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# ARTIFICIAL INTELLIGENCE IN MUSCULOSKELETAL RADIOLOGY: FROM IMAGING BIOMARKERS AND FOUNDATION MODELS TO PRECISION DIAGNOSIS AND PERSONALIZED CARE

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**ABSTRACT:**
Musculoskeletal radiology is undergoing a paradigm shift with the incorporation of artificial intelligence (AI) that moves imaging from morphology-driven interpretation to a quantitative, biologically oriented and individualized assessment. This review aims to explore the evolving role of AI in musculoskeletal imaging, highlighting how imaging biomarkers, molecular and genomic data, multi-omics data, foundation models, and precision medicine converge. Automated detection, segmentation, classification, and extraction of quantitative phenotypes from bone, cartilage, muscle, and soft tissues using AI analysis of radiography, computed tomography, magnetic resonance imaging, and ultrasound. Combination of these imaging phenotypes with genomics, transcriptomics, proteomics, metabolomics, and clinical information offers a chance to describe disease heterogeneity and link the imaging with the molecular mechanisms involved. Radio genomic and multimodal strategies can help identify biologically different disease sub types, composite radio imaging–molecular biomarkers, individualized risk profiles and predictors of the disease progression or therapeutic response. Foundation models also enable further possibilities, such as transferable representations and cross-modal learning that can incorporate a wide range of biomedical data. Important applications of these developments are in the field of osteoarthritis, osteoporosis, inflammatory musculoskeletal diseases, tumors, and muscle diseases. But it is hindered by data heterogeneity, scarcity of paired imaging–omics data, reproducibility, interpretability, bias, privacy, and external validation. Imaging, genomic, and molecular data coupled with standardized longitudinal clinical data will be crucial for the future of AI-driven precision diagnosis and personalized musculoskeletal care in future multicentre studies.

**KEYWORDS:** Artificial intelligence; Musculoskeletal radiology; Imaging biomarkers; Radio genomics; Precision medicine

## INTRODUCTION

Musculoskeletal disorders include a diverse range of conditions that involve the bone, cartilage, joints, skeletal muscle, tendons and ligaments and associated connective tissues. They are now reliant upon radiography, computed tomography (CT) or magnetic resonance imaging (MRI) and ultrasonography for complementary information on structural abnormalities and tissue integrity for their diagnosis. Conventional image interpretation, however, is still affected by reader experience, subtle phenotypic variation and the challenge of deriving complex quantitative data from the high dimensional images. Artificial intelligence (AI) has become a significant method for advancing medical diagnostics by using automated pattern recognition, quantitative feature extraction, and integrating heterogeneous clinical information, which could help standardize diagnostics and facilitate more personalized assessment of the diseases (Akhtar, 2025).

In the field of musculoskeletal medicine, there has been a significant increase in interest around the use of AI, such as machine learning and deep learning for detection of fractures, joint disorders, cartilage abnormality, bone tumors, spinal disease and others. The increasing research activity reflects the shift from experimental algorithms to clinically oriented systems that can assist in detection, segmentation, classification, prognostication and therapeutic decision making. There is a fast-growing trend in AI research related to musculoskeletal diseases, with joint disease, fracture, bone tumors, cartilage disease and spondylitis identified as some of the key research areas (Cao et al., 2024). Thus, AI is not just an automation tool but is also a new paradigm for deriving clinically and biologically relevant information from complex musculoskeletal data.

However, the musculoskeletal radiology field is especially conducive to this transition as medical images provide quantitative phenotypic data that can be used beyond simply what is visually obvious. These repetitive aspects of

radiological evaluation can be reduced, and contemporary AI system can aid image acquisition and reconstruction, lesion detection, segmentation, classification, and prediction. In recent years, deep learning methods have rapidly evolved and started to be explored on various anatomical structures and pathological processes across multiple imaging categories such as radiographs, CT, MRI, and ultrasound (Gitto et al., 2024). However, the potential for wider uses in the musculoskeletal field, including connecting diagnostic images with image-guided interventions and outcome-driven care pathways, points towards a broader potential for AI (Dubey et al., 2026). Thus, AI and machine learning integrated with comprehensive approaches in clinical imaging present opportunities to extract reproducible quantitative phenotypes from intricate anatomical and pathological patterns (Kumar et al., 2024).

Interestingly, the next step in AI-powered musculoskeletal imaging research goes beyond imaging phenotype disease recognition to the understanding of the biology underlying imaging phenotypes. Musculoskeletal disorders are a product of the interplay between genetic susceptibility, regulation of genes, molecular signalling, cellular response, environmental exposures and mechanical factors. Therefore, seemingly identical radiological abnormalities can have multiple, biologically different disease states. Combining quantitative imaging biomarkers with genomic, transcriptomic, proteomic, metabolomic and clinical data may allow a more complete description of disease processes and allow imaging phenotypes to be used as non-invasive markers of the underlying molecular processes. This type of integration is particularly applicable to radio genomics and precision medicine, where one might hope that computational models might link the macroscopic imaging features to molecular and genetic ones.

