Characterization of Enthesitis Burden in Psoriatic Arthritis using Total-Body PET/CT Imaging with the 18F-FDG radiotracer

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Introduction

- Inflammation at sites of tendon and ligament attachment (enthesitis) represents a disease hallmark in psoriatic arthritis (PsA) patients.
- We explored utility of high-sensitivity Total-Body (TB) ^{18}F-FDG PET/CT imaging for the characterization of enthesitis burden in PsA patients.

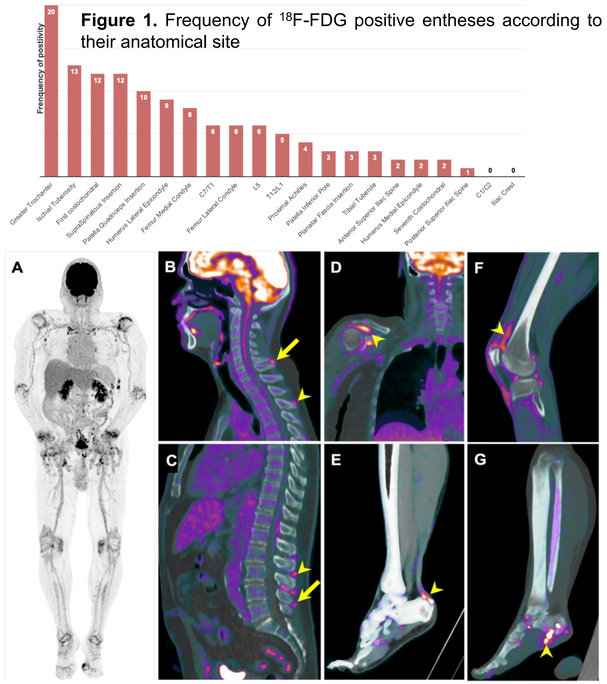

Figure 1. Frequency of ^{18}F-FDG positive entheses according to their anatomical site

Figure 2. Total-Body PET/CT Evaluation of PsA: **(A)** Maximum intensity projection (MIP) view demonstrating multiple active joints (shoulders, sternoclavicular joints, elbows, wrists, knees, ankles, left first MTP). Fused PET/CT images from different participants demonstrating enthesitis patterns throughout the body **(B-G)**. The spine entheses are involved at the cervical (**B**, arrow at C7 and arrowhead at T3), and lumbar regions (**C**, arrow at L5 and arrowhead at L3/L4/L5 inter/supra-spinous ligaments). Other inflamed entheses include right supraspinatus (**D**), Achilles (**E**), and patellar tendons (**F**), and plantar fascia (**G**).

Methods and Materials

- This ongoing work prospectively recruited 15 participants (14 males, 1 female; age of 56.8±16.3 years), with established diagnosis of PsA.
- All subjects underwent rheumatological evaluation including Leeds enthesitis index (LEI) and TB-PET/CT with 77.7±4.7 MBq of ^{18}F-FDG.
- Qualitative and quantitative findings of 38 entheses per participant (38x15=570) were assessed **(Figure 1)**. The evaluated entheses were derived from 6 different enthesitis outcome measures (LEI, San Francisco, MASES, MAJOR, SPARCC, and 4-Point enthesitis measures)[1].
- Each enthesis was visually and quantitatively evaluated ($rSUV_{max}$=SUV_{max} ÷ ascending aorta blood pool SUV_{mean}).

Results

- PET/CT was positive in 127/543 evaluable enthesis (23.4%) from 14 out of the 15 participants.
- On rheumatologic examination and PET/CT, respectively, 7 and 21 out of 82 evaluable LEI entheses were positive. PET/CT was positive in 5/7 tender entheses and detected inflammation in 16 more LEI entheses **(Figure 2).**
- Components of SPARCC and San Francisco measures demonstrated the highest absolute number of positive entheses (66 and 59, respectively).
- Components of LEI were the most active with summed $rSUV_{max}$ of 14.1±9.8 compared to 8.0±5.1 and 7.0±4.8 for SPARCC and San Francisco measures, respectively.

