

Possible morphological substrates in the pathogenesis of rheumatoid arthritis in human finger joints

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Introduction, Material and Methods

Fibrinogen aggregating to a synovial fold in antigen-induced arthritis (1) drew our attention to normal synovial folds (*plicae synoviales*) in the proximal interphalangeal (PIP) joint of the finger. After surveying the PIP-joint ontogeny (2, 3) we studied HR-MRI of the PIP-joint *in situ*, in an otherwise normal anatomical specimen of the finger. Microscopy of part of the PIP-joint capsule, the Proper Collateral Ligament (PCL), was also performed.

Observational Results

From the seventh week, embryonic hands successively show mesenchymal condensation, joint interzone development, and joint space development. Later, convex-concave incongruences between PIP articular surfaces are compensated by vascularized synovial folds (3). Not only dorsal and palmar, but also ulnar and radial synovial folds do persist in adult PIP-joints, as HR-MRI slices testify.

Sagittal HR-MRI slicing shows the PCL's fiber bundles not running parallel, but crossing each other. Histology (Masson Trichrome & Weigert Orcein) confirms this, displaying minimal elasticity of collagenous fibers. Together with their bony attachments, these crossing fiber-strands constituting PCL's superficial and deeper parts can be modeled biomechanically as a crossed 4-bar linkage system ensuring normal PIP motion (4) (Figure 1).

Neurovascular bundles surrounded by connective tissues, pierce through the collagenous strands. Microvascular structures running perpendicular to each other, suggest that they branch off at right angles to each other. Anti-200 kD Neurofilament Heavy antibody staining revealed details of the neurovascular bundles. Several neural structures were found, possibly indicating sympathetic influences on small blood vessels. Neurons in lamellated corpuscles were also observed between the ligament's collagenous bundles, suggesting some functioning as e.g. shear stress micro-sensors (Figure 2).

Discussion and Conclusion

Neurons in lamellated corpuscles within the Proper Collateral Ligament of the PIP-joint seem interesting, because various authors underline the importance of neuropeptides and cytokines in the pathophysiology of rheumatoid arthritis (e.g., 5).

In conclusion, we state that curiosity-driven research after normal synovial folds within the PIP-joint of the finger confirms their actual location. Neurovascular bundles in the normal PIP-joint's capsule, and neurons in lamellated corpuscles within the Proper Collateral Ligament, may shed new light on the pathogenesis of rheumatoid arthritis in human finger joints.

4-bar linkage system of PIP joint

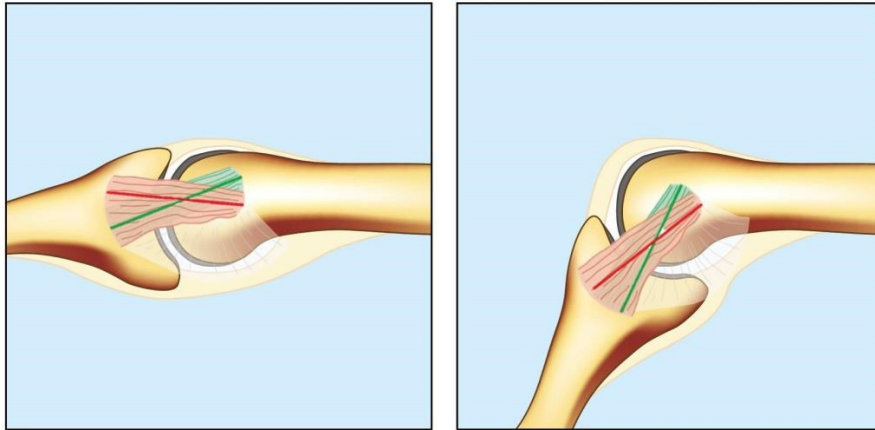


Figure 1.

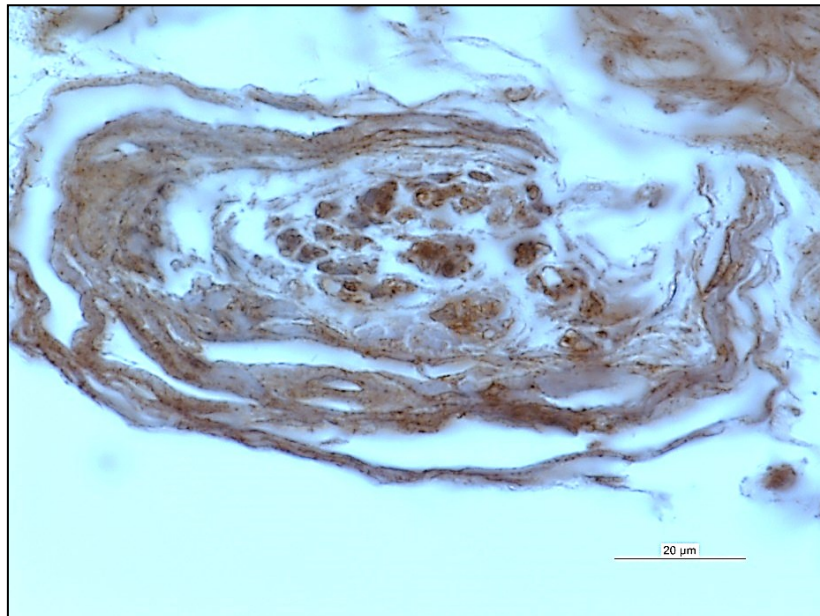


Figure 2.

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References :

1. Sánchez-Pernaute O, López-Armada MJ, Calvo E, Díez-Ortego I, Largo R, Egido J, Herrero-Beaumont G (2003) Fibrin generated in the synovial fluid activates intimal cells from their apical surface: a sequential morphological study in antigen-induced arthritis. *Rheumatology*, 42, 19-25
2. de Bakker BS, de Jong KH, Hagoort J, Oostra R-J, Moorman AFM (2012) Towards a 3-dimensional atlas of the developing human embryo: The Amsterdam experience. *Reproductive Toxicology*, 34, 225-236
3. Landsmeer JMF (1969) Observations on the joints of the human finger. *Annals of the Rheumatic Diseases*, 28, Supplement, 11-14
4. van Zwieten KJ, Lambrichts I, Kosten L, De Munter S, Adriaensens P, Lippens PL (2014) Morphological matching of proximal interphalangeal (PIP) joint arthritis-related entheses. In: *Knowledge for Growth, Flanders Bio Annual Life Sciences Convention, 10th Edition*, Ghent, Belgium, 08/05/2014. *Therapeutics and Diagnostics: Inflammation, Immunology, Infectious and Eye Diseases*, Abstract No. 74, available at: <http://knowledgeforgrowth.be/en/research-detail/morphological-matching-of-proximal-interphalangeal-pip-joint-arthritis-related-entheses> (accessed 15 May 2014)
5. Green PG (2005) Gastrin-releasing peptide, substance P and cytokines in rheumatoid arthritis. *Arthritis Research & Therapy*, 7, 111-113