NOVEL IMAGING IN RHEUMATOLOGY

P. DEHGHAN, MD
ASSOCIATE PROFESSOR OF RADIOLOGY
TALEGHANI HOSPITAL
SHAHID BEHESHTI UNIVERSITY OF MEDICAL SCIENCES

TOPICS TO BE DISCUSSED

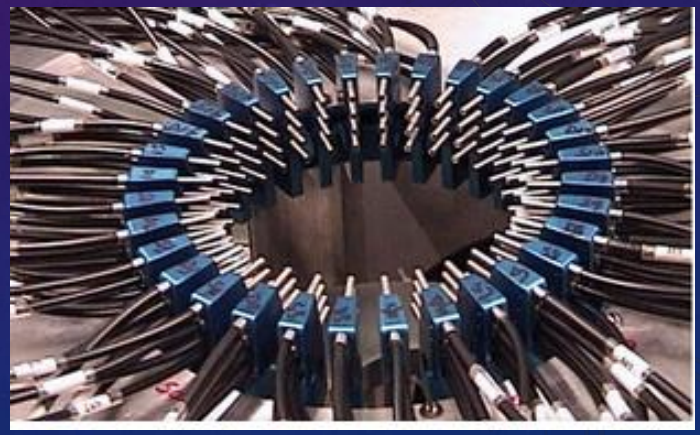
- Optical imaging
- Micro CT
- Whole body MRI
- Advanced MRI techniques

MEDICAL OPTICAL IMAGING

- The use of light as an investigational imaging technique for medical applications.
- Examples include optical microscopy, spectroscopy, endoscopy, scanning laser ophthalmoscopy, laser Doppler imaging, and optical coherence tomography.
- Optical imaging systems may be divided into diffusive and ballistic imaging systems.

DIFFUSE OPTICAL IMAGING (DOI)

- **M**ethod of imaging using near-infrared spectroscopy (NIRS) or fluorescence-based methods
- The technique has many applications to neuroscience, sports medicine, wound monitoring, and cancer detection.
- Typically DOI techniques monitor changes in concentrations of oxygenated and deoxygenated hemoglobin



APPLICATION IN RHEUMATOLOGY

- Valid detection of arthritis in differential diagnosis of joint pain.
- Indocyanin green (ICG)-enhanced fluorescence optical imaging (FOI) is a new imaging method that visualizes inflammation in wrist and finger joints.
- Dependent on the phase evaluated, moderate to good agreement with clinical examination and US.
- No valid study/data available to compare it with MRI as the gold standard for assessment of arthritis
- FOI is currently available for examination of hands and wrists only

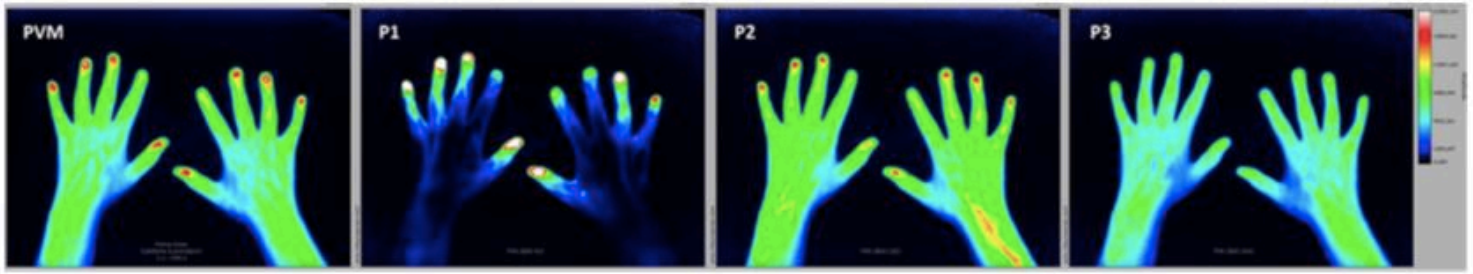


Fig. 1 FOI findings in a patient with arthralgia (group II) without signs of inflammation. P1 describes the period between starting the examination and increased signal intensities in the fingertips, the time point of increased signal intensity in the fingertips is analyzed for evaluation. P2 is defined as the phase with persisting high signal intensities in the fingertips, the time point of a red-colored signal in the fingertips is analyzed for evaluation. P3 begins with the absence of signal intensity in the fingertips, and the time point of a missing (no) signal in the fingertips is analyzed for evaluation. *PVM* automatically generated Prima Vista Mode, *P1–P3* phases 1–3