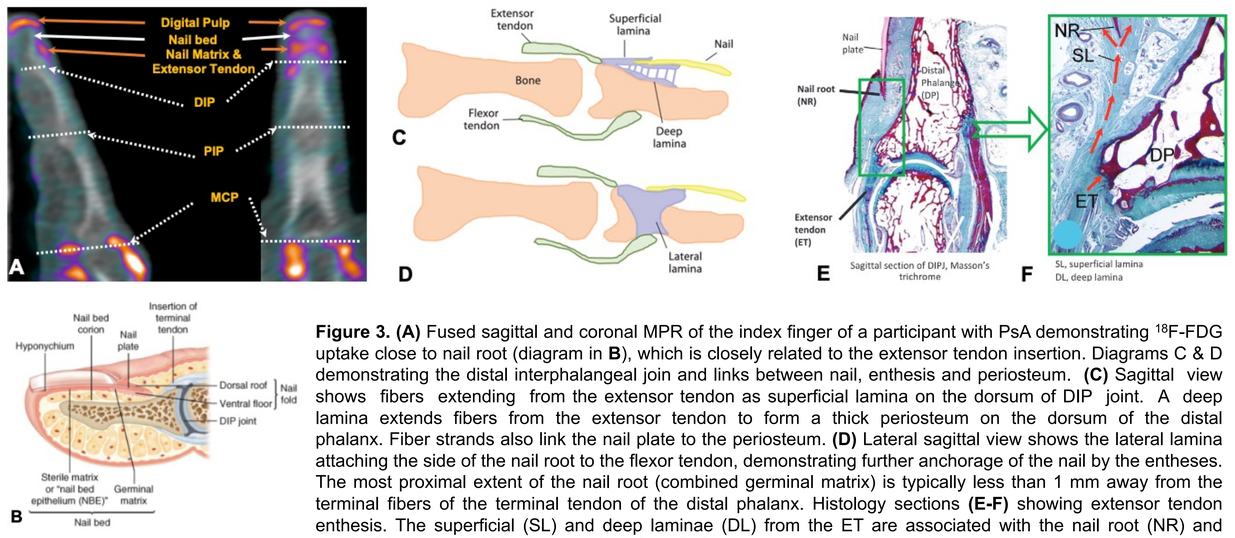

Figure 3. (A) Fused sagittal and coronal MPR of the index finger of a participant with PsA demonstrating ^{18}F-FDG uptake close to nail root (diagram in **B**), which is closely related to the extensor tendon insertion. Diagrams C & D demonstrating the distal interphalangeal join and links between nail, enthesis and periosteum. **(C)** Sagittal view shows fibers extending from the extensor tendon as superficial lamina on the dorsum of DIP joint. A deep lamina extends fibers from the extensor tendon to form a thick periosteum on the dorsum of the distal phalanx. Fiber strands also link the nail plate to the periosteum. **(D)** Lateral sagittal view shows the lateral lamina attaching the side of the nail root to the flexor tendon, demonstrating further anchorage of the nail by the entheses. The most proximal extent of the nail root (combined germinal matrix) is typically less than 1 mm away from the terminal fibers of the terminal tendon of the distal phalanx. Histology sections **(E-F)** showing extensor tendon enthesis. The superficial (SL) and deep laminae (DL) from the ET are associated with the nail root (NR) and matrix. Diagrams and histology sections from Ref.[2-3]

Discussion

- Current clinical measures of enthesitis, based on clinical examination, are driven more by anatomical site accessibility rather than actual disease burden.
- There are probably hundreds of entheses that are not covered by the current enthesitis measures. For example, hand extensor tendon entheses and their immediate relation to the DIP joint and nail matrix/bed **(Figure 3)**.
- Synovio-entheseal complex term has emerged to describe the intimate relationship between each enthesis (organ/functional enthesis) and the neighboring synovial membrane. Evaluation is challenging both on clinical and imaging settings. Resolving this tiny space, requires high spatial resolution and robust motion correction **(Figure 3)**.
- The mismatch between clinical and ^{18}F-FDG findings substantiates that PET could detect subclinical entheseal inflammation. On the other hand, tenderness alone might not be always indicative of active inflammation.
- Accurate quantification of systemic burden of enthesitis could be useful for better stratification of disease extent and severity and could be utilized towards selection of patients for more aggressive therapies or clinical trials.

Conclusion

- Evaluation of enthesitis burden on total-body ^{18}F-FDG PET/CT scans is feasible in patients with PsA.
- Further work is ongoing to recruit more participants, improve spatial resolution, and overcome motion.

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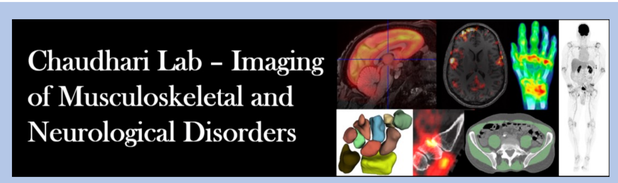

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