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Histological Changes in Dupuytren Contractures Treated with Tamoxifen

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Introduction

Tamoxifen is a synthetic nonsteroidal anti-estrogen drug that may modulate the production of transforming growth factor-β. The beneficial effects of Tamoxifen in Dupuytren disease (DD) have been described both clinically and in vitro.

Objective

To determine if neo-adjuvant Tamoxifen results in measurable histological changes in DD.

Methods

- 14 patients (7 Tamoxifen, 7 Placebo)
    - Inclusion: high-risk DD (diathesis score > 4)
    - Exclusion: revisions, anti-inflammatory use, premenopausal women
- 6 weeks treatment before surgery, continued 12 weeks after surgery
- Tissue analysis (Fig 1):
    - Hematoxylin and Eosin (H&E) staining
    - Masson Trichrome (MT)
    - Immunohistochemistry (IHC) for α-smooth muscle actin (α- SMA) and β-catenin
- Quantification via ImageJ deconvolution (cellularity, collagen, IHC staining) (Fig 2)
- Data analyzed with Student's t-test and Mann-Whitney U test

Results

- No significant difference in cellularity, collagen content, or IHC markers for α-SMA or β-catenin. (Fig 3)
- Slightly higher values in Tamoxifen group, but statistically insignificant
- No difference in number of active zones (Fig 3)
- Findings suggest Tamoxifen does not alter histology after 6 weeks

Conclusion

The clinical benefit of Tamoxifen may be due to post-operative effects. No histological differences were observed after pre-operative administration.

Continuation of Tamoxifen post-surgery might be essential for its therapeutic effect.

Key References

Kuhn et al. J Surg Res. 2002
Kim et al. Nephrol Dial Transplant. 2014
Degreef et al. JBJS. 2014
Schneider et al. Nature Methods. 2012

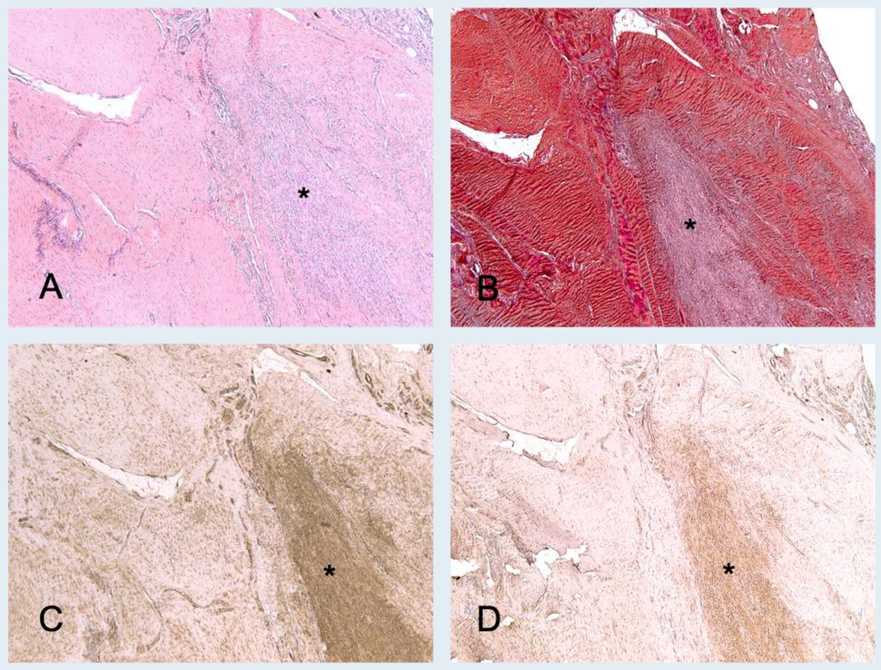

Figure 1: Example demonstrating Comparison of H&E (A) and MT staining (B); and α-SMA (C) and β-catenin (D) IHC staining in samples of the same patient, demonstrating parallel distribution of the different zones, with increased cellularity in linear orientation typical for involutive areas (asterisk).

