Magnetic Resonance Imaging Bone Edema Is Not a Major Feature of Gout Unless There Is Concomitant Osteomyelitis: 10-year Findings from a High-prevalence Population

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ABSTRACT. ***Objective.*** Magnetic resonance imaging (MRI) is commonly used in autoimmune inflammatory arthritis to define disease activity and damage, but its role in gout remains unclear. The aim of our study was to identify and describe the MRI features of gout.

Methods. Over a 10-year period we identified patients with gout who underwent MRI scanning of the hands or feet. Scans were reviewed for erosions, synovitis, tenosynovitis, tendinosis, bone edema, and tophi by a musculoskeletal radiologist and 2 rheumatologists in a blinded manner. MRI features in patients with uncomplicated gout were compared with features where concomitant osteomyelitis was diagnosed.

Results. A total of 47 patients with gout (51 scans) were included: 33 (70%) had uncomplicated gout and 14 (30%) had gout complicated by osteomyelitis. MRI features included tophi in 36 scans (71%), erosions in 35 (69%), bone edema in 27 (53%), synovitis in 15 (29%), tenosynovitis in 8 (16%), and tendinosis in 2 (4%). Uncomplicated gout and gout plus osteomyelitis did not differ for most MRI features. However, "severe bone marrow edema" was much more common in gout plus osteomyelitis, occurring in 14/15 scans (93%) compared with 3/36 scans (8%) in uncomplicated gout (OR 154.0, 95% CI 14.7–1612, $p < 0.0001$). Sensitivity and specificity of "severe bone edema" for concomitant osteomyelitis were 0.93 (95% CI 0.68–0.99) and 0.92 (95% CI 0.78–0.98), respectively.

Conclusion. MRI reveals that gout affects the joints, bones, and tendons. Bone edema in patients with chronic tophaceous gout is frequently mild and this contrasts with the "severe bone edema" observed in patients with concomitant osteomyelitis. (First Release Oct 1 2011; J Rheumatol 2011;38:2475–81; doi:10.3899/jrheum.110477)

Key Indexing Terms:

GOUT | MAGNETIC RESONANCE IMAGING | TOPHUS
SYNOVITIS | BONE EDEMA | EROSION

Imaging in gout has traditionally been performed using plain radiographs. Characteristic findings include asymmetric soft tissue nodules, well-defined "punched out" erosions with overhanging edges, preservation of joint space, intraosseous calcifications, and lack of periarticular osteopenia. However, these changes often occur late and are associated with low sensitivity for a diagnosis of gout[1].

There has been recent interest in other imaging modalities in gout such as computed tomography (CT), dual-energy CT, ultrasonography, and magnetic resonance imaging (MRI). CT enables good visualization of intraarticular tophi and bone erosions and accurate determination of tophus size[2,3,4]. Dual-energy CT can be used to visualize subclinical tophi by color-coding urate deposits and to measure tophus volume[5]. Ultrasonographic features of chronic gout have been reported to include the double-contour sign, which is thought to represent crystalline precipitates of monosodium urate[6]. Tophi seen on ultrasound have been described as hypoechoic to hyperechoic inhomogenous material surrounded by a small anechoic rim[6,7].

MRI is now widely used as an imaging modality in autoimmune inflammatory arthropathies. A well-validated scoring system, the OMERACT-RAMRIS system[8], has been developed as an outcome measure for use in clinical trials. This system grades synovitis, bone erosion, and bone edema at the

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wrist and metacarpophalangeal joints of patients with rheumatoid arthritis (RA). The literature remains sparse regarding the MRI features of gout and the clinical utility of MRI in this setting. Tophi frequently appear as low signal intensity lesions on T1-weighted (T1w) images, and may have variable intensity on T2-weighted (T2w) images with near-homogenous enhancement after intravenous contrast[9,10]. Synovial pannus formation, joint effusions, soft-tissue edema, and bone marrow edema have also been described[10]. MRI has been used to detect subclinical features including tophi[11] and subradiographic bone erosions[12], and in assessing complications from tophaceous gout[9,13]. MRI has also been evaluated for measurement of tophi and it has been suggested that scans without gadolinium enhancement may be preferable for tophus measurement[14].

The aim of our study was to describe the MRI features of chronic tophaceous gout and determine whether these constitute a distinct set that may assist the diagnosis and management of patients with gout. We also investigated the MRI features of gout with concomitant osteomyelitis, and compared these with uncomplicated gout.

MATERIALS AND METHODS

Our study identified all patients with gout in the central Auckland (Auckland District Health Board) and South Auckland (Counties Manukau District Health Board) regions who had been investigated using MRI scans of hands or feet during the past 10 years. Recent data from the Auckland region has shown a high prevalence of gout, affecting 14.9% of Pacific men, 9.3% of Maori men, and 4.1% of European men[15]. This study was approved by the Northern X Regional Ethics Committee, Auckland.