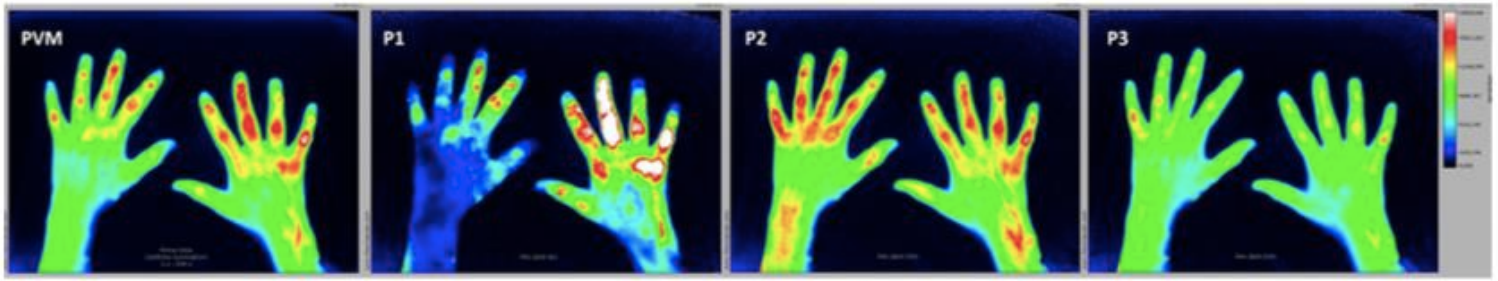


Fig. 2 FOI findings in a 17-year-old patient with clinically active seronegative polyarthritis (group I). Increased signal intensities as a sign of active inflammation (synovitis) can be seen in both hands especially in P1 as follows: high signal intensities (FOIAS grade 3) in MCP 4 + 5, PIP 3 + 5, and DIP 3 of the right hand; moderate signal intensities (FOIAS grade 2) in MCP 2, PIP 2 + 4, and DIP 2 of the right hand; and FOIAS grade 1 in IP of the right hand and DIP 2 + 3 and PIP 2 + 3 + 5 of the left hand. *PVM* Prima Vista Mode, *P1–P3* FOI phases 1–3

