

# THIGH MUSCLE CHANGES CAN WORSEN SUBSEQUENT KNEE OA CLINICAL OUTCOMES: USE OF DEEP LEARNING AND PROPENSITY-SCORE MATCHING ON OAI DATA

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## Introduction and Objectives.

Thigh muscles play an important role in knee joint biomechanical stability, and changes in their size and quality are associated with knee OA incidence. There are currently no known disease-modifying medications for mitigating knee OA-related symptom worsening and delaying TKA. Therefore, non-surgical, non-pharmacological approaches targeting thigh muscle strengthening and composition have important clinical implications. The structural therapeutic effects of such interventions can be quantified using muscle MRI. However, no conclusive longitudinal data is available on the association of quantitative thigh muscle MRI markers with knee OA-related clinical outcomes.

We aimed to investigate the longitudinal changes in quantitative muscle cross-sectional area (CSA) and adipose tissue in knee OA and their association with downstream symptom worsening and TKA. We trained, tested, and implemented a fully automated supervised deep learning model to segment longitudinal thigh MRIs of a large sample of the OAI participants

## Materials and Methods.

In an analysis of OAI data, knees of participants with available quality thigh MRIs at baseline and at least one follow-up visit were included and classified as with and without knee OA according to baseline radiographic KLG  $\geq 2$  and matched for confounders using propensity score matching. An automated deep learning model for thigh MRI 2D-segmentation was developed and tested. Markers of muscle CSA and intramuscular adipose tissue (intra-MAT) were measured at baseline, 2nd and 4th-years follow-up (period-1) and compared between knees with and without knee OA using linear mixed-effect regression models. Furthermore, in knees with knee OA, the association of period-1 changes in muscle markers with risk of TKA (Cox proportional-hazards) and symptom worsening (mixed-effect models) during the 4th- to 9th-year (period-2) was evaluated.

## Results.

This study included 4,634 matched-thighs (2,317:2,317 with:without knee OA) of 2,344 participants (mean age $\pm$ SD:62 $\pm$ 9, 1,292 females). Compared with those without, knees with knee OA had a decrease in quadriceps CSA (mean difference: -8.21mm<sup>2</sup>/year, p:0.004) and an increase in quadriceps intra-MAT (1.98mm<sup>2</sup>/year, p:0.007). Decreased CSA and increased intra-MAT of quadriceps during period-1 predicted downstream (period-2) knee OA symptom worsening (WOMAC total score, odds ratios:0.24 (negative association), p<.001, and 1.38, p:0.019, respectively). Quadriceps CSA changes, negatively associated with higher future TKA risk (hazard ratio:0.70, p<.001).

## Conclusion.

Knee osteoarthritis was associated with longitudinal MRI-derived decreased quadriceps cross-sectional area and increased intramuscular adipose tissue. These potentially modifiable risk factors predicted downstream symptom worsening and knee replacement.