Patients were included in the analysis if there was a diagnosis of gout based on the American College of Rheumatology diagnostic criteria[16] and they had undergone an MRI scan of the hands or feet. We used the radiology Picture Archiving Communication System to identify patients. The search used the following keywords: gout, MRI hand/wrist, and MRI ankle/foot. This search included both inpatient and outpatient populations. In patients with more than 1 MRI scan, the latest scan was selected if the scans were performed within the same clinical presentation. However, if the MRI scans were performed for a different clinical presentation, both scans were included in the analysis. Clinical details recorded included indications for the scan and clinical features of gout at the time of the scan including presence of tophi, serum urate, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). Data regarding the presence of osteomyelitis were obtained based on documented clinical findings, white blood cell count, and inflammatory markers (CRP/ESR) plus bacteriological confirmation in a subgroup.

MRI scans. All MRI scans were performed on a 1.5-Tesla scanner (Siemens or Siemens Avanto, Erlangen, Germany) with a dedicated wrist coil (Siemens) in the case of upper limb scans. Of the 51 MRI scans, 30 included sequences taken after injection of intravenous gadolinium diethylenetriamine pentaacetic acid (Gd-DTPA).

All MRI scans were reviewed by a musculoskeletal radiologist (AD) and 2 rheumatologists (ND, FMM) who were blinded to the clinical history. Features were scored by consensus. The MRI features recorded were as follows: presence of bone edema, bone erosion, synovitis, tenosynovitis, tendinosis, and tophus. Bone marrow edema on MRI was defined as a lesion within trabecular bone with ill-defined margins and demonstrating low signal intensity on T1w images, increased signal intensity on T2w images, and enhancement with contrast. We graded the severity of bone edema as follows: Grade 0 (no bone marrow edema); Grade 1 (mild/moderate edema), defined as involvement of < 50% of bone; or Grade 2 (severe edema), defined as involvement of > 50% of bone. Bone erosion was defined as a sharply marginated bone lesion with loss of normal low signal intensity of cortical bone and loss of normal high signal intensity of trabecular bone on non-fat suppressed T1w images. Synovitis was defined as an area in the synovial compartment that showed enhancement with contrast, with a thickness greater than the width of the normal synovium. Tenosynovitis was scored if there was tendon sheath fluid, thickening, and/or enhancement postcontrast. Tendinosis was defined as thickening of the tendon associated with contrast enhancement. Tophi were defined as amorphous and sometimes nodular regions of low signal intensity on T1w images, variable intensity on T2w images, and variable, patchy enhancement after intravenous contrast. Tophi were recorded as intraarticular, subcutaneous, or intratendinous.

Statistical analysis. Data were analyzed using GraphPad Prism (v5, GraphPad Software, San Diego, CA, USA). Clinical data are presented as median (range) or as percentages. Differences between the uncomplicated gout and concomitant osteomyelitis groups were analyzed using contingency tables. A value of $p < 0.05$ was considered significant. Subgroup analyses were performed to investigate whether results were influenced by bacteriological confirmation of osteomyelitis, use of intravenous contrast on MRI scanning, or ethnicity.

RESULTS

Patient characteristics. Using the search criteria, a total of 47 patients were identified. There were 43 men (92%). The majority of the patients (51%) were of Pacific or Maori ancestry. There were 13 (28%) patients with aspirate-proven gout and 20 (43%) patients with visible subcutaneous tophi at the time of the MRI examination. Twenty-six patients (55%) were taking allopurinol, 17 (33%) colchicine, 6 (12%) nonsteroidal antiinflammatory drugs, and 4 (8%) prednisone at the time of the MRI scan. Patients' clinical details are shown in Table 1. In 33 patients (70% of total group), a diagnosis of uncomplicated gout was made. In 14 patients (30%), a diagnosis of gout and concomitant osteomyelitis was made and of these, bacteriological confirmation of osteomyelitis was obtained

Table 1. Patient characteristics.

Characteristics	
Age, yrs, median (range)	63.3 (35–91)
Male, n (%)	43 (92)
Ethnicity, n (%)	
Caucasian	20 (43)
Pacific	18 (38)
Maori	6 (13)
Fijian	1 (2)
Indian	2 (4)
Disease duration, yrs, median (range)	7.5 (1–31)
Presence of tophi, n (%)	20 (43)
Aspirate-proven gout, n (%)	13 (28)
Allopurinol use, n (%)	26 (55)
Colchicine use, n (%)	17 (33)
Nonsteroidal antiinflammatory drug use, n (%)	6 (12)
Prednisone use, n (%)	4 (8)
CRP, mg/l, median (range)	54.75 (< 1.0–442)
ESR, mm/h, median (range)	60.0 (4–138)
Serum urate, mmol/l, median (range)	0.49 (0.26–0.78)
White cell count, $\times 10^9$/l, median (range)	8.30 (4.59–53.00)

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

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in 6 (43%). In the group with concomitant osteomyelitis, MRI scans were performed at presentation prior to the commencement of antibiotics in 8 patients, and in the others, scans were obtained after diagnosis while patients were receiving intravenous antibiotics (at 4–14 days after commencing treatment).