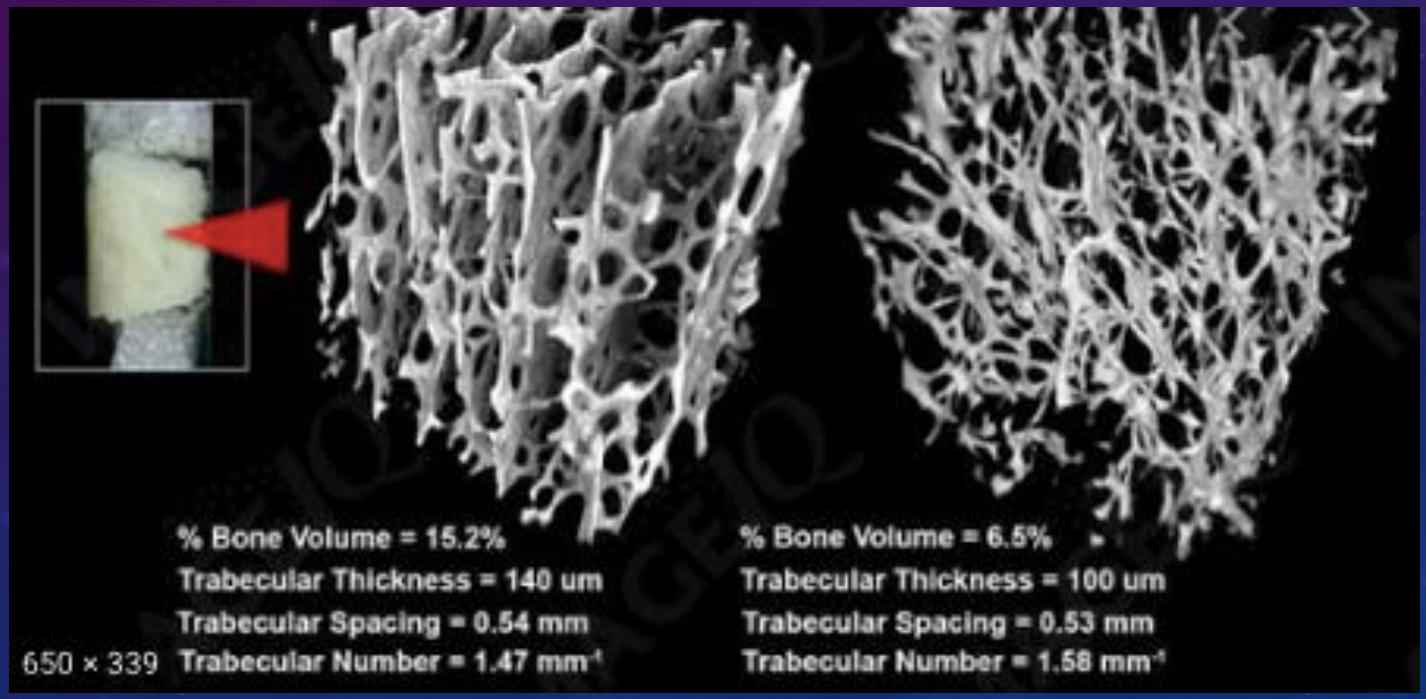
ARTHRITIS RESEARCH & THERAPY (2017) 19:233

MICRO COMPUTED TOMOGRAPHY OR "MICRO-CT"

- **x-ray imaging** in 3D, by the same method used in hospital **CT scans**, but on a small scale with massively increased resolution.

- It really represents 3D microscopy

BONE VOLUME FRACTION (BV/TV, %), BONE SURFACE/BONE VOLUME (BS/BV, MM 1), TRABECULAR THICKNESS (TB.TH, MM), TRABECULAR SEPARATION (TB. SP, MM), STRUCTURE MODEL INDEX (SMI), TRABECULAR NUMBER (TB.N, MM 1), AND DEGREE OF ANISOTROPY (DA).



WHOLE BODY MRI IN RHEUMATOLOGY

Current and Potential Indications

- ✓ Seronegative rheumatologic disease
- ✓ Aseptic multifocal osteitis related to SAPHO (synovitis, acne, pustulosis, hyper- ostosis, osteitis) syndrome

WHOLE BODY MRI PROTOCOLS FOR ONCOLOGIC AND RHEUMATOLOGIC PATIENTS

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Table 4

Whole-Body MR Imaging Protocol for the Work-up of Pelvic-spinal Arthritic Disease

Protocol	Plane	Sequences
Whole body	Coronal	T1-weighted, STIR, T1-weighted fat-saturated gadolinium-enhanced*
Whole spine	Sagittal	T1-weighted, STIR, T1-weighted fat-saturated gadolinium-enhanced*
Sacroiliac joint	Coronal oblique	T1-weighted, STIR
Hindfeet*	Sagittal/axial, oblique	STIR

Note.—Section thickness: body, 4–6 mm; spine, maximum 3 mm advised. Examination duration: 30–45 minutes. Detailed protocols used at the author's institution may be found in Appendix E2 (online); other examples of protocols can be found in the literature (102,122,126).

* Optional, not routinely performed.

Table 2

Whole-Body MR Imaging Protocol for the Work-up of Metastases and Hematologic Cancers

Protocol	Plane	Sequences
Whole body	Coronal, axial	T1-weighted, STIR*, DWI†
Whole spine	Sagittal	T1-weighted*, STIR
Brain*, lung*, liver*	Axial	T1-weighted, T2-weighted, enhanced T1-weighted

Note.—Section thickness: body, 4–6 mm; spine, 3–4 mm. Examination duration: 30–45 minutes. Detailed protocols used at the author's institution may be found in Appendix E2 (online); other examples of protocols can be found in the literature (8,11,99).

