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THE ROLE OF IMAGING IN KNEE PATHOLOGY: CURRENT STATE AND FUTURE PROSPECTS

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Abstract

Knee trauma account for the majority of the lesions of the knee and is an increasing cause of access to the ER in an international scenario where the common effort is to reduce the costs of healthcare . Despite being so common, trauma is not the only cause of knee-involving disease: tumor, hereditary disease, idiopathic illness and rheumatological conditions may affect this marvelous joint as well.While traditional diagnostic tools like x-ray or ultrasounds seems to have expressed their full potential already, more recent imaging techniques appear to offer unprecedent possibilities. The new aim of modern radiology is to wisely employ latest technologies available both as a complementary approach to older diagnostic method and as a springboard to new diagnostic horizons, combining clinical knowledge and laboratory findings to the imaging interpretation. In this study we tried to focus reader's attention toward classical radiological findings of well-known common, and not so common, disease while exploring the new fields that MRI is unveiling and that may seem to be extraordinary today but may become common and widely spread in just a few years.

Keywords: *Knee, MRI, labelling, baker cyst, state of art, future prospects*

Introduction

WHO identify Physical inactivity as the fourth leading risk factor for death in both developed and developing countries, nonetheless physical inactivity levels are rising in many places, with major implications for the general health of the global population [3]. Substantial changes in lifestyle and physical activity can be seen spreading from time to time in restricted areas, however, surprisingly, levels of inactivity are twice as high in high-income countries compared to low-income countries, moreover, insufficient activity levels increased by 5% in those counties between 2001 and 2016 and there has been no improvement in global levels of physical activity since 2001[4]. Despite those data, sports-related knee lesions represents the most common type of knee damage, accounting for 43.9% of total knee injuries, and are more commonly seen in patients 15 to 24 years of age [5], linking directly with increased physical competency [6]. Another 43,8% of injuries occur in the house, commonly in over 65 patients. Trauma is then the most common cause of knee pathology in young, adults and old patients and represent the main reason why they seek for medical assistance when affected by knee pain.

Background

Both the clinical practice of radiology and the imaging acquisition have had an enormous evolution throughout the last decades. Early descriptions of knee injuries appeared possible on radiographs only. Lately, magnetic resonance has deepened our understanding of the pathophysiology and pathological anatomy of those issues [7]. Knee damage assessment should always begin with a detailed history that can help narrow down the nature of the injury. Examination can be hard to perform in the acute setting and may need to be repeated 3 days after the first encounter with the patient. Fractures can usually be evaluated with plain X-rays but sometimes CT scan will be needed to confirm the diagnosis. MRI has a pivotal role in depicting soft tissue injuries that wouldn't be visible otherwise in both adults and children [8]. Ultrasound are seldom used and only to assess knee derangement. Management's aim is to reduce pain, resolve swelling and allow quadriceps activation. If there is a suspect of fracture, the use of radiography is first choice in adults with isolated knee pain [9].

