

AI-Enabled Quantification of Osteosarcopenia Progression Using Musculoskeletal Biomarkers in a Retrospective Prostate Cancer Patient Population

Saleh Tabatabaei^{1,2}, Tayler D. Ross^{1,3,4}, Teodora Vujovic¹, Kazi Rahman¹, Cari M. Whyne^{1,2,3,4}, Urban Emmenegger^{1,3}, Michael Hardisty^{1,3}

¹Sunnybrook Research Institute, ²Institute of Biomedical Engineering, Faculty of Engineering, University of Toronto, ³Institute of Medical Science, Temerty Faculty of Medicine, University of Toronto, ⁴Division of Orthopaedics, Department of Surgery, University of Toronto, Toronto, ON, Canada
s.mirzatabatabei@mail.utoronto.ca

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INTRODUCTION: Osteosarcopenia is a musculoskeletal condition with the coexistence of osteopenia (decreased bone mineral density) and sarcopenia (loss of skeletal muscle mass and strength). Sarcopenia and osteopenia are both common conditions particularly secondary to prostate cancer. Cancer patients have prolonged survival because of advanced therapeutics; however, the period of active disease and treatment has a detrimental and irreversible impact on individuals' musculoskeletal (MSK) health because of the progressive nature of osteosarcopenia during this period. Sarcopenia and osteoporosis have primarily been studied in isolation and the true impact of osteosarcopenia has been poorly elucidated. Osteopenia and sarcopenia in isolation have been shown to have deleterious effects on quality of life, independence, falls, fractures, hospital readmission, and patient-reported outcomes in cancer cohorts. Osteosarcopenia is a progressive syndrome with weakness, frailty, and bone strength deteriorating over time. Given this, there is a crucial need for better tools to improve understanding of osteosarcopenia progression and to allow routine clinical osteosarcopenia measures of progression. Assessments of osteopenia and sarcopenia, DEXA and 2D assessments of computed tomography (CT) scans, used in previous investigations focus on a single timepoint, neglecting the temporal progression in osteosarcopenia. Current methodologies often treat osteoporosis and sarcopenia as separate entities.

Objective: Quantify musculoskeletal biomarkers in a large retrospective cohort of advanced prostate cancer patients to study osteosarcopenia progression.

Hypotheses: Sarcopenia will progress in advanced prostate cancer patients, manifesting as decreases in muscle quality and quantity. Further bone mineral density will increase with time in these advanced prostate cancer patients because of the presence of metastatic disease leading to sclerotic lesions.

METHODS: Musculoskeletal biomarkers were calculated for 87 patients with advanced prostate cancer treated with systemic therapy at the Sunnybrook Odette Cancer Centre (Toronto, ON, Canada) between January 2009 and January 2021. Retrospective computed tomography imaging (1-4 per annum/patient) was used to calculate MSK biomarkers. The research protocol was approved by Sunnybrook Health Science Centre research ethics board.

3D computed tomography imaging was used opportunistically for this study with imaging initially ordered to monitor progression of prostate cancer disease. Analysis was restricted to CT imaging that contained the lumbar spine (abdominal or pelvis). Imaging was reconstructed to nominally a 1mm isotropic voxel size from diagnostic axial, sagittal and coronal reconstructions using a custom iterative approach for high-resolution image reconstruction.

The biomarker extraction pipeline (Figure 1) identifies and segments lumbar vertebral bodies (L1 to L5) and psoas muscles using a combination of convolutional neural network (CNN) architectures (vertebral instance segmentation CNN and U-Net models). The superior and inferior boundary of the psoas muscle used to quantify muscle biomarkers was defined based on the L2/L3 to L4/L5 intervertebral disc mid points and automatically calculated based on the vertebral body segmentations. Specific biomarkers extracted were bone density of lumbar vertebral bodies and the volume and density of the major psoas muscles. The pipeline takes an approximate duration of 30 seconds per image to meticulously derive the desired biomarkers.