Advances in AI are also bringing about a shift towards foundation models and multimodal learning. Instead of writing individual imaging algorithms for each of a series of imaging tasks, these methods can learn generalizable representations from large collections of data and then adapt to multiple diagnostic tasks. AI already has potential applications in musculoskeletal conditions in radiological interpretation, trauma assessment, orthopaedic management and rehabilitation, but robust datasets and clinically generalizable algorithms are needed (Román-Belmonte et al., 2023). In the future, it is anticipated that multimodal systems may be able to jointly analyse imaging, molecular, genomic, laboratory and clinical information, thereby providing more biologically informed patient representations that can be used for improving earlier diagnosis, molecular stratification, individualized risk prediction, and treatment-response assessment.

In this review, we explore how AI has evolved from quantitative imaging biomarkers towards radio genomics, multi-omics integration and foundation models, focusing on its integration with molecular and genomic medicine in musculoskeletal radiology. These technologies offer an opportunity to interpret beyond morphology to precision diagnosis and personalized musculoskeletal care by linking imaging phenotypes with underlying biological heterogeneity.

**Objectives:**

To examine the role of AI in extracting and interpreting quantitative musculoskeletal imaging biomarkers and relating imaging phenotypes to underlying molecular and genomic characteristics.

To evaluate emerging radio genomic, multi-omics, and foundation-model approaches for integrating imaging with genetic, molecular, and clinical information in musculoskeletal disorders.

To explore the translational potential, current limitations, and future directions of biologically informed AI for precision diagnosis, patient stratification, prognosis, and personalized musculoskeletal care.

## 2. Molecular and Genomic Foundations of Musculoskeletal Imaging Phenotypes

### 2.1 Genetic Architecture and Molecular Basis of Musculoskeletal Disorders

Musculoskeletal disorders are due to a combination of genetic predispositions, aging, mechanical stresses, metabolic factors and environmental exposures. Genetic variation may affect cartilage homeostasis, bone remodelling, muscle function, extracellular-matrix organization and inflammatory pathways leading to differences in disease susceptibility and progression. Biomarker profiling can be used alongside the traditional clinical and radiologic assessment of the disease to identify biological processes involved in early disease and progression in OA (Coleman et al., 2025). These molecular differences might account for the fact that the same radiologic abnormalities can be biologically different disease states.

### 2.2 Molecular Pathways and Tissue-Level Imaging Manifestations

Imaging abnormalities can reflect molecular and cellular processes occurring on a macroscopic level. The degradation of cartilage is characterized by disruption of the extracellular-matrix, inflammatory signalling and alterations in chondrocytes, while bone abnormalities may be a consequence of dysregulated remodelling. In a like manner, muscle and soft-tissue modifications can occur because of inflammation, fibrosis, metabolic disturbance, or failure to regenerate. The combination of molecular and musculoskeletal imaging is an opportunity to shift the paradigm from anatomical imaging to a biologically based characterization of abnormalities within tissues (Klontzas et al., 2020).

### 2.3 Genotype–Phenotype Relationships

Imaging can offer an intermediate step between molecular changes and clinical manifestations (phenotypes). Some features like bone morphology, cartilage thickness, muscle volume, tissue composition and lesion architecture can mean underlying genetic or molecular variation. This correlation is especially applicable in the context of genetically driven neuromuscular disorders, where computational genomic methods can aid in the characterization and diagnosis of such diseases (Kumar & Dwivedi, 2025). The combination of genomic and quantitative imaging data could therefore help identify genotype–phenotype relationships and could be used to fine-tune molecular subclassification of musculoskeletal disorders.

### 2.4 Multi-Omics Characterization and Imaging Integration

Genomics represents one level of musculoskeletal disease biology. Transcriptomics describes the pattern of changes in gene expression; proteomics represents the changes in functional protein changes and metabolomics represents the downstream metabolic changes. They can be combined with imaging and clinical information to provide a more complete picture of disease heterogeneity. Diagnostic methods are evolving towards the integration of advanced imaging techniques, biomarkers, and clinical evaluation to enhance the characterization of musculoskeletal diseases (Kumar et al., 2025). AI can help with this integration as well, by recognizing high-dimensional relationships between imaging and molecular variables. Table 1 lists main molecular and genomic determinants of musculoskeletal imaging phenotypes, and their importance for precision diagnosis.

**Table 1. Molecular and genomic determinants of musculoskeletal imaging phenotypes**

| Biological level | Major factors/processes | Potential imaging manifestation | Relevance to precision diagnosis | References |
|---|---|---|---|---|
| Genetic variation | Disease susceptibility variants and inherited predisposition | Variation in bone morphology, cartilage integrity, muscle phenotype, and disease susceptibility | Supports genotype–phenotype characterization and risk stratification | Coleman et al. (2025); Kumar and Dwivedi (2025) |
| Gene expression | Altered transcriptional programs and regulatory pathways | Tissue degeneration, inflammatory changes, and structural remodeling | May connect imaging phenotypes with active molecular pathways | Ou et al. (2025) |
| Cellular and molecular pathways | Inflammation, extracellular-matrix remodeling, bone turnover, tissue repair | Cartilage loss, bone remodeling, edema, and soft-tissue alterations | Provides biological interpretation of imaging abnormalities | Klontzas et al. (2020) |
| Proteomic profiles | Altered proteins, enzymes, cytokines, and signaling molecules | Potential association with tissue composition and disease activity | Supports biomarker-based disease characterization | Kumar et al. (2025) |
| Metabolic profiles | Metabolites reflecting cellular and tissue dysfunction | Potential compositional and functional imaging changes | May identify metabolically distinct disease phenotypes | Ou et al. (2025) |
| Integrated multi-omics | Combined genomic, transcriptomic, proteomic, and metabolomic information | Composite imaging–molecular phenotypes | Enables biologically informed patient stratification | Kumar et al. (2025); Ou et al. (2025) |