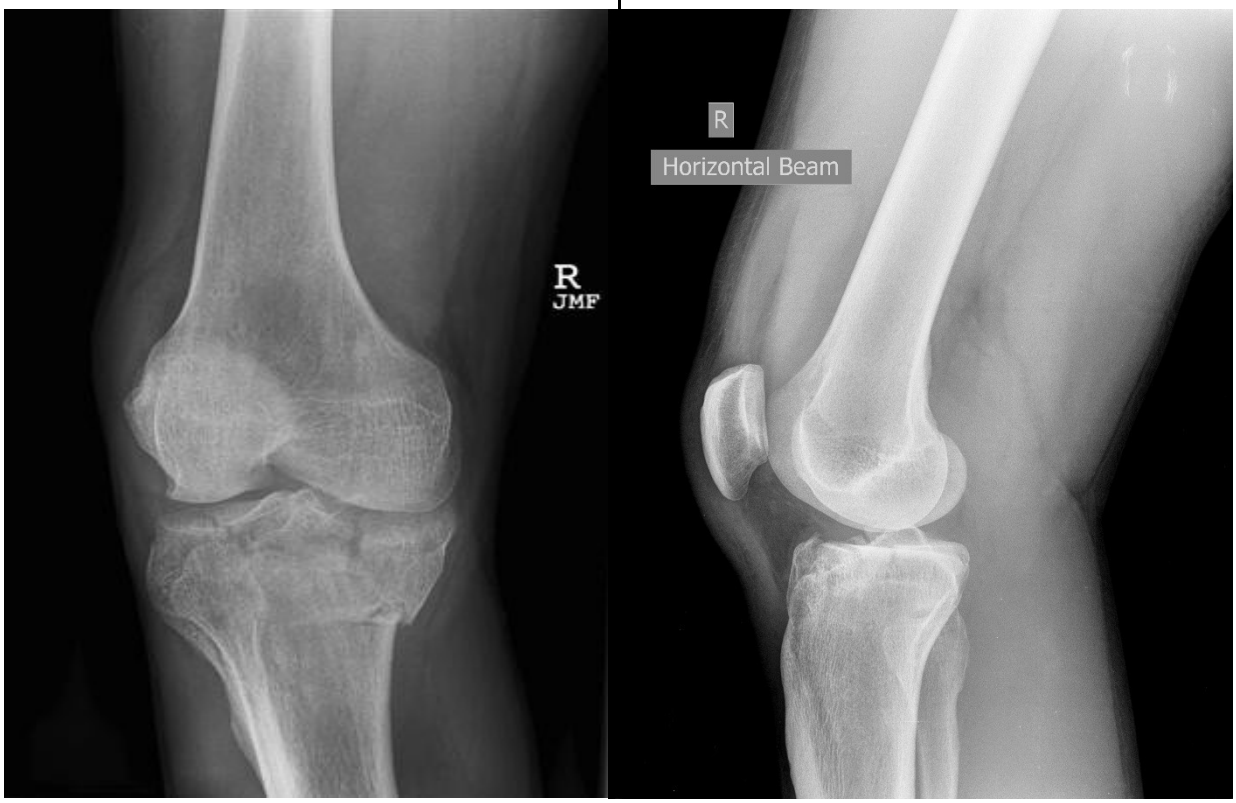
X-Ray

Plain radiogram is the eldest method used to assess traumatic knee injury. According to Ottawa rules physicians should ask for an x-ray imaging if one or more of these findings are encountered in knee trauma: 55 years of age or older; isolated tenderness of the patella; tenderness at the head of the fibula; inability to flex the knee to 90°; inability to weight bear (4 steps, unable to transfer weight twice onto each lower limb regardless of limping) [10]. In a regular knee x-ray the radiologist will report an uninterrupted bone profile without periarticular bone fragments, no subchondral density variations and a regular position of the tibial condyles that shouldn't go beyond the correspondent femoral condyle for more than 5 mm. Patella is usually clearly visible through the femoral bone [11]. The distance between the patella and tibial tuberosity should be equivalent to the patellar length itself in LL radiogram [12]. Beside classical traumatic injuries there are some uncommon findings that can guide us to specific pathologies., hereby briefly listed.

Tibial plate fracture

Tibial plate fracture usually appears after violent trauma like car crashes, fall or during sportive activities. Lateral plate fracture is four times more common than medial plate fracture and it's commonly associated with medial collateral ligament lesion. Every time there's an anamnestic suspicion for a tibial plate fracture, regardless if it's the medial or the lateral one, we should check for four different things: smooth bone profile with no stratification; no sub-chondral density augmentation that would be meaningful for a compression fracture; no tibial borders dislocation and, on LL radiograms, no clear appearance of a fat-fluid level [13]. This last radiographic sign is seen every time the over-patellar bag gets infiltrated by inflammatory fluid, causing an anterior dislocation of the pre-femoral adipose tissue.

Thickness of the peri-femoral fatty tissue is supposed to be less than 5 mm [14].



