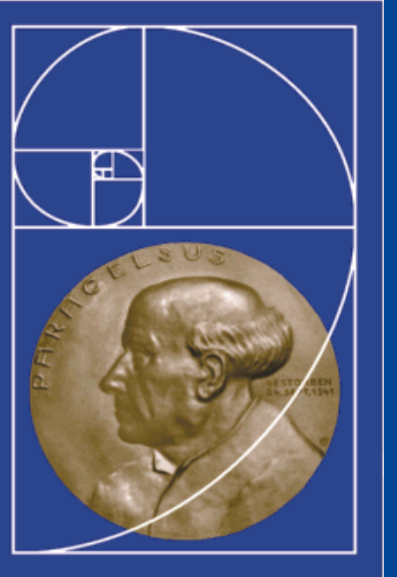


# IMAGING-BASED CHARACTERIZATION OF OA ENDOTYPES DERIVED FROM BIOCHEMICAL MARKERS – DATA FROM THE OBSERVATIONAL MULTICENTER APPROACH COHORT

J. Bacardit<sup>1</sup>, F. Roemer<sup>2,3</sup>, M. Jansen<sup>4</sup>, S. Maschek<sup>5,6</sup>, A. Marijnissen<sup>4</sup>, S. C. Mastbergen<sup>4</sup>, A. Wisser<sup>5,6</sup>, F. Lafeber<sup>4</sup>, A. Lalande<sup>7</sup>, H. Weinans<sup>4</sup>, F. Blanco<sup>8</sup>, F. Berenbaum<sup>9,10</sup>, L. A. van de Stadt<sup>11</sup>, M. Kloppenburg<sup>11</sup>, I. K. Haugen<sup>12</sup>, C. Ladel<sup>13</sup>, A-C. C. Bay-Jensen<sup>14</sup>, Y. Henrotin<sup>15,16</sup>, A. Struglics<sup>17</sup>, A. Mobasher<sup>18</sup>, F. Eckstein<sup>5,6</sup>, W. Wirth<sup>5,6</sup>



<sup>1</sup>Newcastle Univ., Newcastle, United Kingdom, <sup>2</sup>Univ. of Erlangen, Erlangen, Germany, <sup>3</sup>Boston Univ., Boston, MA, <sup>4</sup>Univ. Utrecht, Utrecht, Netherlands, <sup>5</sup>Paracelsus Med. Univ., Salzburg, Austria, <sup>6</sup>Chondrometrics GmbH, Freilassing, Germany, <sup>7</sup>Servier, Suresnes, France, <sup>8</sup>INIBIC-Univ. de A Coruña, A Coruña, Spain, <sup>9</sup>Sorbonne Univ., Paris, France, <sup>10</sup>AP-HP Saint-Antoine Hosp., Paris, France, <sup>11</sup>Leiden Univ. Med. Ctr., Leiden, Netherlands, <sup>12</sup>Diakonhjemmet Hosp., Oslo, Norway, <sup>13</sup>Independent Consultant, Darmstadt, Germany, <sup>14</sup>Nordic BioSci., Herlev, Denmark, <sup>15</sup>Artialis SA, Liège, Belgium, <sup>16</sup>Univ. of Liège, Liège, Belgium, <sup>17</sup>Lund Univ., Lund, Sweden, <sup>18</sup>Univ. of Oulu, Oulu, Finland



APPROACH is a 5-centre, 2-year prospective follow-up cohort project that included patients with a high likelihood of joint space width (JSW) loss and/or increased or sustained knee pain over the course of the study. With the help of machine learning approaches, three endotype clusters were identified in the APPROACH cohort. Based on patterns of serum and urine biomarker concentrations, the three clusters were characterized as: systemic inflammation, low tissue turnover and structural damage (Fig. 1).

## OBJECTIVES

- To evaluate whether joint tissue pathologies, (MRI Osteoarthritis Knee Scores (MOAKS)) and femorotibial joint (FTJ) cartilage thickness differ between the three clusters
- To study whether the 2-year changes in MOAKS scores and FTJ cartilage thickness differ between clusters.

## METHODS

- APPROACH enrolled 297 participants with knee OA (age: 66.5±7.1 years, BMI: 28.1±5.3 kg/m<sup>2</sup>, 77.5% women, 55% with KLG 2-4, 2 participants excluded, because of missing data).
- Of the remaining 295 participants, 93 assigned to the low-tissue-turnover (LTT) cluster, 110 to the structural-damage (SD) cluster, and 92 to the systemic-inflammation (SI) cluster.
- Semi-quantitative MOAKS scores assessed at months 0 and 24 by an experienced radiologist:
  - cartilage damage (#regions, max. score of cartilage damage and full thickness damage)
  - bone marrow lesion (BML, #regions, max score)
  - osteophytes (#regions, max score)
  - meniscus (max. damage and extrusion)
  - effusion and Hoffa synovitis
- Weight-bearing femorotibial cartilage thickness computed at 0 and 24 months from manual, quality-controlled segmentations of the femorotibial cartilages based on 3D SPGR MRI.
- X<sup>2</sup> tests used for comparing frequencies and t-tests used for comparing quantitative FTJ cartilage thickness measures between clusters.