### 2.5 Toward Biologically Informed Imaging Phenotypes

Combining quantitative imaging with molecular and multi-omics profiles will give a basis for musculoskeletal phenotyping, done in the context of biological knowledge. AI is being used more in clinical, imaging and omics fields in the context of OA, which can help to delineate different disease phenotypes and predict disease progression and treatment response (Ou et al., 2025). Radiological features can be correlated with genomic, transcriptional, proteomic and metabolic data to turn imaging biomarkers into tools to describe the disease biology, which serves as the basis for radio genomics, precision diagnosis and personalized musculoskeletal care. Figure 1 illustrates the progression from molecular and genomic determinants to tissue alterations, AI-derived imaging phenotypes, and clinically relevant outcomes.

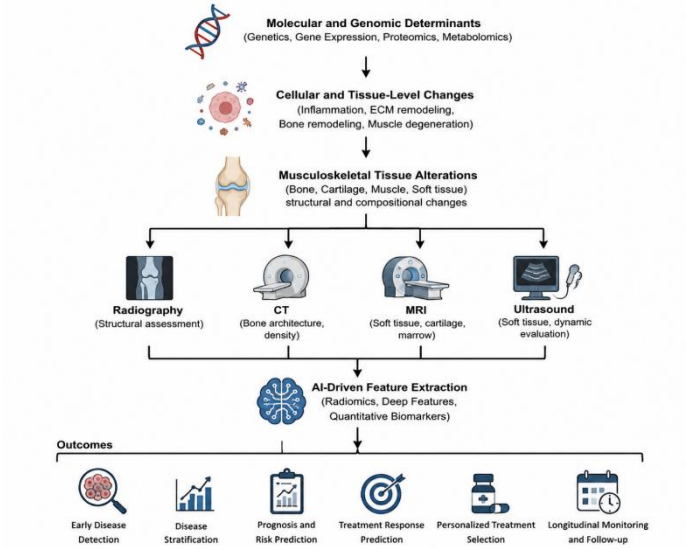


**Figure 1. Molecular-to-Imaging Pathway in Musculoskeletal Disease**

## 3. AI-Driven Imaging Biomarkers and Quantitative Musculoskeletal Phenotyping

### 3.1 Quantitative Imaging Biomarkers in Musculoskeletal Radiology

Imaging biomarkers are the measurable features of the structure, composition, and activity of the disease of the tissue that can be useful for diagnosis, prognosis, and monitoring of therapy. The complementary quantitative information on bone, cartilage, muscle and soft tissue can be obtained from radiography, CT, MRI and ultrasound. Advanced techniques in body-composition imaging also allow for objective measurements of muscle mass, adipose distribution, and tissue quality, paving the way for descriptive radiologic assessments to transition into quantitative precision medicine (Ko et al., 2026). AI can augment this process by automatically pulling out the subtle imaging characteristics that may not be simply quantifiable by the naked eye.

### 3.2 AI-Based Detection, Segmentation, and Quantification

With the advent of machine learning and deep learning, musculoskeletal image analysis can be automated to an even greater extent. Algorithms can be used for the detection, segmentation, quantification and classification of anatomical structures in different imaging modalities and detection of abnormalities and quantification of lesions. In orthopaedic imaging, there is ample evidence of the potential of AI to enhance the interpretation of imaging, with varying levels of performance and generalizability across different applications (Longo et al., 2025). Such abilities will allow for reproducible quantitative phenotyping and may help to minimise observer dependent phenotyping variability.

### 3.3 AI-Derived Phenotypes in Osteoarthritis and Osteoporosis

AI-assisted quantitative imaging is well suited to the detection of two very specific diseases which involve a progressive structural change over time: osteoarthritis and osteoporosis. Machine-learning techniques can be used to examine the joint space properties, cartilage structure, bone density, trabecular structure and other imaging features, aiding in the early detection and classification of the disease. The use of machine learning in the imaging of OA and osteoporosis has seen a rise in recent years, showcasing its ability to achieve a more granular detection of abnormalities and enhance the accuracy of diagnosis beyond what is currently performed by humans (Ming et al., 2026). This could, therefore, help in the early detection and objective severity assessment of bone and joint imaging using AI (Oladele, 2025).