Case courtesy of Dr Victoria Ho, Radiopaedia.org, rID: 44857

Patellar sleeve avulsion fracture

Beside the common traumatic injuries of the kneecap, chondral or osteochondral avulsion injury may be sometimes encountered in clinical practice. Mostly located at the inferior pole of the patella usually this damage is subsequent to a sudden contraction of the quadriceps muscle, especially in young athletes [15], and can very seldomly involve the upper pole. This diagnosis could be life-changing because the displaced bone-forming tissue may continue to grow and ossify, enlarging, and sometimes duplicating the patella.

Case courtesy of Dr Benoudina Samir, Radiopaedia.org, rID: 77495

Segond fracture

Segond fracture is the name usually given to avulsion fracture of the knee associated with disruption of the anterior cruciate ligament (ACL) and of the lateral collateral ligament. This injury involves the lateral side of the tibial plateau in three of four cases [16]. Usually it's the result of internal rotation and varus stress and it's due to falling or sports damage. Orthopaedic disagree to some extent about the exact cause of this pathological entity, pointing out from time to time lateral capsular ligaments or the iliotibial band [17]. General consensus has been rising lately around the lateral meniscus [18] involvement which may be an excellent theoretical explanation but fail to be identified on MRI scan. The typical appearance of a Segond fracture is the detachment of a curvilinear or elliptic bone fragment from the lateral tibial cortical profile, usually seen right next to the lateral aspect of the tibial plateau. This has been referred to as the lateral capsular sign [19], best seen on the anteroposterior view of the knee.

Case courtesy of Dr Maulik S Patel, Radiopaedia.org, rID: 20287

Ultrasound

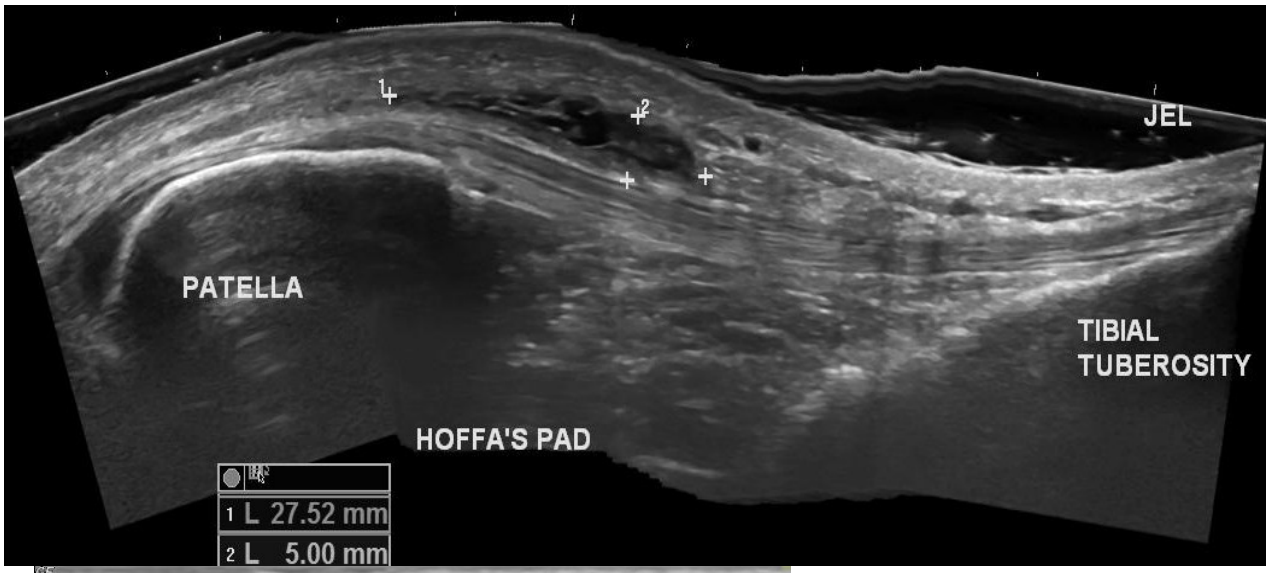
Ultrasound of the knee joint allows high-resolution imaging of superficial articular anatomy, consenting the evaluation, to some extent, of few of the tendons and ligaments. This imaging investigation method is poorly efficient when compared with similar examinations of other joints because the cruciate ligaments and the meniscus are usually hard, if not impossible, to visualize on ultrasound [20]. The US hold a niche role in the knee joint evaluation but its contribute is incredibly valid for some, very specific, pathological conditions.