* Optional, not routinely performed.

† Advised low *b* values were between 50 and 150 sec/mm^2; high *b* values were between 800 and 1000 sec/mm^2.

WHOLE BODY MRI VS DEDICATED MRI

- In arthritis of the axial skeleton, whole-body MR imaging performs as well as MR imaging dedicated to the lumbar spine and pelvis for lesion detection

- extends the screening to additional sites of disease activity, in the thoracic spine and wall, pelvic and shoulder girdles, and peripheral entheses and joints.

33-YEAR-OLD MAN WITH A 1-YEAR HISTORY OF INFLAMMATORY PAIN

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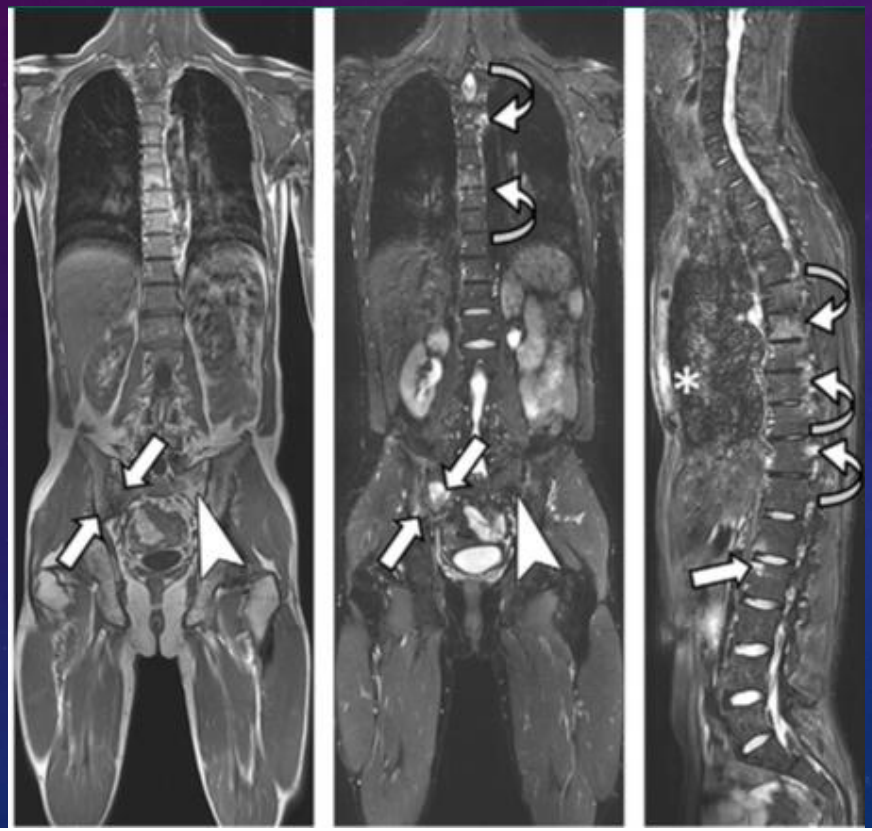
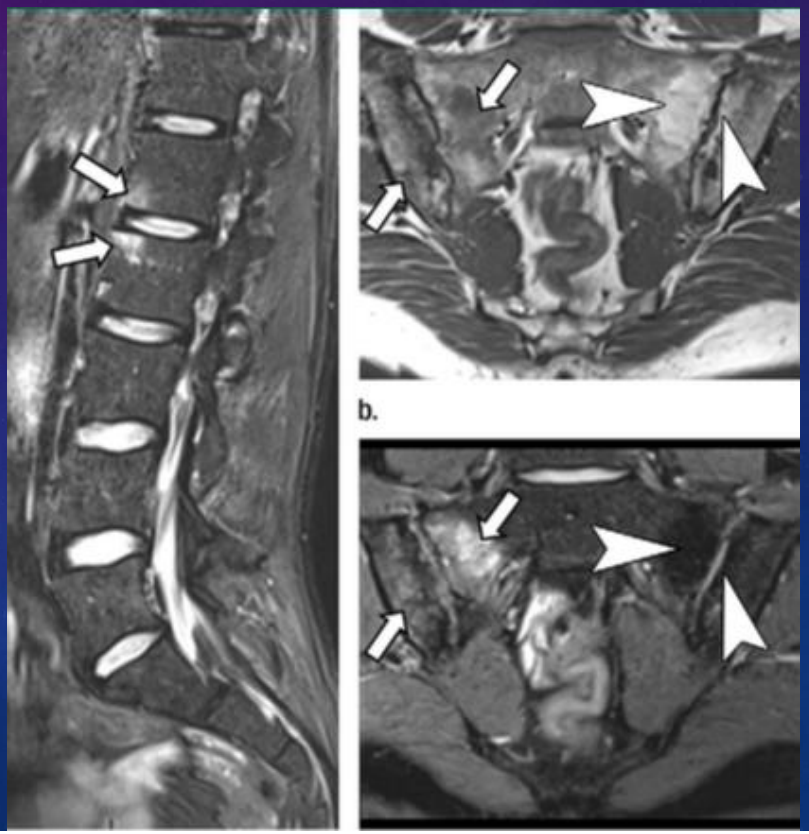
Whole body MRI