## REFERENCES

[1] Angelini et al., Ann Rheum Dis 2022. 81(5):666-675.

## ACKNOWLEDGEMENT

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CONTACT: wirth@chondrometrics.de

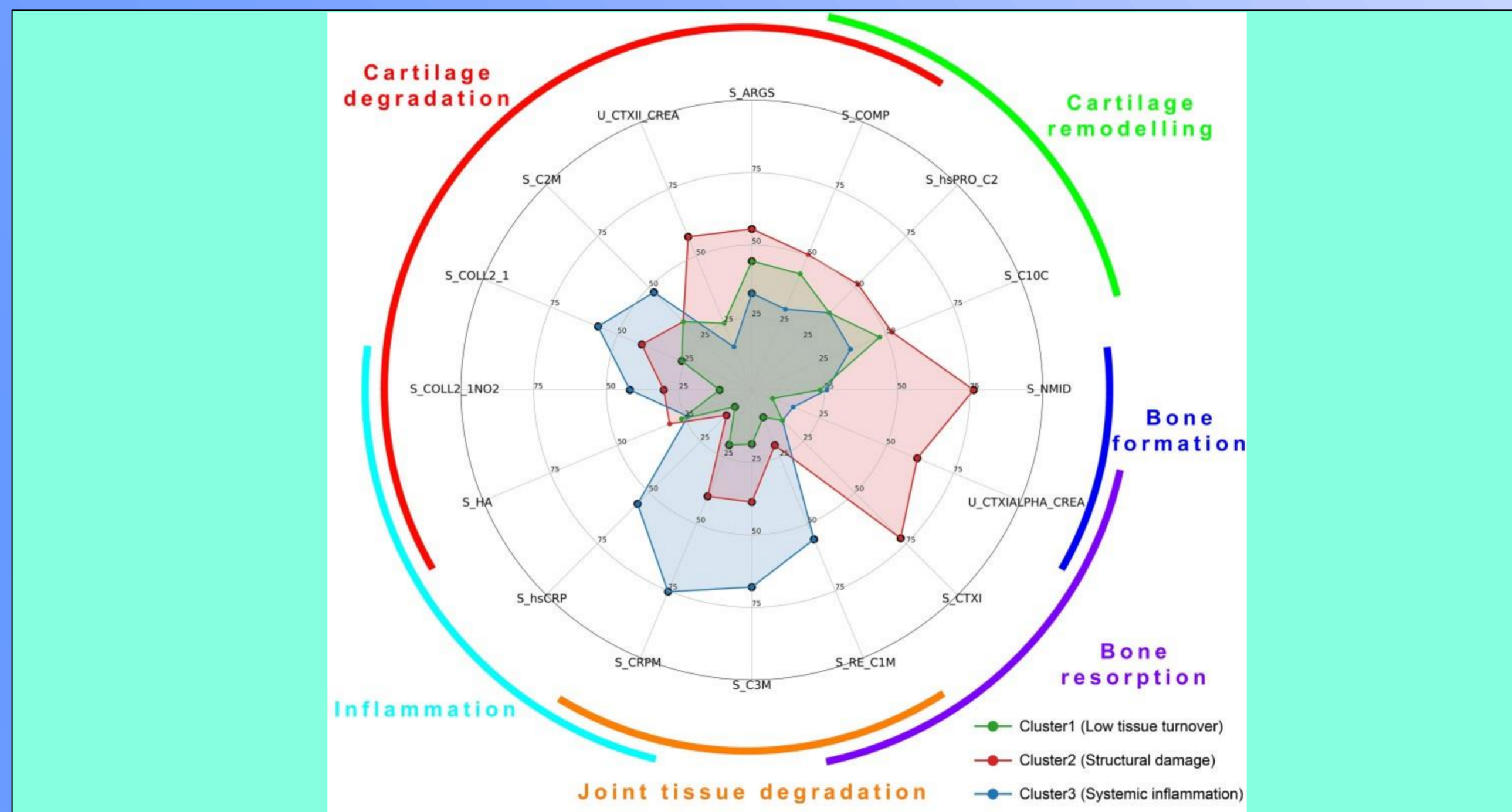


Figure 1: Radar-plot showing the 3 identified endotypes and the associated serum and urine markers