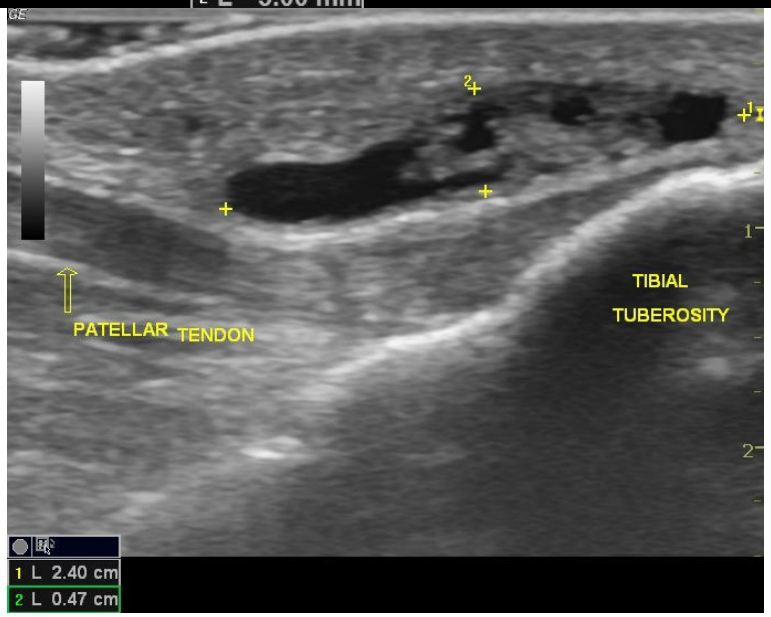
Patellar tendon rupture

Patellar tendon rupture is a common knee injury that follows high energy trauma in young people, involving almost invariably either the patellar or tibial insertion of the patellar tendon. Association with small avulsion fractures is not uncommon, usually involving the inferior pole of the patellar bone and should always be looked for in plain radiogram [21]. Complete rupture is easily identified thanks to the elevation of the bone (patella alta) associated with an increased Insall-Salvati ratio [22]. Commonly associated features are blurring of posterior margin of patellar tendon into the Hoffa fat pad and avulsion fracture. High-frequency linear transducer probe are recommended in order to obtain the best image quality. Normal tendon appears as a continuous hyperechoic structure with well defined borders. Hypoechoic tendon with interruption of the regular pattern have to be assessed to tendon rupture. Early surgical repair may be necessary to ensure good functional outcome [23].

Patellar bursitis

Inflammation of bursae around the insertion of the distal patellar tendon (clergyman's knee) or of the prepatellar bursa, (housemaid's knee). Usually associated with fluid collection and subcutaneous edema, the inflamed bursa may be superficial (anterior to the distal patellar tendon) or deep (posterior to the distal patellar tendon [24]. Main clinical features are knee pain and sweeling, which is easily detected both In MRI and US. Trauma and repetitive knee joint stress bring liquid accumulation in the bursa, sometimes linked with haemorrhagic damage. Seldomly infection, gout or auto-immune disease are responsible for this clinical pattern [25]. US quickly shows hypoechoic soft tissue swelling, contestually located debris, prepatellar soft tissue calcification. When haemorrhage occurs, the fluid signal appears to be more hyperechoic with hematinic spots. The wall of the bursa may show increased thickness and irregular profile [26]. A classic anti-inflammatory therapy is usually sufficient to get rid of the problem, using high doses of NSAID and Corticosteroids. Resistant cases are treated with open bursectomy [27].



