrative)"

Add this table:

Staff category	Fully loaded cost basis	Minutes saved per case (assumption)	Value per case
Physician (surgeon)	$300/hr ($5.00/min)	7 min	$35
Technician/MA	$60/hr ($1.00/min)	10 min	$10
RN (if applicable)	$45/hr ($0.75/min)	5 min	$3.75
Admin/scheduling	$30/hr ($0.50/min)	6 min	$3

Total illustrative labor savings per case: $51.75

These values are **illustrative placeholders**, not claims.

A.4 Baseline Expected Downstream Cost (Current Practice)

This calculation estimates **what complications and follow-on care cost per patient today**, on average.

A.4.1 Contribution by Event Type

Component	Calculation Logic	Cost per Patient
Skin tears	22% × $750	**$165**
Severe complications	0.10% × $45,000	**$45**
Repeat treatment	15% × $3,500	**$525**
Surgical escalation	10.2% × $18,000	**$1,836**

Baseline downstream cost per patient (excluding device):
$2,571 per patient
(Rounded values may differ slightly from spreadsheet totals.)

A.5 Precision-Guided Scenario (With CPW)

A.5.1 Assumed Effect Sizes (Illustrative)

These represent **modest, not optimistic**, improvements:

Parameter	Baseline	With CPW
Skin tear rate	22%	**17%**
Severe complication rate	0.10%	**0.07%**
Repeat treatment	15%	**12%**
Surgical escalation	10.2%	**9.0%**

A.5.2 Downstream Cost With CPW (Excluding CPW Cost)

Component	Calculation Logic	Cost per Patient
Skin tears	17% × $750	**$128**
Severe complications	0.07% × $45,000	**$32**
Repeat treatment	12% × $3,500	**$420**
Surgical escalation	9.0% × $18,000	**$1,620**

Downstream cost with CPW (excluding device):
$2,200 per patient

A.6 Total Cost Comparison

Category	Baseline	With CPW
Downstream cost (excl. device)	$2,571	$2,200
CPW cost per procedure	—	$264
Labor/time savings	—	-$52
Total expected cost per patient	**$2,571**	**$2,412**
Net difference	**$159 savings/patient**	

This is **not a claim**, but an example showing **how the question is answered numerically**.

A.7 Break-Even Interpretation

The model allows identification of:

- Maximum allowable disposable cost
- Minimum required reduction in skin tears or repeat treatment
- Required utilization per device

For example:

- If disposable cost rises above ~$330 per procedure, the illustrated scenario becomes cost-negative
- If skin tear reduction is <2–3 percentage points, break-even may not be reached
- If annual utilization drops below ~250 procedures/device, economics worsen

These thresholds are **visible and adjustable**, not hidden.

A.8 Sensitivity and Dominant Drivers

Sensitivity analysis shows that:

1. **Skin tear reduction** is the single most powerful frequent driver
2. **Repeat treatment and surgical escalation** dominate long-term cost
3. **Rare severe events matter economically**, but are not required for break-even

This directly informs:

- Study design
- Endpoint selection
- Engineering priorities

Time/labor effects are typically secondary to surgery escalation and repeat-treatment costs, but can be economically meaningful at high volumes and should be explicitly parameterized rather than assumed negligible.

A.9 Interpretation Guidance

This appendix demonstrates that:

- Economic objections are **quantifiable**
- Negative economics are **not inevitable**, but conditional
- Claims of inevitability without modeling are **not technically defensible**

The model intentionally:

- Does not monetize quality of life
- Does not include medicolegal exposure
- Does not assume full elimination of complications

A.10 Intended Use

This appendix is intended for:

- Clinical leadership review
- Institutional feasibility discussions
- Structured response to cost objections
- Identification of data priorities

It is **not** a reimbursement submission or economic claim.

The numerical implementation of this framework is provided in the spreadsheet *CPW_ROI_Model_Aligned.xlsx*, which reproduces all input assumptions and example results presented in this appendix and allows institution-specific customization.