### 3.4 Radiomics and High-Dimensional Imaging Phenotypes

Radiomics takes quantitative imaging to the next level, by extracting many shape, intensity, texture and spatial features from medical images. These capabilities can be integrated with AI and be used to describe disease heterogeneity and to derive imaging signatures that relate to diagnosis, prognosis or response to treatment. The current applications of AI in musculoskeletal imaging are growing in terms of automated quantitative analysis of bone, joint, muscle and soft tissue diseases (Shariatnia et al., 2025). Importantly, evaluation of high dimensional imaging phenotypes in conjunction with genomic or other omics data, can also offer a link to molecular profiling. The Table 2 shows the summary of the AI-generated quantitative imaging biomarkers from major musculoskeletal imaging modalities and their clinical applications.

**Table 2. AI-derived imaging biomarkers across major musculoskeletal imaging modalities**

| Imaging modality | AI-derived/quantitative biomarkers | Major MSK applications | Potential clinical value | References |
|---|---|---|---|---|
| Radiography | Joint-space measurements, alignment, bone texture, fracture characteristics | Osteoarthritis, fractures, skeletal abnormalities | Screening, detection, severity assessment | Longo et al. (2025); Oladele (2025) |
| CT | Bone density, cortical/trabecular characteristics, lesion morphology, body composition | Osteoporosis, fractures, tumors, muscle assessment | Quantification, opportunistic screening, risk assessment | Ko et al. (2026); Shariatnia et al. (2025) |
| MRI | Cartilage thickness, tissue composition, marrow abnormalities, muscle volume and lesion characteristics | Osteoarthritis, soft-tissue disease, spine disorders | Early phenotyping, prognosis, longitudinal monitoring | Ming et al. (2026); Stefanou et al. (2026) |
| Ultrasound | Tissue architecture, echogenicity, morphology, functional characteristics | Tendon, muscle, joint, and soft-tissue disorders | Accessible quantitative assessment and monitoring | Shariatnia et al. (2025) |
| Radiomics | Shape, texture, intensity, and spatial features | Tumors, degenerative disorders, heterogeneous lesions | High-dimensional phenotyping and biomarker discovery | Shariatnia et al. (2025) |
| AI-based body composition | Muscle quantity, quality, adipose distribution | Sarcopenia and metabolic/degenerative MSK conditions | Objective phenotyping and longitudinal assessment | Ko et al. (2026) |

### 3.5 Biomarker Interpretation and Clinical Translation

Imaging biomarkers derived from AI must have the three properties of reproducibility, biological relevance and clinical validity to support precision medicine. In the field of spine imaging and the diagnosis and treatment of lower-back pain, for instance, novel biomarkers are being explored, and AI can detect complex patterns in correlation with disease characteristics and outcomes (Stefanou et al., 2026). Performance of biomarkers may however vary depending on differences in imaging protocol, scanners, patient population, and computational pipelines. Standardisation and external validation are therefore crucial. Finally, connecting quantitative imaging with strong imaging phenotypes derived from AI with molecular and genomic features has the potential to turn quantitative imaging into a non-invasive 'biology window' for musculoskeletal diseases. Figure 2 presents the AI-driven workflow for musculoskeletal imaging biomarker discovery, from image acquisition and preprocessing to quantitative biomarker generation.

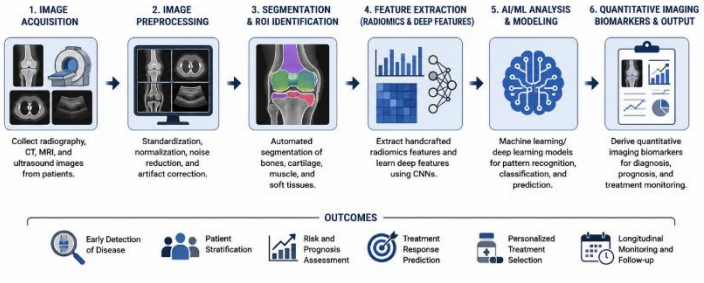


**Figure 2. AI Pipeline for Imaging Biomarker Discovery**

## 4. Radio genomics and AI-Based Integration of Imaging with Multi-Omics

### 4.1 Radio genomics in Musculoskeletal Disease

Radio genomics is the correlation of quantitative imaging phenotypes to underlying genomic and molecular traits and is a non-invasive method to gain understanding of biological heterogeneity. In musculoskeletal disorders, this framework can be used to link abnormalities in imaging techniques that are structural and functional in nature with genetic susceptibility, molecular pathways, and disease activity. This integration is especially pertinent in the context of immune-mediated disorders, which are increasingly being diagnosed and managed using a precision medicine approach that leverages molecular profiling and advanced computational methods guided by biomarkers to precision the diagnosis and therapeutic decision making (Al-Ewaidat & Naffaa, 2025).

### 4.2 Integration of Imaging and Multi-Omics Data

Radiological data can be used to integrate with genomics and transcriptomics, proteomics, and metabolomics, to give a more complete picture of musculoskeletal disease than any one data modality. Multimodal fusion techniques can help analyse imaging characteristics in relation to clinical and biological variables, which may help uncover associations between abnormalities in tissues and the underlying molecular processes (Jacob et al., 2026). The multimodal imaging itself also enhances this approach by integrating complementary anatomical and functional data to aid in the characterization of diseases and facilitate clinical translation (Luo et al., 2025).