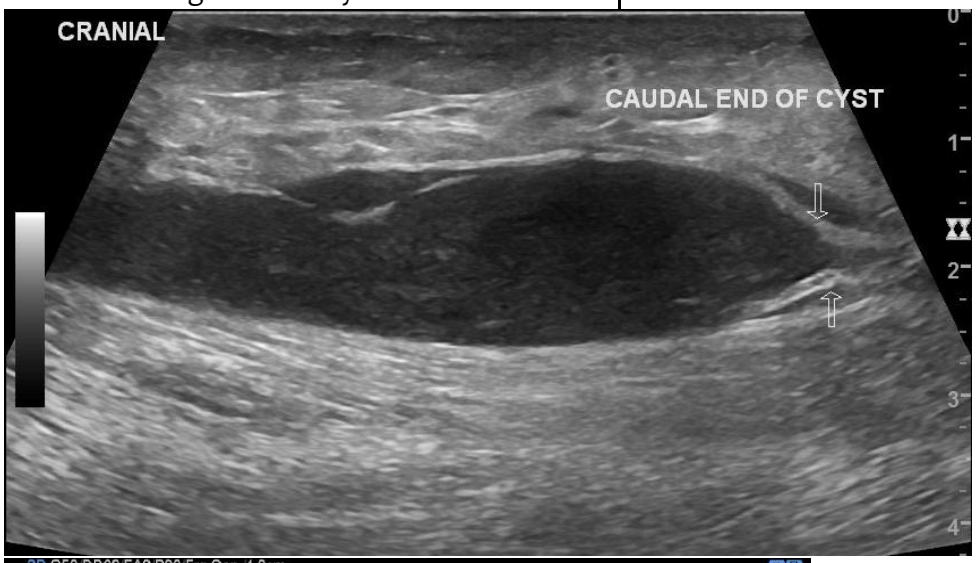


Case courtesy of Dr Maulik S Patel, Radiopaedia.org, rID: 72987 and Case courtesy of Dr Maulik S Patel, Radiopaedia.org, rID: 32224

Baker cysts

Also known as popliteal cysts, these are common fluid-filled synovial lesions arising in the popliteal fossa at 35-70 years[28] . Most commonly located between the medial head of the gastrocnemius and the semimembranosus tendons, they are not exactly a true cyst, as they occur as a communication between the posterior joint capsule and the gastrocnemius-semimembranosus bursa [29]. Usually, a Baker cyst is an incidental finding while performing knee's diagnostic imaging but symptomatic presentation may be acute when rupture occurs. Chronic/subacute presentation appear as as a popliteal fossa mass sometimes associated with pain. The pathological process that explain the onset of such disease is a valve-like connection between the knee joint and the gastrocnemius-semimembranosus bursa, resulting in fluid being pushed outward. US represents the first line imaging investigation [30]. Typical finding is a well-defined cyst with a narrowing at its deepest extent, if this 'neck' is not identified a proper diagnosis cannot be made, this has been referred to as shaped like a "speech bubble" or "talk bubble" [31] . Like all other cyst it is usually anechoic but may contain internal debris. In children, most of the popliteal cyst spontaneously resolve within 10-20 months

[32]. Aspiration may be useful, steroid injection is useful in reducing cyst size and improve pain. If the symptoms persist and/or the cyst is large, surgical excision is the last line option [33]. Rupture is a sudden event that allows the leaking of baker cyst's fluid into the popliteal fossa, the subsequent edema may cause compression of tibial nerve and popliteal vessel with sudden severe pain. In a few cases compartment syndrome may arise requiring immediate surgical therapy [34].



Case courtesy of Dr Alex Lim Tat Leong, Radiopaedia.org, rID: 71478 and Case courtesy of Dr Maulik S Patel, Radiopaedia.org, rID: 66675

Magnetic Resonance Imaging

MR provides the highest quality images when it comes to knee scanning, with no need for ionizing radiations, replacing long ago the conventional arthrography and plain radiography in the evaluation of the menisci and ligaments [35]. MRI allows excellent visualization not only of the bone structure of the knee but, maybe even more importantly, also of the soft tissues of the same region, in different orthogonal planes [36]. Thanks to its high spatial resolution and anatomical detail MR is now established as the diagnostic gold standard in various disease of the lower limb joint and may play a key role in all the disease described so far. Despite that, MR most exciting aspects involve new clever applications, some of the most intriguing ones are stressed out and listed below.