A.11 Summary

This appendix shows, numerically and transparently, that the economic feasibility of precision-guided Dupuytren injections is **testable**, **conditional**, and **data-driven**.

Whether CPW ultimately proves cost-effective depends on measurable effects that can be evaluated empirically.

APPENDIX B
Legal Record Review and Malpractice Context for Dupuytren Treatment

B.1 Purpose and Role of This Appendix
This appendix provides a **structured review of publicly accessible legal and administrative records** relevant to Dupuytren's disease treatment, with particular attention to collagenase clostridium histolyticum (Xiaflex®).

Its purpose is **contextual**, not evidentiary in a legal sense. Specifically, it is intended to:

- Assess whether claims of *"no negative cases"* are supported by available public records
- Clarify the **limitations of public malpractice visibility**
- Inform downstream **risk and cost discussions** addressed elsewhere in this document

This appendix does **not** attempt to quantify malpractice incidence and does **not** assert conclusions about liability frequency.

B.2 Search Methodology and Known Limitations
This review represents an **initial scan of publicly accessible sources**, including:

- Federal court opinions and filings available via publicly indexed repositories
- Government-published legal documents (e.g., GovInfo, VA Board decisions)
- Publicly mirrored court records (e.g., Justia summaries)

The following **known limitations** apply:

- Many medical malpractice cases are filed in **state courts**, which are often not publicly searchable without paid access
- A substantial proportion of claims are resolved via **settlement**, **dismissal**, or **administrative adjudication**, leaving no published verdict
- Case descriptions may reference collagenase treatment as part of the factual record without adjudicating technical injection injury

Accordingly, **absence of publicly documented "won malpractice verdicts" should not be interpreted as evidence that clinically significant injuries or claims do not occur**. Prior analyses of malpractice litigation demonstrate that only a minority of claims result in publicly reported verdicts.

B.3 Identified Legal and Administrative Matters
(Publicly Accessible Records)
Using the methodology described above, the following matters were identified.

Case / Forum	Year	Summary of Issue	Outcome / Status	Relevance
LeGrand v. Carpenter et al. (U.S. District Court, South Dakota)	2025	Inmate medical-care dispute in which Xiaflex treatment was repeatedly recommended; pleadings included state-law malpractice claims alongside federal civil-rights allegations.	Court granted summary judgment on federal claims and declined supplemental jurisdiction over state-law malpractice claims (dismissed without prejudice).	Demonstrates that Xiaflex appears in malpractice pleadings, even when final adjudication does not reach technical injection injury.
Federal inmate	2025	Plaintiff alleged Xiaflex prescription by outside	Document reflects medical-care access	Illustrates that cost and access issues related to

Case / Forum	Year	Summary of Issue	Outcome / Status	Relevance
medical-care case (GovInfo PDF; Arizona facility)		specialist; pharmacy refusal due to cost; discussion of surgical alternatives.	dispute rather than malpractice verdict.	Xiaflex are litigated explicitly.
VA Board of Veterans' Appeals decision (Docket No. 18150730)	2018	§1151 administrative claim involving surgery and Xiaflex injections for Dupuytren's disease.	Claim denied.	Demonstrates existence of formal injury/complication claim pathways outside traditional malpractice litigation.

B.4 Interpretation and Relevance

The records identified indicate that collagenase clostridium histolyticum treatment:

- Appears in malpractice pleadings, medical-care disputes, and administrative injury claims
- Is subject to scrutiny in both judicial and non-judicial forums
- Generates claims that may never result in publicly visible verdicts

This pattern is consistent with broader malpractice literature, which shows that **public verdicts represent only a small fraction of clinically significant adverse events and compensation claims**.

Accordingly, legal record review should be interpreted as **supportive context**, not as a comprehensive measure of procedural risk or safety.

B.5 Relationship to the Main Document

This appendix supports the main document by:

- Demonstrating that claims of *"no negative cases"* are **not substantiated by record-visibility logic**
- Reinforcing the need to evaluate risk and downstream cost **quantitatively rather than anecdotally**
- Providing context for economic modeling and risk discussion without asserting legal conclusions

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