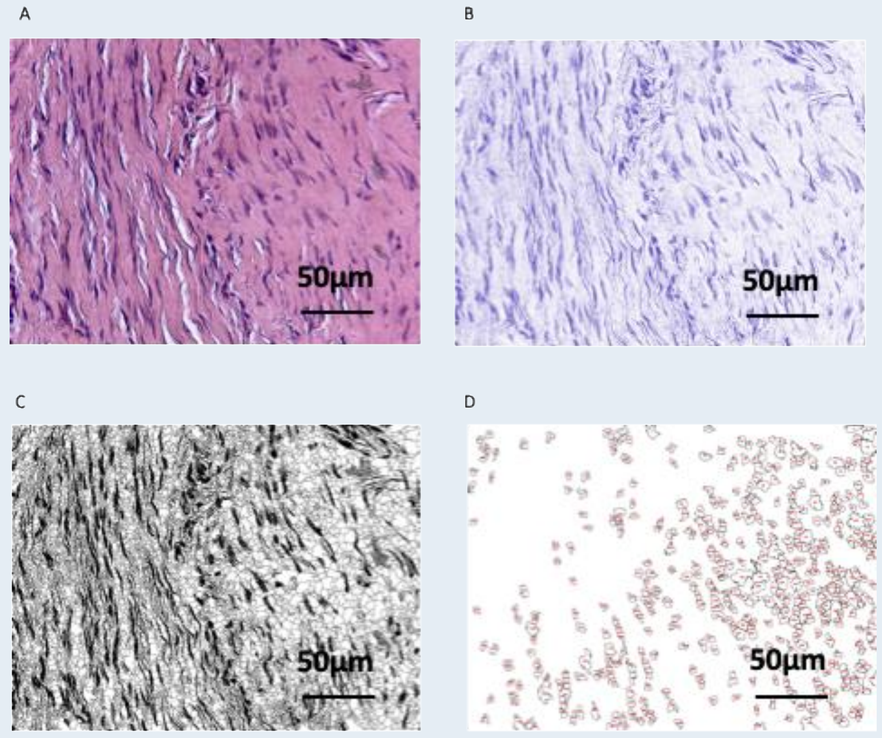

Figure 2: Example demonstrating deconvolution method and technique used to count the cells on the blue staining of an H&E-stained section in ImageJ. On the original image of the H&E staining (A), we extract the blue colour with the deconvolution technique, using a fixed threshold (B). This blue colour represents the cellularity on the H&E staining. The image is converted to a binary image (C). And the cells are counted using the "Analyse Particle plugin" in the ImageJ software (D). Manual count was performed in stains with few cells

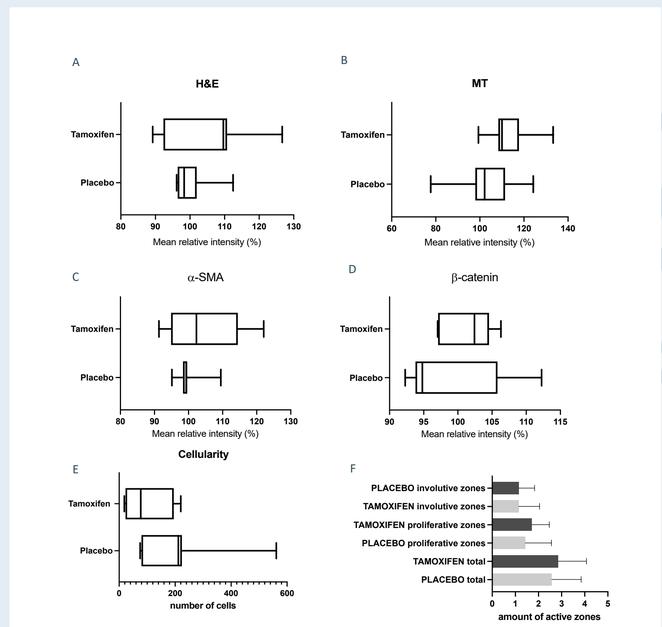

Figure 3: Box plot graphs representing mean and +/- 95% CI of the mean relative % intensity as quantified on H&E (A), MT (B) staining, α-SMA (C) and β-catenin (D) immunohistochemical detection, number of cells estimated on the H&E stainings (E). The bar graphs represent the mean with standard deviation of the number of active zones (proliferative and involutive) in the 2 groups.