Metabolic syndrome and osteoarthritis

Osteoarthritis (OA) is among the commonest musculoskeletal disorder a physician will

encounter during worktime and an ordinary cause of disability [37]. Mechanical damage and aging process were, inevitably, considered the main reason for the arising numbers of this pathological condition in the first place. While ageing and trauma are certainly linked to knee

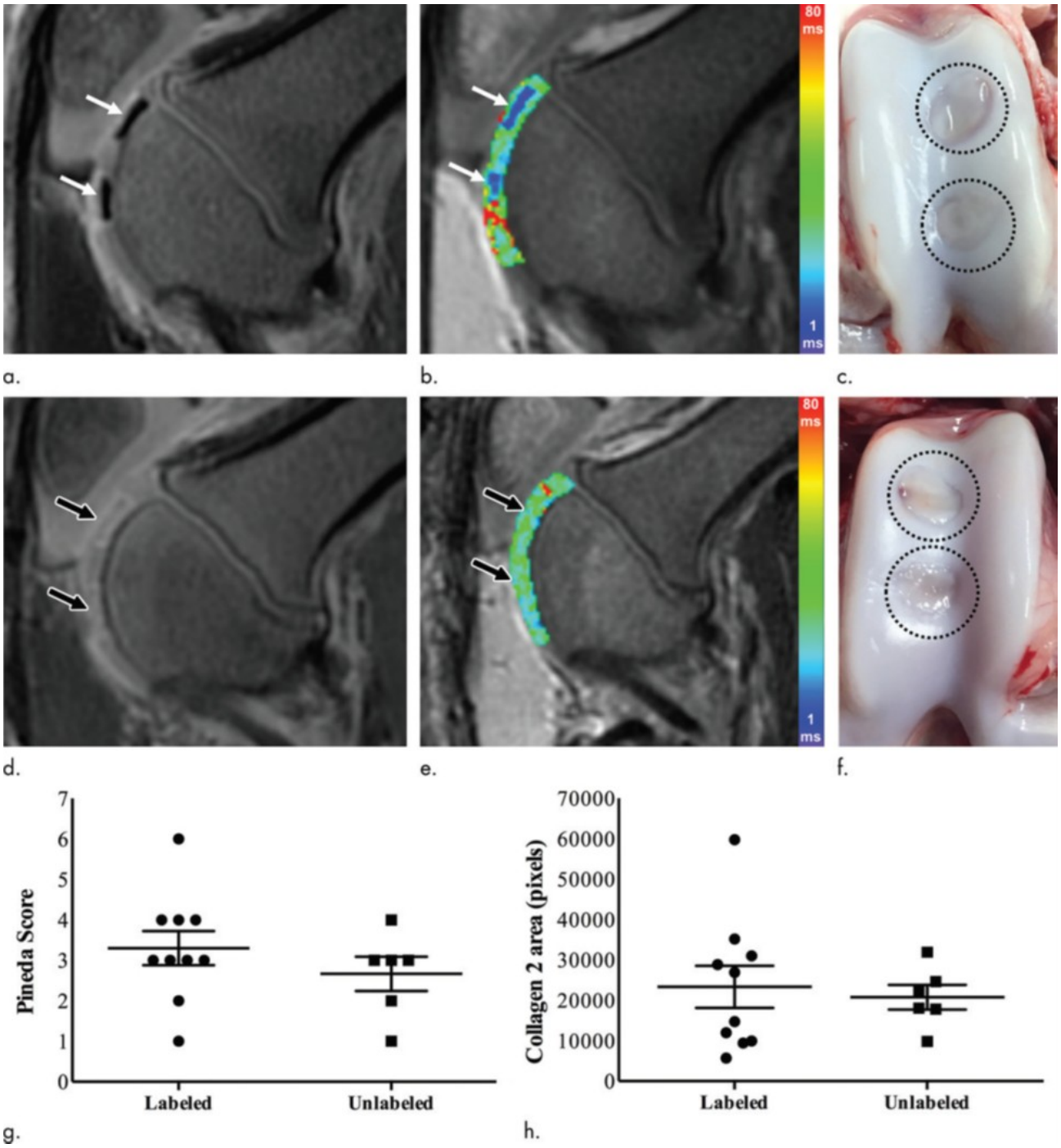
seems to be more challenging to explore because there is a blurred line that divide damage due to direct mechanical effect attributable to overweight and the one linked to the prostaglandins released by the fat tissue[41, 42]. New theories hypothesize a role of insulin resistance in synovium damage and of oxidized low-density lipoprotein in ectopic bone formation and cartilage damage [43]. MRI is a gold standard imaging technique in the assessment of knee osteoarthritic damage which allows punctual morphological evaluation and, sometimes, biochemical changes detection before a clinical onset is reported by the patient [44]. So far the MRI with contrast injection has been considered too expensive and too slow to be extensively used in everyday clinical practice despite the incredible advantages and the very few contraindications. Current OA score systems include an evaluation of the bone marrow, cartilage, ligaments, osteophytes and synovitis, combined with joint effusion [45]. Based on MR evaluation five different phenotypes have been proposed (inflammatory, meniscal, bone, hypertrophic and atrophic) each one has its proper specific characteristic but a certain overlapping between different phenotypes can be seen [46]. Inflammatory type is defined by joint effusion and synovitis; bone phenotype is characterized by large bone marrow lesions; meniscal phenotype comes quite obviously with meniscal damage or extrusion. Hypertrophic or atrophic phenotypes usually refers to the presence of osteophytes with cartilage damage, the former, or with cartilage loss, the latter, which is extremely rare [47]. Regardless the specific subtype of OA MetS and low HDL level strongly correlates with reduction of cartilage volume and bone marrow structural changes. These findings uncover the possibility of changing the disease evolution by modifying host's metabolic factors [48]. Recent studies found that, furthermore, MetS is also linked osteoarthritis new findings identify a pivotal role in systemic inflammation and in its causes like obesity and metabolic syndrome (MetS) [38,39]. This idea of a systemic regulation of localised inflammatory disease is not new to the medical field [40] but this particular scenario