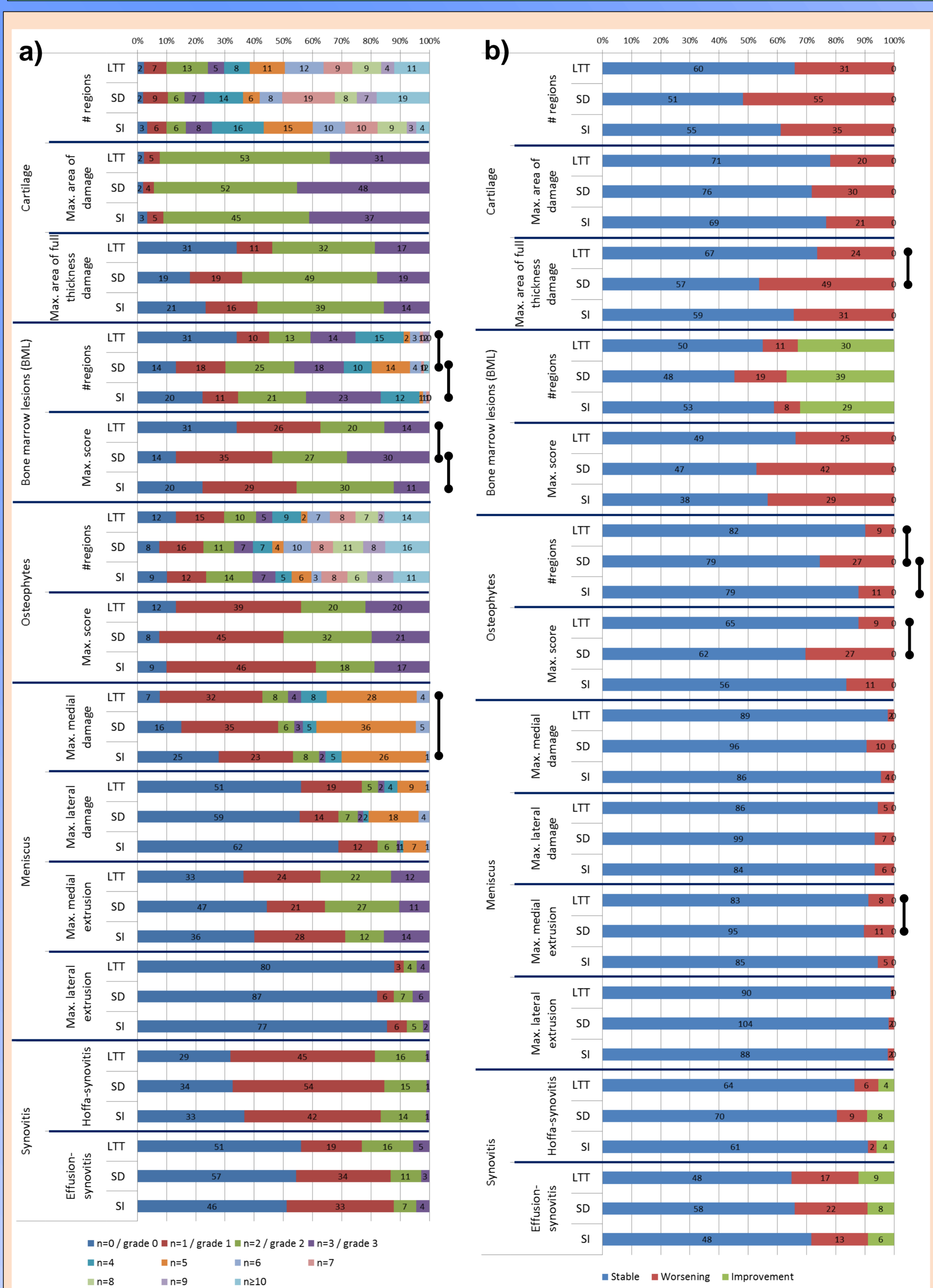


Figure 2: Baseline frequency (a) and two-year change in MOAKS pathologies (b) observed in the low tissue turnover (LTT) cluster, the structural damage (SD) cluster, and the systemic inflammation (SI) cluster (vertical bars indicate statistically significant differences between clusters (p<0.05)).