### 4.3 AI for Multimodal and Molecular Data Fusion

AI offers computational approaches for merging high-dimensional data of very diverse nature and scale. Multi-modal models can simultaneously analyse data from imaging, molecular biomarkers, omics profiling and clinical information, which are all able to discover latent patterns related to disease sub-types, prognosis and therapeutic response. These methods are becoming more recognized as key elements in personalized healthcare, as they can integrate several information sources from the biological and diagnostic fields into comprehensive predictive models (Parvin et al., 2025). Table 3 summarizes the integration of imaging information with the information from other omics (genomic, transcriptomic, proteomic, metabolomic, and clinical) for precision musculoskeletal medicine.

**Table 3. Integration of musculoskeletal imaging with genomic and multi-omics information**

| Data layer | Information captured | Integration with imaging | Potential output | Precision-medicine relevance | References |
|---|---|---|---|---|---|
| Genomics | Genetic variants and susceptibility profiles | Association of variants with quantitative imaging traits | Imaging–genotype signatures | Genetic risk and disease stratification | Al-Ewaidat and Naffaa (2025) |
| Transcriptomics | Gene-expression patterns | Correlation of expression profiles with imaging phenotypes | Imaging–transcriptomic signatures | Identification of active molecular pathways | Zheng et al. (2026) |
| Proteomics | Protein and signaling profiles | Association with structural or functional imaging changes | Composite protein–imaging biomarkers | Disease activity and response prediction | Parvin et al. (2025) |
| Metabolomics | Metabolic | Integration with | Metabolic– | Biological | Zheng et al. |

| | | | | | |
|---|---|---|---|---|---|
| | alterations | quantitative tissue characteristics | imaging phenotypes | endotyping | (2026) |
| Multimodal imaging | Complementary anatomical and functional characteristics | Fusion of multiple imaging modalities | Integrated imaging phenotype | Improved disease characterization | Luo et al. (2025) |
| Clinical + imaging + omics | Demographic, clinical, imaging, and molecular information | AI-based multimodal fusion | Patient-specific disease representation | Precision diagnosis and personalized care | Jacob et al. (2026); Rajurkar Ali (2026) |

**4.4 Imaging–Molecular Phenotypes and Disease Stratification**

The combination of imaging and molecular information could help identify biologically distinct disease phenotypes not evident by traditional radiologic evaluation. In the context of heterogeneous inflammatory and rheumatic diseases, multimodal AIs and generative methods can integrate visual data with other patient-specific information to enhance the diagnostic characterization and personalized treatment approach (Rajurkar Ali, 2026). Imaging–molecular signatures could hence be composite biomarkers to identify disease endotypes, predict the risk of progression, and determine those patients most likely to benefit from a particular therapy.

**4.5 Toward Multi-Omics Precision Musculoskeletal Medicine**

Precision musculoskeletal medicine can be realized by combining AI, imaging and multi-omics. Large-scale data and AI are now more frequently targeting endotyping of disease, prediction of therapeutic responders, and the transitioning of regenerative strategies to personalized care in the field of knee OA (Zheng et al., 2026). This framework could be expanded to other musculoskeletal disorders, allowing AI systems to make links between imaging features and genomic and molecular mechanisms that might help to diagnose disorders earlier in the disease course, stratify patients based on biology, and select the treatments best suited to the patient. Radio genomics thus is an important link between traditional musculoskeletal radiology and precision medicine guided by genomics. Figure 3 illustrates the AI-based integration of imaging, genomic, transcriptomic, proteomic, and metabolomic data for biomarker discovery and precismusculoskeletal care.

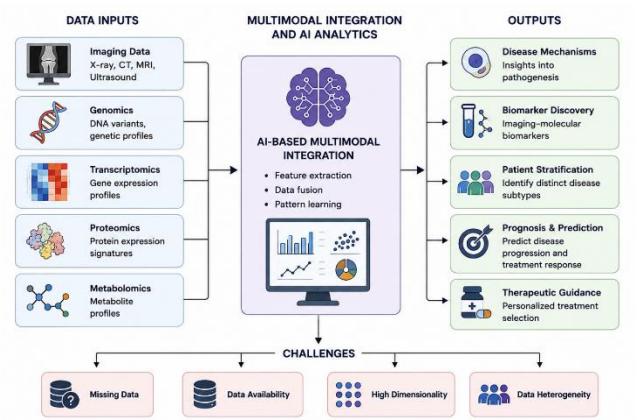


**Figure 3. Radio genomic and Multi-Omics Integration Framework**

**5. Foundation Models and Multimodal AI in Musculoskeletal Radiology**

**5.1 Emergence of Foundation Models in Musculoskeletal Imaging**

The emergence of foundation models has moved AI from being task-specific to models trained on large and diverse datasets which can be fine-tuned for a variety of downstream applications. In musculoskeletal radiology, this can help in the detection, segmentation, classification, quantitative phenotyping and prediction of outcome for various imaging modalities. In the larger scope of AI-assisted medical imaging, progress in identifying intricate disease patterns and facilitating early detection has showcased the potential of computational models in the field (Singh et al., 2026). This type of model could decrease the need for algorithms trained on a narrow range of data and offer models of musculoskeletal anatomy and disease that are more broadly transferable.