RESULTS SECTION: Our analysis covered 278 studies comprising a total of 87 patients with all identifying as male (100%). The average age at time of first imaging was 71.27 years (53-85). The duration of imaging follow-up was on average 1084 days (median 890; 112 to 3284 days). Throughout this period, we found an average increase in bone mineral density and a decrease in psoas volume and density (Figure 2). In assessing temporality, we compared the patient's final imaging and compared it with their initial. We found that the average Hounsfield Units (HU) of L2-L5 vertebral bodies increased 19.91% (median -1.13%; -46.43 to 259.95%) over time. Additionally, we found that both psoas volume and psoas density decreased over time. Psoas volume had a less pronounced decrease with a 7.43% (median -8.46; -76.99 to 190.52%) volume loss. The most drastic decrease in biomarkers was seen in the psoas density (HU). Psoas density decreased 12.33% (median -10.87%; -186.83 to 180.29%) over the study duration. Interestingly, we found that 47/87 (54.02%) were stable or had a loss in bone density. Additionally, 23/87 (26.44%) had a greater than 30% increase in L2-L5 Bone Mineral Density (BMD). Further analysis of the psoas density relationship over time showed that 64/87 (73.56%) had a decrease in density over the study. Psoas volumes decreased from baseline (58/87 [66.67%]). Only 5/87 patients showed an increase over >30% in psoas volume. The temporal rate of change of the MSK biomarkers were significantly correlated (psoas volume vs bone density $R^2=0.57$, $p<0.001$, psoas density vs bone density $R^2=0.29$, $p<0.01$).

DISCUSSION: This study quantified changes in muscle and bone imaging biomarkers over an extended period, demonstrating important changes over the length of the disease. The results confirmed our hypotheses: greater than 2/3 of advanced prostate cancer patients showed losses in muscle quality and quantity, and bone mineral density showed an increase with time. Inspection of imaging studies suggests that the changes in bone mineral density were explained by development of sclerotic metastatic lesions. The findings were consistent with previous reports that showed loss of muscle quality and quantity in prostate cancer patients, however, the study here shows larger changes, probably because of the greater length of time studied. The study was limited to several important aspects that will be addressed in future work. The study considered only one site and did not consider potentially explanatory variables such as disease status, age, or treatments. The quantitative 3D imaging biomarkers investigated here have the potential to be more sensitive to changes than 2D biomarkers because of their invariance to patient positioning.

SIGNIFICANCE/CLINICAL RELEVANCE: Imaging-derived biomarkers of osteosarcopenia progression for advanced prostate cancer can be easily integrated into clinical practice by analyzing routine imaging. Mounting evidence shows understanding osteosarcopenia is crucial for understanding a patient's quality of life and outcome. Osteosarcopenia progression as measured by the biomarkers here can be used to predict patient outcomes and if shown to be related to treatment or disease course, would highlight the need for osteosarcopenia monitoring with metastatic progression in routine cancer care and other diseases that affect bone and muscle health.

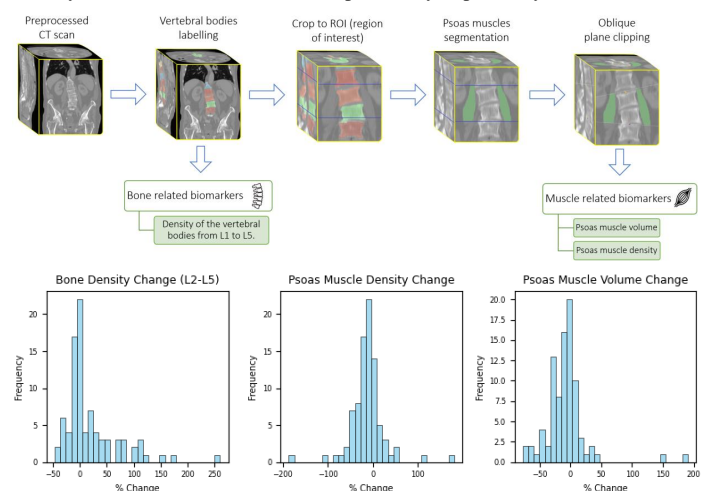


Figure 1. Biomarker extraction pipeline implemented in Python 3 using 3D Slicer (version 5.03).

Figure 2. Distributions of Cumulative Percentage Changes of MSK Biomarkers