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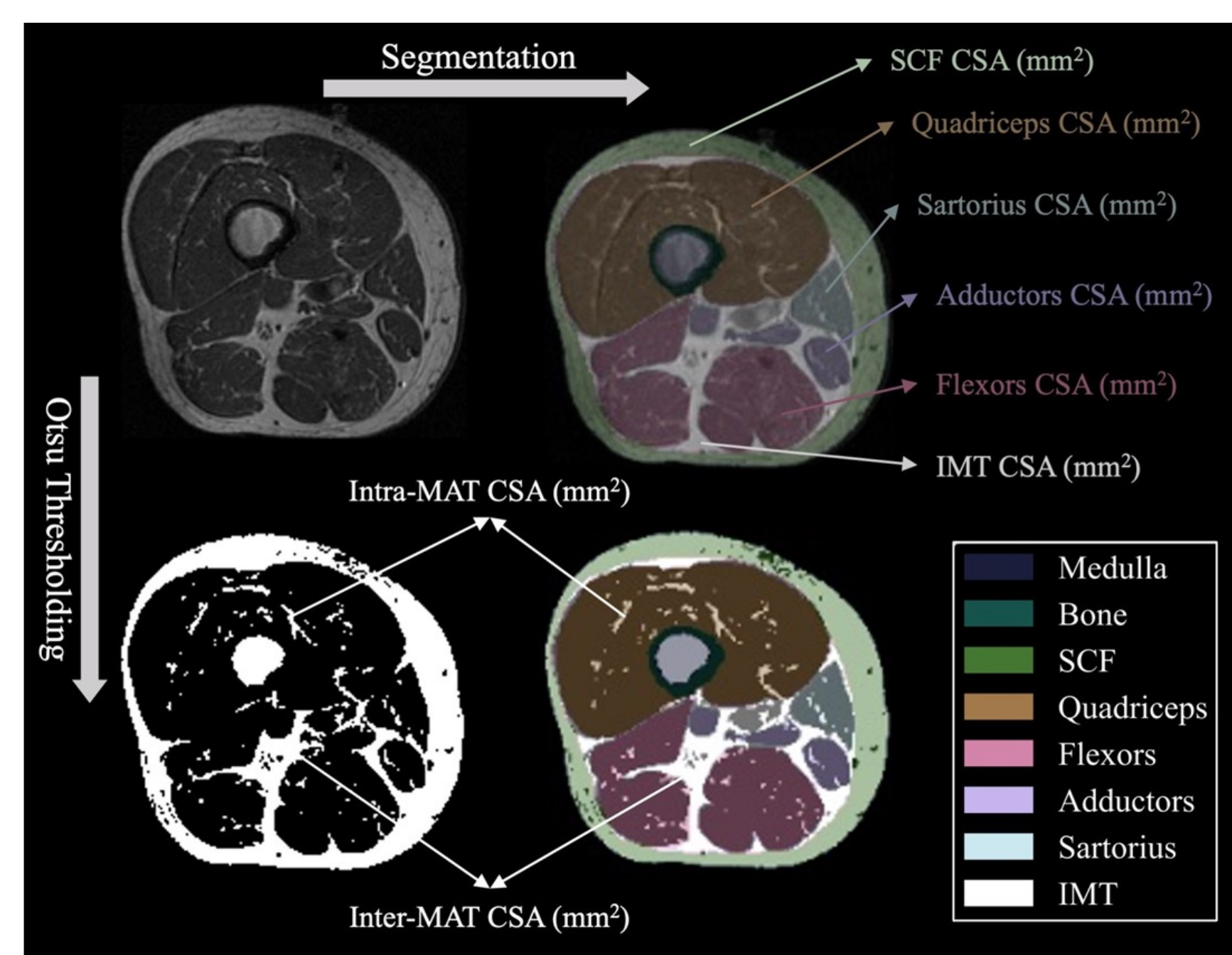
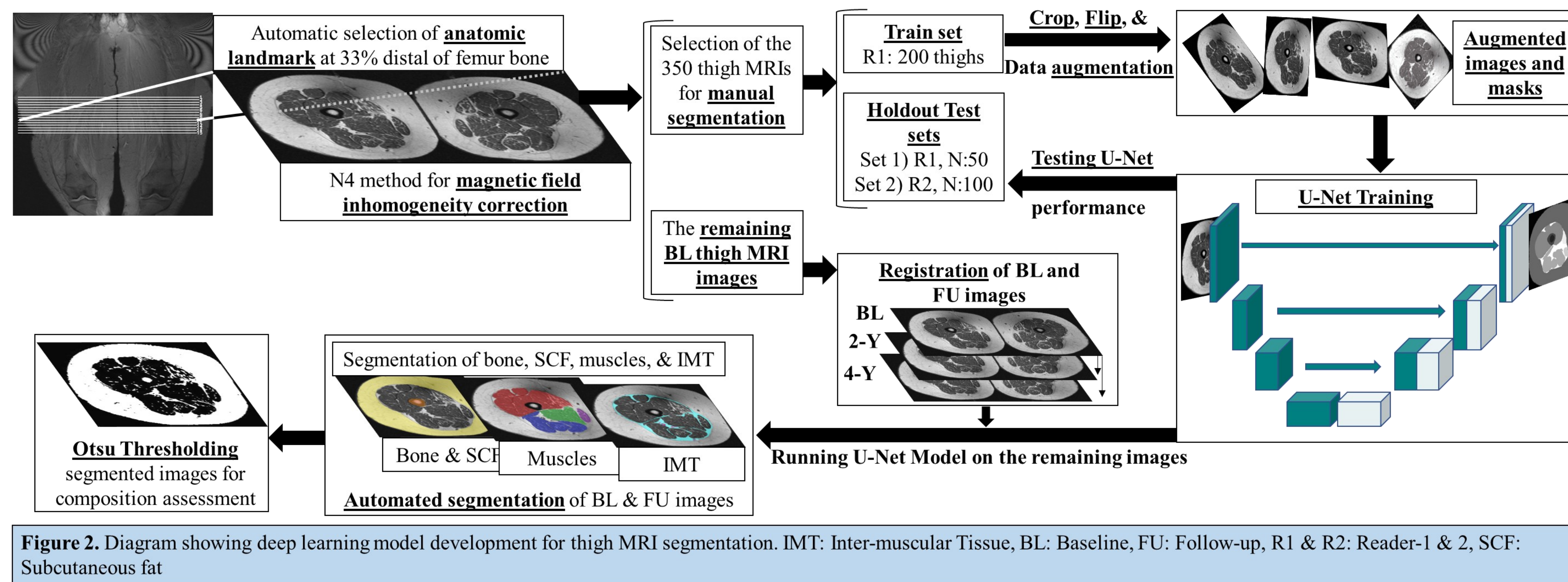
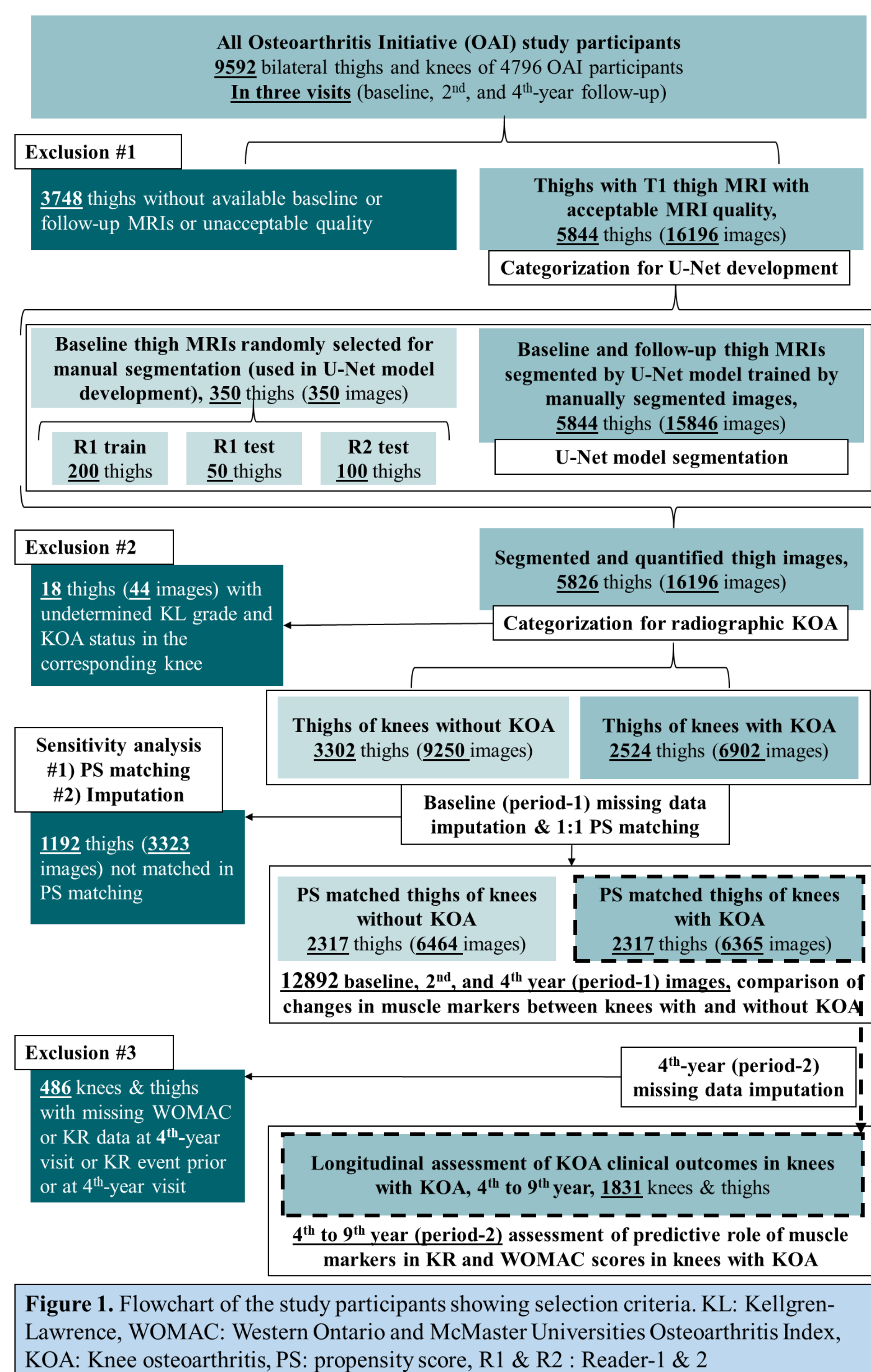
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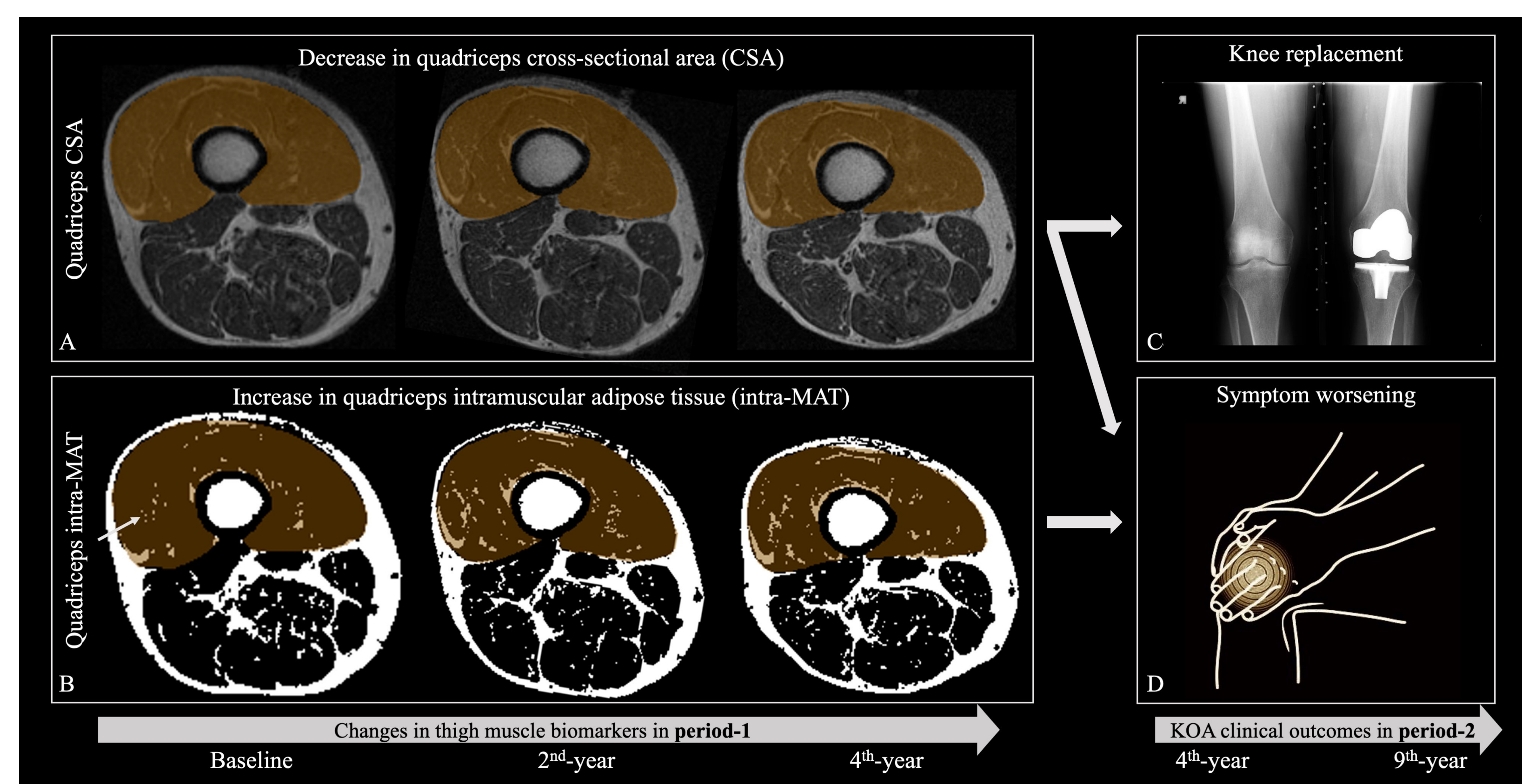
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**Our measurements for more than 16,000 thigh MRIs are publicly available. [Scan here!](#)**



**Figure 3.** Illustration of study outcome variables of muscle size and quality. CSA: Cross-sectional Area, IMT: Inter-muscular Tissue, Inter-MAT: Inter-muscular Adipose Tissue, Intra-MAT: Intra-muscular Adipose Tissue, SCF: Subcutaneous Fat.



**Figure 6.** Illustration of main study findings. Axial non-contrast T1-weighted MRIs of the quadriceps region at 33% distal femur length of left thigh of a 58-year-old male participant with KOA. Baseline to 4th-year (period-1) follow-up thigh MRIs show a decrease in quadriceps CSA (A) and an increase in quadriceps intra-MAT (B). During period-2 (4th- to 9th-year), this participant underwent left knee replacement at 7.7 years after baseline visit (C) and had increased KOA-related symptoms in WOMAC pain, stiffness, disability, and total scores (D). Thigh muscle changes in period-1 predicted KOA clinical outcomes in period-2, regardless of KOA grade at the start of period-2. CSA: Cross-sectional area, Intra-MAT: Intramuscular adipose tissue, KOA: Knee osteoarthritis, WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.