**5.2 Foundation Models for Quantitative Imaging Biomarkers**

One of the largest opportunities for foundation models is to automatically extract strong quantitative imaging biomarkers. For musculoskeletal MRI, one of the key requirements is the potential to retain clinically valuable biomarker information in the process, which can also enable predictive applications, an essential aspect for transferring large pretrained models to precision imaging pipelines (Hoyer et al., 2026). These models can be used to learn complex representations of cartilage, bone, muscle and other tissues, and may be able to recognize subtle phenotypic changes before any overt structural changes and offer quantitative assessment of disease progression.

**5.3 Cross-Modal Learning and Musculoskeletal Digital Twins**

In many cases, AI systems can leverage information from one data type to another through a process known as cross-modal learning, which could be useful in cases where one modality is incomplete representation of disease. New combinations of foundation models and musculoskeletal digital twins highlight the potential for uncertainty-aware detection of subclinical cartilage abnormalities from knowledge shared across modalities (Feng & Peng, 2026). Digital

twins take this one step further and can model a patient in the digital world in a dynamic matter, for example incorporating anatomical, physiological and longitudinal information to aid in personalised diagnosis and treatment planning (Sun et al., 2023).

### 5.4 Multimodal Foundation Models and Molecular Integration

A unified model incorporating both radiograph, CT, MRI, clinical records, laboratory findings and possibly genomic and multi-omics profiles will likely be the next generation of musculoskeletal AI models. These multimodal systems might be used to link imaging phenotypes with molecular features and offer patient-specific models of disease. The ability of computational methods to process and combine complex information in biomedical applications is already illustrated in the field of medical diagnostics and imaging with the use of AI. Widespread use of foundation models in image and molecular (and genomic) data would help identify imaging–molecular associations and facilitate biologically informed disease stratification. Table 4 provides an overview of the key approaches to transferring knowledge from the foundation model to musculoskeletal radiology, such as cross-modal learning, multimodal AI, and digital twins.

**Table 4. Foundation-model approaches and their potential roles in musculoskeletal radiology**

| AI approach | Principal capability | MSK application | Molecular/precision relevance | Major considerations | References |
|---|---|---|---|---|---|
| Imaging foundation models | Large-scale pretrained image representations | Segmentation, detection, quantitative phenotyping | Scalable extraction of imaging biomarkers | Domain adaptation and external validation | Hoyer et al. (2026) |
| Self-supervised models | Learning representations from largely unlabeled images | Feature extraction and downstream MSK tasks | May reveal latent disease phenotypes | Biological interpretability | Hoyer et al. (2026) |
| Cross-modal models | Transfer of information between modalities | Early/subclinical tissue characterization | Combines complementary phenotypic information | Cross-modal harmonization | Feng and Peng (2026) |
| Multimodal foundation models | Joint processing of heterogeneous data | Integrated diagnostic and predictive modeling | Potential integration of imaging, genomics, omics, and clinical data | Data availability and modality imbalance | Singh et al. (2026) |
| Digital twins | Dynamic patient-specific computational representation | Disease simulation and longitudinal monitoring | Supports individualized prediction and intervention | Requires robust longitudinal multimodal data | Sun et al. (2023) |
| Explainable/validated AI | Interpretable model outputs and clinically tested predictions | Decision support | Links computational features with biological meaning | Transparency, bias, and generalizability | Tordjman et al. (2026); Valavanidis (2023) |

### 5.5 Interpretability, Validation, and Clinical Readiness

Although promising, foundation models must be thoroughly assessed prior to their routine use for musculoskeletal applications. Factors such as training-population characteristics, imaging protocols, institutional differences and disease prevalence may have an impact on their performance. It is also unclear whether learned representations are clinically or biologically meaningful features. Critical reflections on AI in musculoskeletal imaging highlight the importance of separating "hype from impact" and the need for proper validation and generalizability (Tordjman et al., 2026). Therefore, future research and development should focus on explainability, external validation, biomarker reproducibility and compatibility with molecular data to make the contribution of foundation models to precision diagnosis and personalized musculoskeletal care reliable.

## 6. Clinical and Translational Applications Across Musculoskeletal Disorders

### 6.1 Osteoarthritis and Degenerative Joint Disease

As structural alterations in cartilage, subchondral bone and joint morphology can be quantified across imaging modalities, osteo-arthritis is a large application area for AI. Machine-learning methods can be used to help in identifying subtle patterns between the images which could indicate the occurrence of advanced radiography disease beforehand, and also to help identify and assess its severity (Prabha, 2025). In combination with molecular and imaging biomarkers, these methods could also help to further differentiate disease phenotypes and to predict progression and response to therapy.