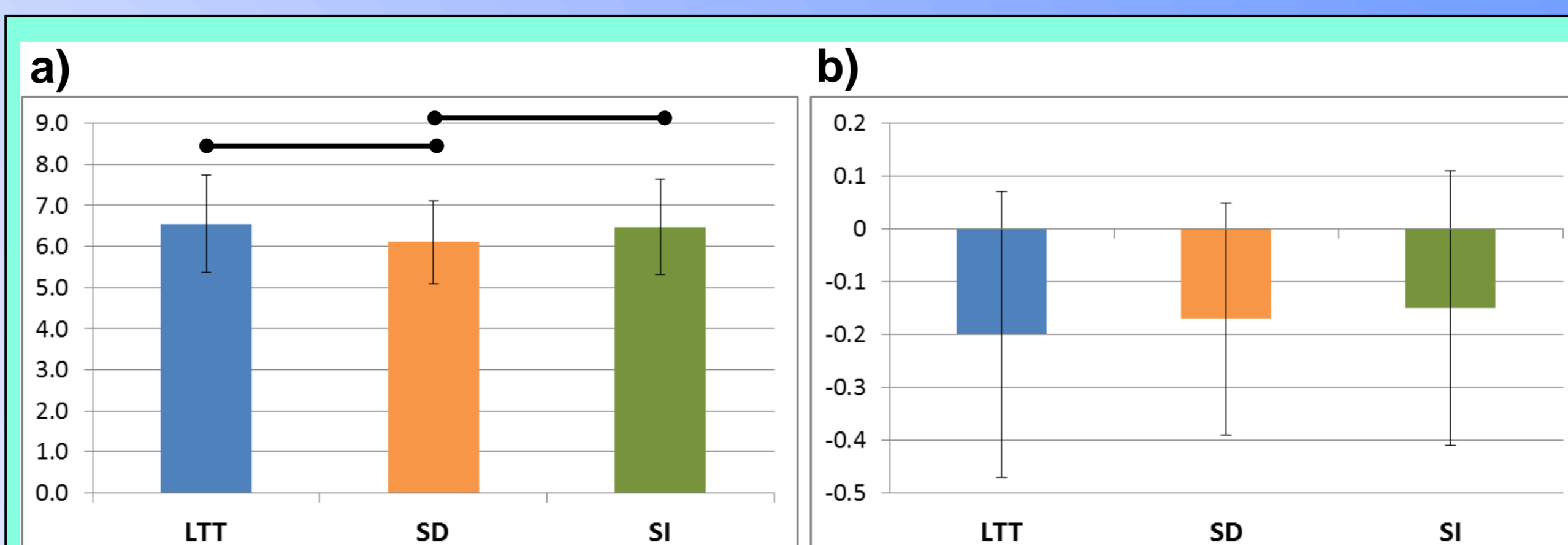


Figure 3: Baseline cartilage thickness (a) in the entire femorotibial joint (FTJ) and two-year change in FTJ cartilage thickness (b) observed in the low tissue turnover (LTT) cluster, the structural damage (SD) cluster, and the systemic inflammation (SI) cluster (mean ±SD in mm, horizontal bars indicate statistically significant (p<0.05) differences between clusters).

## RESULTS

### Cross-sectional comparison:

- MOAKS cartilage damage, osteophytes, effusion-synovitis, as well as Hoffa-synovitis did not differ between the 3 clusters (Fig. 2a).
- BMLs were observed in more subregions per knee and were more severe in the SD than in the other clusters.
- Medial meniscus damage was greater in the LTT than in the SI cluster, whereas other meniscus scores did not differ between clusters (Fig. 2a).
- FTJ cartilage thickness was lower in the SD than in the other 2 clusters (Fig. 3a).

### Longitudinal comparison:

- No differences observed between clusters for change in BMLs and synovitis scores (Fig. 2b).
- Change in number of regions with cartilage damage and the change in the maximum size of cartilage damage did not differ between clusters, whereas the change in the maximum size of full thickness cartilage damage was greater in the SD than in the LTT cluster (Fig. 2b).
- Knees from the SD cluster showed more medial meniscus extrusion worsening (Fig. 2b).
- Increase in the number of osteophyte locations and maximum osteophyte scores was greater in the SD cluster when compared to the LTT cluster (Fig. 2b). The increase in the number of osteophyte regions was also greater in the SD cluster than in the SI cluster (Fig. 2b).
- Change in femorotibial cartilage thickness did not differ between clusters (Fig. 3b).

## CONCLUSIONS

- Imaging features and cartilage loss patterns did not appear to be highly specific for the three clusters derived from baseline biochemical markers.
- Some of the cartilage and bone-related markers were, however, elevated in the SD cluster at baseline as well as over the 2-year follow-up period.
- These findings indicate that systemic biochemical markers may characterize endotypic clusters, reflecting different disease processes in large joints such as the knee, but may be of limited use for enriching clinical trials with knees likely to show fast structural progression (i.e., cartilage loss).