Lumbar and SIJ MRI



QUANTITATIVE MRI (QMRI) AS QUANTITATIVE IMAGING BIOMARKERS (QIB)

- Measurement of particular physical tissue characteristics, such as cellularity, diffusion, perfusion and fat content, in cartilage, synovium and bone.

- The ability of qMRI techniques to measure specific tissue characteristics (potentially independent of the hardware and software used to acquire the images) qualifies these measurements to be used as quantitative imaging biomarkers (QIBs)

- Sullivan et al. define a QIB as ***'an objectively measured imaged characteristic derived from an in vivo image as an indicator of normal biologic processes, pathological processes, or response to a therapeutic intervention'***

ADVANTAGES

- The QIB framework enables

✓ Rigorous evaluation and/or validation of imaging methods (substantial body of literature that can guide the validation process)

✓ Statistical approaches for measuring the accuracy, precision (including repeatability and reproducibility), biological validity and ultimately clinical utility of candidate QIBs are well-described

✓ Measurements can be compared between scanners, between different hospitals and across time points, and therefore offer greater objectivity than image assessment using conventional MRI.

✓ This can reduce the subjectivity associated with conventional MRI assessment and visual scoring approaches commonly used in research

✓ Further, the use of numeric data in qMRI maps can support automation and machine learning approaches to image analysis

DISADVANTAGES

- Availability
- Expensive
- Technically challenging
- Lack of adequate experience in technicians, radiologists and clinicians

QUANTITATIVE MRI TECHNIQUES USED IN MUSCULOSKELETAL IMAGING

- Diffusion weighted imaging (DWI)
- Dynamic contrast enhanced imaging (DCE-MRI)
- T1rho imaging
- T1rho (T1ρ)
- Delayed gadolinium-enhanced MRI of cartilage
- T2 relaxation time mapping
- Fat-Water MRI
- Ultra-short echo time and zero echo time

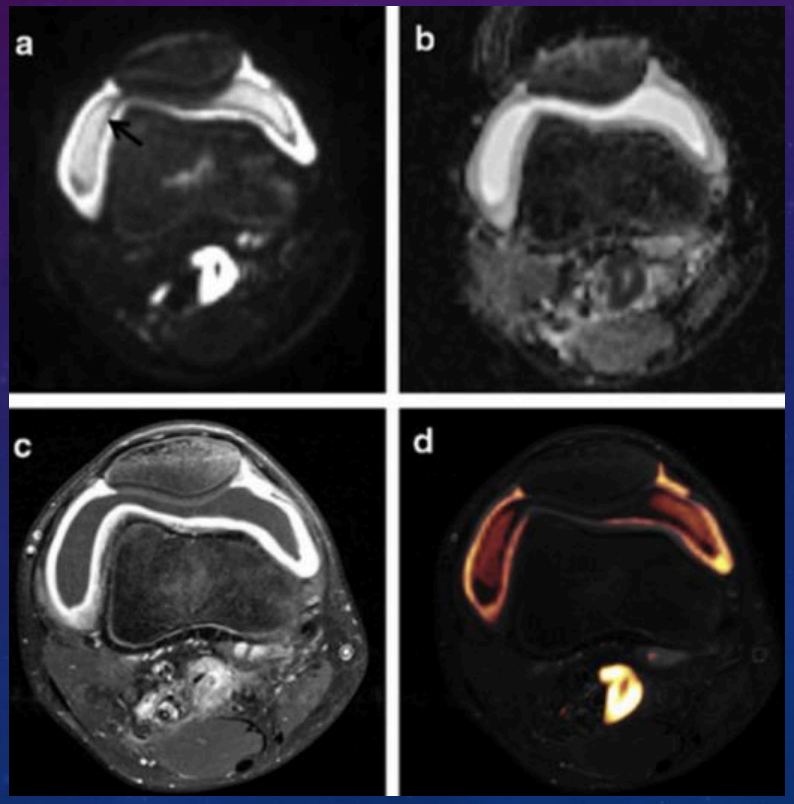
DIFFUSION-WEIGHTED IMAGING (DWI)