### 6.2 Muscle and Soft-Tissue Disorders

AI can help in the characterization of muscle and soft-tissue abnormalities with automated segmentation and tissue classification, quantitative feature extraction, and recognition of diseases. These applications can help to enhance the

evaluation of soft-tissue heterogeneities and offer objective phenotypic data that are relevant for diagnosis and treatment planning (Al-Raeei, 2026). An AI-enabled opportunistic assessment of muscle quantity and quality from images routinely acquired in the clinic is a particularly pertinent example as they can extend AI's use beyond opportunistic assessment to individual rehabilitation and longitudinal monitoring (Wang et al., 2026).

**6.3 Musculoskeletal Interventions and Image-Guided Care**

AI's impact is not just in the diagnosis but also in musculoskeletal interventions. AI-driven tools have the potential to further enhance procedural planning, anatomical localization, image guidance, and patient selection, and integrate imaging data into interventional workflows (Dubey et al., 2025). Eventually, integration with molecular biomarkers and/or patient-specific clinical characteristics may permit interventions to be tailored to both anatomical abnormalities and molecular disease profiles.

**6.4 Clinically Deployable AI in Musculoskeletal Radiology**

In the clinical translation, AI systems must deliver more than just technical performance; they need to offer significant improvements in diagnostic accuracy, efficiency, and decision support. Potential use cases soon are fracture detection, automated measurements, opportunistic screening, segmentation, and quantitative assessment of both degenerative and structural abnormalities (Ruitenbeek et al., 2024). In the field of orthopaedics, applications can extend from diagnosis to follow-up, including treatment planning and postoperative assessment, highlighting the dynamic shifts in the role of the clinician and the machine in decision-making (Yapıcı, 2026).

**6.5 Toward Molecularly Informed Clinical Applications**

The highest translational potential may be for the imaging phenotypes, generated by AI, combined with genomic, molecular, and clinical data. A combination of these could allow musculoskeletal conditions to be categorised based on biological mechanism and not imaging alone to aid more accurate patient stratification and individualised management. The goal of automated image interpretation, across musculoskeletal diseases, is now being replaced, therefore, by a clinical goal which aims to integrate quantitative imaging biomarkers with disease biology. This trajectory is a roadmap for how AI can evolve from a diagnostic aid to precision diagnosis, prognosis, treatment choice and precision musculoskeletal care. Table 5 shows the main clinical / translational uses of AI in key musculoskeletal conditions or care pathways. Figure 4 illustrates the integration of musculoskeletal imaging, molecular and genomic information, clinical records, and sensor data through AI to support personalized patient care.

**Table 5. Clinical and translational applications of AI across musculoskeletal disorders**

| MSK condition/application | AI/imaging role | Relevant biomarkers or phenotypes | Potential precision-care application | References |
|---|---|---|---|---|
| Osteoarthritis | Detection, segmentation, severity assessment, progression analysis | Cartilage morphology, joint-space characteristics, bone changes | Early detection and individualized progression assessment | Prabha (2025) |
| Muscle/soft-tissue disorders | Segmentation, classification, quantitative tissue analysis | Muscle volume, composition, lesion characteristics | Objective phenotyping and treatment planning | Al-Raeei (2026) |
| Sarcopenia | Opportunistic screening and automated body-composition assessment | Muscle quantity and quality | Risk stratification and personalized rehabilitation | Wang et al. (2026) |
| Fracture/bone disorders | Automated detection, classification, and quantitative assessment | Fracture patterns and bone characteristics | Rapid diagnosis and clinical decision support | Ruitenbeek et al. (2024) |
| Musculoskeletal interventions | Planning, localization, image guidance, procedural support | Anatomical and quantitative imaging characteristics | Patient and procedure selection | Dubey et al. (2025) |
| Orthopaedic care pathway | Diagnosis, treatment planning, and follow-up | Integrated imaging and clinical phenotype | Personalized longitudinal management | Yapıcı (2026) |

