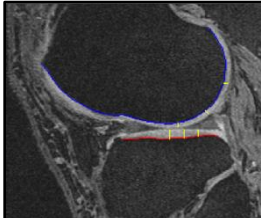
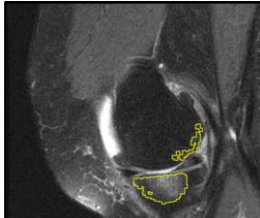
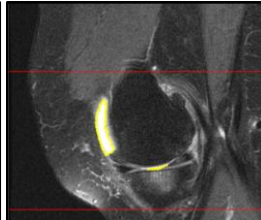


Knee osteoarthritis (KOA) is a leading global cause of pain, disability, and arthroplasty. Despite a promising therapeutic development pipeline, there are currently no available therapies proven to reduce or reverse osteoarthritis (OA) disease progression. A primary obstacle to the development and FDA registration of OA therapies is the absence of valid and discriminative structural outcome measures that reflect OA pathology of the whole knee. Magnetic resonance (MR) imaging can support accurate and sensitive quantification of whole-knee OA joint damage, but legacy scoring systems are burdensome and expensive to deploy.

#### MR Composite Metrics: A Novel Way to Conceptualize and Define Knee Osteoarthritis Progression

MR Composite Metrics: A Novel Way to Conceptualize and Define Knee Osteoarthritis Progression		
<b>Cumulative Damage</b> <i>Reflects the accumulation of damage attributable to KOA over the course of</i>	<b>Disease Activity</b> <i>Reflects a patient's current state of disease and symptoms</i>	
<b>Cartilage Damage Index</b>	<b>Bone Marrow Lesion</b> (Femur, Tibia, Patella)	<b>Effusion-Synovitis</b> (Whole Knee)
		

Over the past 15 years, with continuous funding from NIAMS and FDA, Tim McAlindon and Jeff Driban led a team of researchers in developing and validating proprietary analytic algorithms and software to efficiently quantify *whole-knee* structural damage using MRI.

Development work generated and validated algorithmic measurement scores that differentiate into two domains reflecting OA pathology and meaningful patient outcomes:

1. *Cumulative damage* (reflecting whole knee cartilage damage)
2. *Disease activity* (reflecting structural inflammation, bone marrow lesions, effusion-synovitis)

These composite metrics provide continuous scores of “whole-knee” OA structural pathology that are optimized to detect change and can be acquired with standard 20-minute MR scans and measured by technicians with minimal training in a few minutes.

**Patent** awarded for the algorithms supporting these Image Biomarkers (US Patent *Objective Assessment of Joint Damage* 17/609,226).

**FDA** accepted our Qualification Plan (DDT-BMQ-000087-QP-1) into the CDER/CBER Biomarker Qualification Program as filling “an existing scientific knowledge gap and would potentially enable identification of patients who are more likely to experience disease progression of KOA”.

**Arthrometrics Inc.** formed in 2023 to further develop and commercialize this promising technology.

#### Construct Validation to Date:

	Relates to Concurrent Outcomes		Predicts Future Outcomes		
	KL Grade	Pain	KL Grade	iSxOA*	TKR
<b>CDI</b>	√+				
<b>BML</b>	√+	√+	√+	√	
<b>Effusion-Synovitis</b>	√+		√+	√	
<b>Disease Activity</b>	√+	√+	√+	√	√
<b>Cumulative Damage</b>	√+		√+	√	
<b>End-stage KOA</b>	√+	√+		n/a	√+

\*iSxOA: incident symptomatic OA; n/a: not applicable. √+ = published. √ = abstract

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