- Quantifies the freedom of water diffusion in tissue.
- Following acquisition of images with multiple diffusion weightings (b-values), a signal model is fitted to the acquired data, allowing estimation of the diffusion coefficient for the tissue.
- The diffusion coefficient gives an indication of the freedom with which water molecules diffuse.
- Tissue diffusion is typically estimated using a simple monoexponential model with a single ‘apparent’ diffusion coefficient (ADC).
- ADC measurements provide a useful ‘summary’ measure of tissue diffusion

LIMITATIONS

- Relatively low spatial resolution
- Low signal-to-noise ratio
- The reproducibility of ADC measurements between different scanners and within patients is also relatively poor.

A 15-YEAR OLD PATIENT WITH ACTIVE KNEE ARTHRITIS
DWI WITH B-VALUE 800 S/MM2 (A) AND ADC50/800 MAP (B) DEMONSTRATING HIGHER ADC IN EFFUSION AS COMPARED TO SYNOVIUM.
THE POST-CONTRAST IMAGE (C) SHOWS SYNOVIAL UPTAKE OF CONTRAST AGENT
(IMAGE FROM LI 2019, WORLD J PEDIATR. 2019).



DYNAMIC CONTRAST-ENHANCED MRI (DCE-MRI)

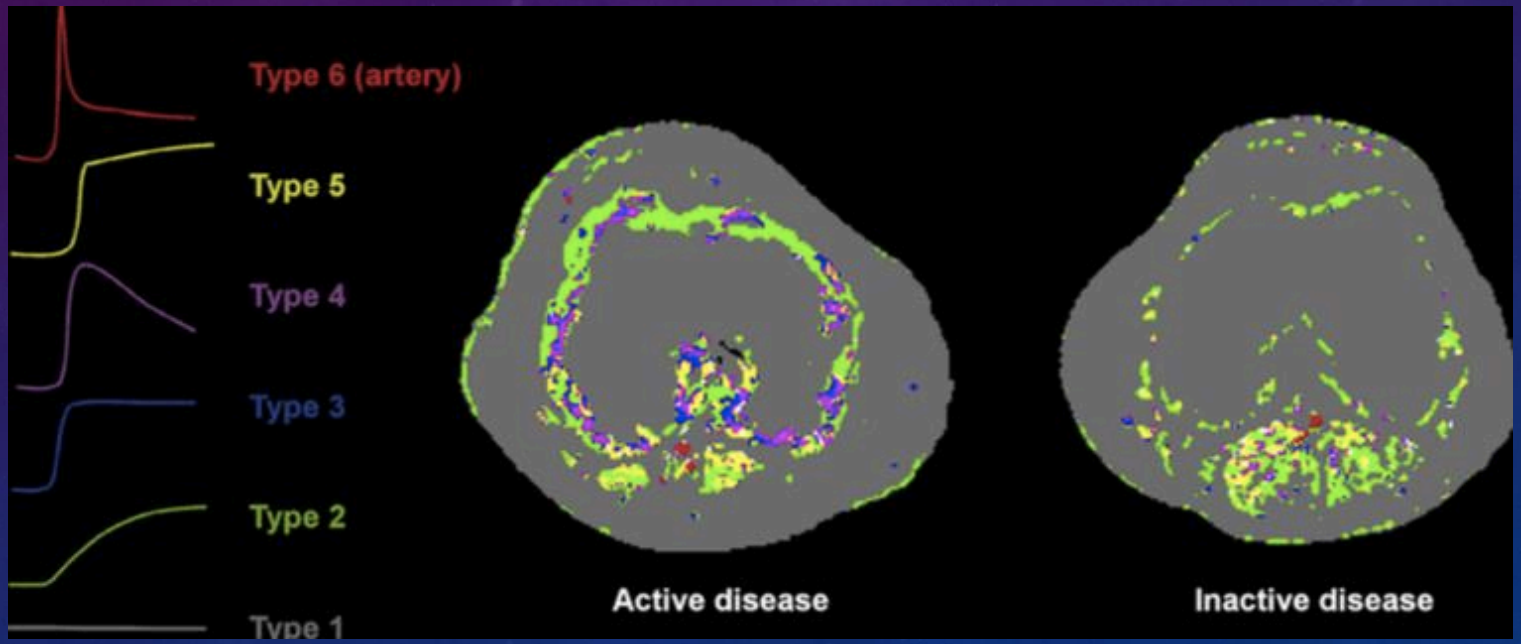
- A method for measuring tissue perfusion, relying on the acquisition of rapidly repeated images during intravenous administration of gadolinium-based contrast agent (GBCA).
- Changes in signal intensity over time are analysed to derive maps of specific ‘microvascular’ parameters.
- The descriptive or heuristic method, describes the shape of the signal intensity curves of contrast enhancement over time within the tissue of interest