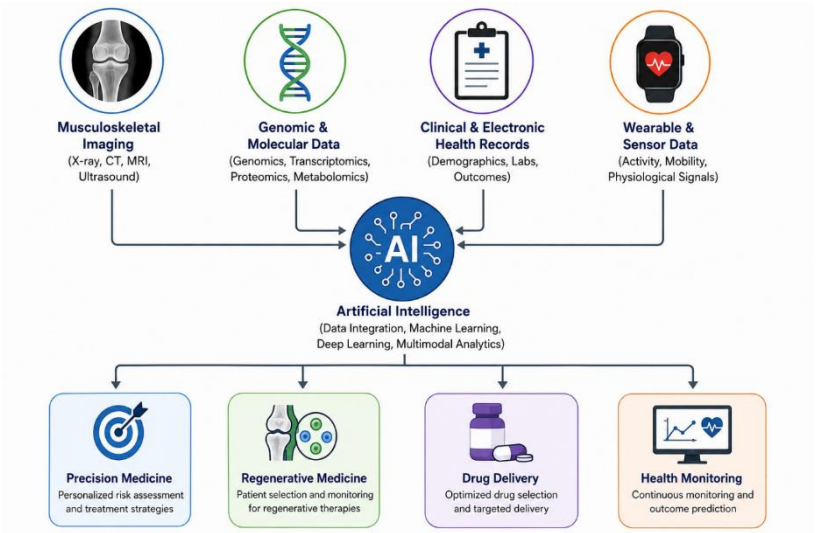


**Figure 4. Translation of AI Across the Musculoskeletal Care Continuum**

## 7. Precision Diagnosis and Personalized Musculoskeletal Care: Challenges and Future Directions

The combination of artificial intelligence, quantitative imaging biomarkers, molecular profiling and genomic information is paving the way towards precision medicine in musculoskeletal diagnosis. AI-based systems could instead categorize disease not just based on structural abnormalities, but by also incorporating imaging phenotypes, genetic susceptibility, molecular biomarkers, clinical characteristics and longitudinal information to find biologically meaningful patient subgroups. In the context of precision medicine in orthopaedics, there is a growing focus on technologies that can aid patient-specific risk assessment, therapeutic selection and outcome prediction, as well as an overall shift towards patient-specific management (Sadoghi et al., 2026). This integration might be especially useful in heterogeneous situations where patients with similar radiological phenotypes have different rates of progression and/or therapeutic responses.

AI must also progress from diagnosis to treatment planning and intervention to offer personalized musculoskeletal care. The future of AI and robotics in orthopaedic surgery showcases the potential of computational systems to aid in personalized surgical planning, precision during the procedure, and post-surgical care. Likewise, AI could be strategically leveraged in musculoskeletal interventions to augment the application of imaging data with patient-specific information to optimize the selection of appropriate interventions and enable precision-care models tailored to individual patients (Isaac et al., 2026). In the future, systems that integrate genomic and multi-omics profiles may take this paradigm one step further by defining different endotypes of diseases at the molecular level and determining which patients may most benefit from a particular pharmacological, regenerative, surgical or rehabilitation approach.

Multiple barriers, though, exist that prevent translation into routine care. The characteristics of the population, imaging modalities, acquisition protocols, annotation, model architecture, and the definition of the outcomes vary across musculoskeletal AI studies. Such variation can decrease the reproducibility and the generalizability to other settings. Evaluation of clinical translation suggests that many algorithms still have a long way to go until they are ready for use: the lack of proper prospective evaluation and validation across diverse real-world populations are persistent limitations (Ghazanfar et al., 2026). The inclusion of genomic and molecular data introduces additional difficulties due to the high dimensionality of the data, missing data, batch effects, genetic variability across different populations, data harmonization, privacy concerns, and given the lack of large, paired imaging–omics datasets.

As a result, the focus for future development should be placed on explainable and biologically interpretable AI as well as predictive accuracy. The models should show reproducible relationships of imaging signatures and latent features with clinically relevant phenotypes, molecular pathways or therapeutic responses. With the advent of AI in orthopaedic research, it is also essential to report and validate any research with external or transparent analysis of bias and clinical utility before generalizing for routine use (Misir & Yuce, 2025). Multicentre imaging–genomic repositories, harmonized biomarker definitions, federated learning, and prospective studies may help to bolster evidence while safeguarding patient sensitive information.

Finally, multimodal foundation models that can combine information from radiological images, genomic variants, gene-expression profiles, additional omics data, laboratory results and longitudinal clinical data will be able to offer more complete representations of patients. Biologically informed AI would bring about a change in musculoskeletal radiology from morphology-based interpretation to molecular-based diagnosis, individual risk prediction, monitoring treatment response, and personalized care. This transition will require a close collaboration between radiologists, geneticists, molecular scientists, orthopaedic experts, bioinformaticians and AI researchers.

## 8. CONCLUSION

AI is transforming musculoskeletal radiology by enabling the quantitative, biological and patient-specific assessment of images moving beyond the traditional morphological assessment. Automated detection, segmentation, classification, and extraction of imaging biomarkers using AI analytics of radiography, CT, MRI, and ultrasound data can be used to help

characterize subtle changes in bone, cartilage, muscle, and soft tissues. Importantly, by integrating these imaging phenotypes with genetic, genomic, transcriptomic, proteomic and metabolomic information, a link between radiological manifestation and molecular mechanisms involved in musculoskeletal disease can be achieved. Radio genomics and the integration of multi-omics are important advances to biologically distinguish disease phenotypes, stratify patients and to develop composite imaging–molecular biomarkers. Foundation models and multimodal AI can potentially further drive this shift, by acquiring transferable representations across imaging, molecular and clinical datasets. They may help to facilitate early disease detection, risk stratification, prognosis prediction, treatment decision-making, and long-term management of both osteoarthritis and osteoporosis as well as inflammatory diseases, musculoskeletal tumors, and muscle diseases. However, standardized imaging and molecular data, external validation, reproducible biomarkers, biological interpretability, fair model performance and suitable safeguards of the genomic and clinical data are necessary for successful clinical translation. More attention should be paid to establish large-scale multicentre imaging–omics data resources and clinically validated multimodal imaging–omics models. In conclusion, the intersection of AI, imaging biomarkers, genomics, and molecular biology holds the promise of revolutionizing musculoskeletal radiology, making it a vital part of precision diagnosis and personalized care.

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