with greater medial tibial cartilage volume loss and a higher number of bone marrow lesion in the same area [49]. The mechanism lipoproteins damage cartilage and bone tissue may be oxidation and deposit into cartilage itself, reducing blood supply to the knee joint and causing an intense inflammatory response [50]. Despite lipoprotein been directly involved in OA no findings suggest the same hypothesis for Hypertension or hyperglycaemia [51], nonetheless a higher number of components of MetS simultaneously found in the same patient seems to correlate with more severe cases of OA [52]. These studies may open up to new treatment possibilities and, to the author's knowledge are the first to link a specific biomarker, simply evaluated trough blood samples, with consistent pathological MR findings. While this article is being written more and more studies are moving toward the same direction , trying to connect imaging with biochemical findings.

Possible future use of MRI starts today

Trauma, degenerative pathologies, inflammatory condition and overuse pain involving the knee affects approximately 20% of all adults [53]. Damage of bones and cartilages do not heal fast and require the activation of bone marrow derived mesenchymal stromal cells (MSCs) which will differentiate into chondrocytes. Sometimes this process may be too slow or inefficient and the steam cells are directly provided by the surgeon in an attempt to repair an injured cartilage [54]. Ferumoxytol labelling of this cellular population may bring useful information, providing a persistent iron signal in the cartilage if there is a favourable repair outcome after matrix-associated stem cell implants (MASI) [55]. The underlying idea is to use the MRI to detect the signal intensity of