DCE-DERIVED TIME INTENSITY CURVE SHAPE MAPS OF TWO PATIENTS WITH JIA.

-THE FIRST PATIENT DEMONSTRATED ACTIVE SYNOVIAL INFLAMMATION AND THE DCE MRI OF THIS PATIENT SHOWS AN INCREASED NUMBER AND PERCENTAGE OF TIC-4 SHAPES

-THE SECOND PATIENT, WHO HAS NO SYNOVIAL INFLAMMATION ON MRI.

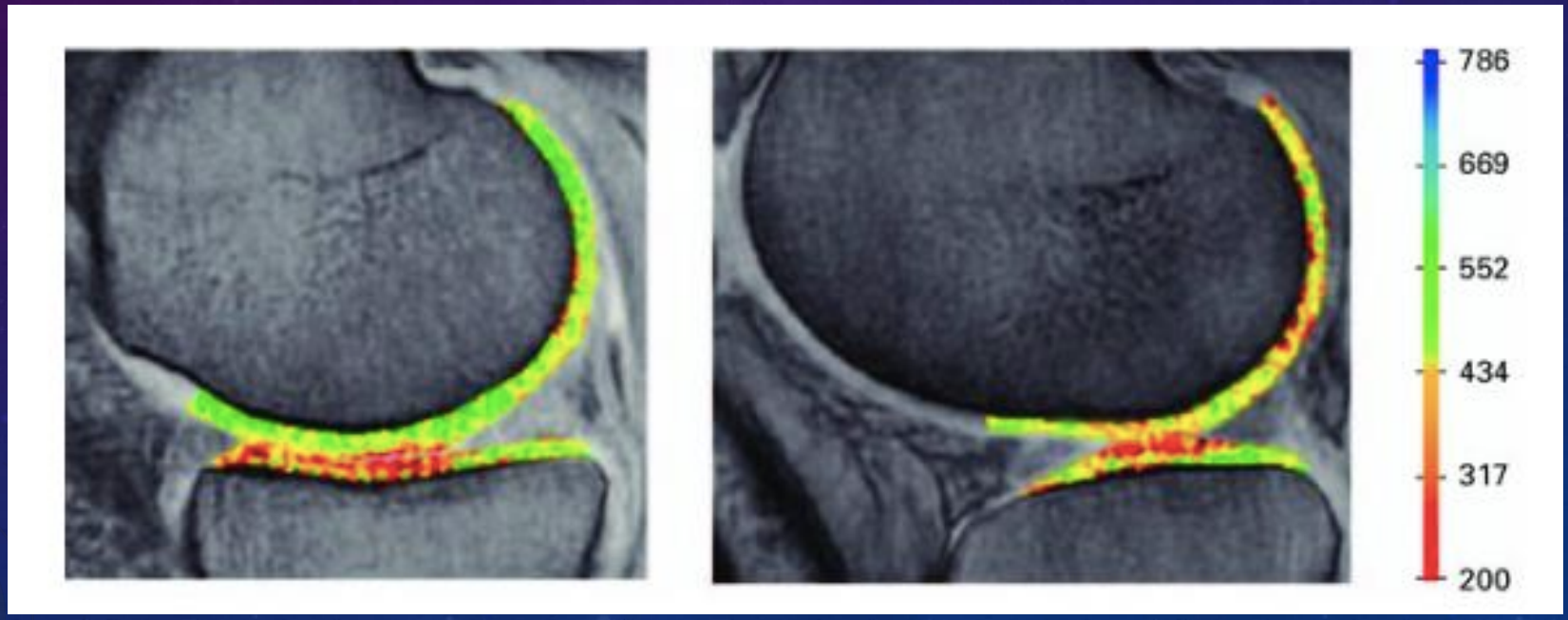
(FROM HEMKE 2014, EUROPEAN RADIOLOGY).