the treated knee to understand the outcome of our procedure [56]. Ferumoxytol is proven to be safe and is metabolized in 2 weeks [57] but seems to cause a limited blooming effect on MRI [58]. Up to date the time needed to detect a successful MASI at MRI range within months [59], when it's late to correct transplant failure. Early detection of an impending graft failure may be pivotal in planning and performing rescue interventions [60]. MSC used in MASI may be labelled with iron oxide nanoparticles to be tracked in vivo [61], this hasn't been made in human yet because of potential safety issue involving cartilage restoration process. Theruvath et al. performed MASI on cohorts of minipigs with ferumoxytol MSC labelling, showing that ferumoxytol labelling enables an early diagnosis of failing MASIs in full-thickness cartilage defects and confirmed that rapid disappearance of iron signal, therefore of iron - labelled MSCs from the transplant site is associated with poor cartilage repair outcomes. Apoptotic MSC lost their signal in a short amount of time while viable MSC keep providing iron signal for up to six weeks before getting phagocytosed by macrophages [62]. First differences between apoptotic MSC and viable cells were visible 2 weeks after the implant, persisted for at least 4 weeks but were not seen any more at 3 months [63]. It is still unknown if the MSC helps repairing process trough differentiation into chondrocytes or providing growth factors [64]. This fascinating imaging approach could soon become reality and spreads widely to detect early stage complication of organ transplantation.



Reprinted from: 60. Tracking Stem Cell Implants in Cartilage Defects of Minipigs by Using Ferumoxytol-enhanced MRI Ashok J. Theruvath, MD * • Hossein Nejadnik, MD, PhD* • Olga Lenkov, MSc • Ketan Yerneni, • ai Li, PhD • Lara Kuntz, PhD • Cody Wolterman, MSc • Jutta Tuebel, BSc • Rainer Burgkart, MD, PhD • Tie Liang, EdD • Stephen Felt, DVM • Heike E. Daldrup-Link, MD, PhD, Radiology

Functional imaging

Functional imaging refers broadly to the visualization of organ or tissue physiology using medical image modalities, like nuclear medicine. [65-67] Nuclear medicine imaging uses small amounts of radioactive material to diagnose, evaluate or treat a variety of diseases. [68-70] These include many types of cancers [71-73], metabolic, gastrointestinal, endocrine, or neurological disorders and other abnormalities. [74] Because nuclear medicine exams can pinpoint molecular activity, they have the potential to identify disease in its earliest stages. They can also show whether a patient is responding to treatment. [75]

Scintigraphy is a proven complementary modality to x-ray and MRI in many patients with postoperative knee pain. [76] Bone scintigraphy is especially favored bymany radiologists and orthopedists as a fast and easy wayto obtain an overview of areas with increased blood flowand bone metabolism. [77]

Three-phase Bone Scintigraphy (BS) displays perfusion, bloodpool and osteoblastic activity after knee surgery. BS enables combined assessment of bone remodeling around the prosthesis, mechanical alignment, component position, and structural changes. Bone scintigraphy can demonstrate changes in the subchondral bone during the evolution of osteoarthrosis. Histology of the subchondral bone in areas with increased tracer uptake shows increased vascularity and new bone formation. [78]

Nuclear medicine techniques can be helpful in differentiate aseptic from septic loosening before surgery.: a normal bone scan virtually excludes loosening, and combined imaging of bone marrow and 111In-labeled white blood cells is the current best practice for the assessment of suspected prosthetic infections. [79]

The use of SPECT-CT methodology with dedicated radiopharmaceuticals is established in imaging bone metabolism and postoperative management after prosthetic implantation. In periprosthetic fractures, SPECT/CT may be warranted to assess the fracture healing process and to detect nonunion, which is especially important in case of comminuted fractures to diagnose or exclude necrotic bone fragments. SPECT/CT offers vastly improved localization, increased accuracy, and only a very marginal extraradiation dose when scanning the postoperative knee. [80]

Conclusion

Knee pain held a key role in the quality of life of our patients and, despite remaining statical for decades, modern approaches may be life changing not only providing a pathway for the diagnostical process but also in detecting the disease even before the symptom's onset. New trends may open us to unprecedent possibilities, which will improve therapy success rate and provide global information about the patient well-being. It is mandatory to not start exploring those new discovered fields to benefit both medical science and our patients, therefore, further studies are needed.

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