DELAYED GADOLINIUM-ENHANCED MRI OF CARTILAGE (DGEMRIC)

- Quantifies the composition of cartilage, particularly with respect to glycosaminoglycans (GAGs).
- Following intravenously administered negatively-charged anionic contrast agent (Gd-DTPA), contrast diffuses into cartilage in a dose-dependent manner but uptake is inhibited by the presence of GAGs, which are negatively charged.
- Thus, uptake of contrast is inversely related to GAG density.
- In healthy cartilage, GAGs are abundant.
- In GAG-depleted joints, such as those affected by arthritis, the net charge of the cartilage matrix increases, and contrast uptake increases.
- T1 relaxation time can be used to calculate the remaining cartilage GAG concentration expressed as the dGEMRIC index; a shorter dGEMRIC index indicates cartilage damage.

DGEMRIC SCAN OF THE KNEE SHOWING SLICES FROM THE MEDIAL (LEFT) AND LATERAL (RIGHT) COMPARTMENTS.
THE SCALE (MS) REPRESENTS THE DGEMRIC INDEX (T 1GD), THE COLOUR SCALE APPLIED TO THE IMAGE FACILITATES VISUAL INTERPRETATION.
HIGHER VALUES OF T 1GD REPRESENT INCREASED GLYCOSAMINOGLYCAN (GAG) CONTENT THE SCAN DEMONSTRATES THE PHYSIOLOGICAL REDUCTION IN CONCENTRATION OF GAG AS ONE MOVES FROM THE DEEP TO SUPERFICIAL CARTILAGE ZONES, PARTICULARLY CLEARLY FOR THE TIBIAL CARTILAGE OF THE LATERAL COMPARTMENT.
THE TIBIAL CARTILAGE OF THE MEDIAL COMPARTMENT DEMONSTRATES A RELATIVE DEPLETION OF GAGS ANTERIORLY COMPARED WITH POSTERIORLY, IN THE ABSENCE OF CHONDRAL EROSION, SUGGESTING EARLY ANTEROMEDIAL OSTEOARTHRITIS (IMAGE PROVIDED BY DR DEBORAH BURSTEIN, BETH ISRAEL DEACONESS MEDICAL CENTER, BOSTON).



LIMITATIONS

- The delay between injection of the contrast agent and the time of optimal imaging is long, substantially prolonging standard imaging protocols.
- The optimal time interval for imaging is unknown and delays of between 30 and 120 min have been described and it is likely that the interval influences the dGEMRIC index.
- Exercise probably accelerates cartilage uptake of contrast, but the size of this effect is unknown.
- Finally, there are no studies correlating the histopathological cartilage composition with dGEMRIC values in rheumatic diseases.

Thank you for your attention

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