MRI scans. There were 51 MRI scans identified; 37 were of the foot/ankle region and 14 the hand/wrist region. MRI scans were most frequently requested in these patients because of clinical suspicion of osteomyelitis (49%). Other indications for scans are listed in Table 2. There were 2 MRI scans performed in the nonacute setting, both prior to elective surgery. One had no synovitis, whereas another had mild synovitis demonstrated on MRI.

MRI features in patients with uncomplicated gout. MRI features for the group of patients with uncomplicated gout are described in Table 3. In this group, the majority of MRI scans, 23/36 (64%), had no evidence of bone marrow edema. There were 10/36 (28%) scans demonstrating mild-moderate bone marrow edema (Figure 1A, 1B). More than half the MRI scans demonstrated erosions (64%) and tophi (67%), with 31% demonstrating synovitis. In this group, intraarticular tophi were seen in almost half the scans (47%; Figure 2), and there were 4 scans (11%) that showed intratendinous tophi. All intratendinous tophi were observed in the flexor tendons of the hands (Figures 3 and 4). In our series, 3 of the imaged tophi were subsequently excised and histologically confirmed to be tophi. There were 6 scans (17%) with tenosynovitis involving the flexor tendons of the hands, tibialis anterior tendon, peroneal longus tendon, and Achilles tendon. Tendinosis was found in 2 MRI scans (6%; at the Achilles tendon and peroneus brevis tendon).

MRI features in patients with concomitant osteomyelitis. The MRI features for the group of patients with concomitant osteomyelitis are described in Table 3. Most scans from these patients (93%) demonstrated bone edema and in all cases this was "severe bone edema" with > 50% involvement of the bone (Figure 1C, 1D). The majority of scans also demonstrated erosions (80%) and tophi (80%). Tenosynovitis was seen in 2 MRI scans involving the extensor tendons of the hands, tibialis anterior, extensor digitorum longus, the peroneal longus tendon, and tibialis posterior. "Any bone edema" and "severe bone edema" were observed more frequently in patients with concomitant osteomyelitis than in those with uncomplicated gout (Table 3). The sensitivities of "any bone edema" and "severe bone edema" for concomitant osteomyelitis were 0.93 (95% CI 0.7–1.0) for both (Table 4). Specificities for "any bone edema" and "severe bone edema" for concomitant osteomyelitis were 0.64 (95% CI 0.5–0.8) and 0.92 (95% CI 0.8–1.0), respectively. In contrast, there were no significant differences between the 2 groups with respect to other MRI features or laboratory results including CRP, ESR, and white blood cell count (data not shown).

Because MRI findings might have influenced the diagnosis of concomitant osteomyelitis in patients where there was a typical clinical picture but no bacteriological confirmation, a subgroup analysis was performed using data only from those where there was bacteriological confirmation of osteomyelitis. "Any bone edema" and "severe bone edema" remained much more common in this group than in those with uncomplicated gout (OR 22.6, 95% CI 1.2–434.1, p = 0.0052; and OR 124.4, 95% CI 5.7–2709, p < 0.0001, respectively). We also investigated for an effect of ethnicity on the results of the analysis and found none (data not shown).

Table 2. Clinical indications for MRI scan.

Indication	No. MRI scans (%)
Clinical suspicion of osteomyelitis	25 (49)
Persistent pain	11 (21)
Mass/nodule	6 (12)
Nonhealing ulcer	6 (12)
Ruptured tendon	1 (2)
Flexion contracture	1 (2)
Preparation for carpal tunnel surgery	1 (2)

MRI: magnetic resonance imaging.

Table 3. MRI features in uncomplicated gout and gout with osteomyelitis.

	Uncomplicated Gout, n = 36 Scans (%)	Gout and Concomitant Osteomyelitis, n = 15 Scans (%)	OR (95% CI)	p
Any bone edema	13 (36)	14 (93)	24.8 (2.9–210.6)	0.0002
Severe bone edema	3 (8)	14 (93)	154.0 (14.7–1612)*	< 0.0001
Erosions	23 (64)	12 (80)	2.3 (0.54–9.5)	0.33
Synovitis	11 (31)	4 (27)	1.01 (0.26–4.0)	1.0
Tenosynovitis	6 (17)	2 (13)	0.77 (0.14–4.3)	1.0
Tendinosis	2 (5.6)	0 (0)	0.45 (0.02–9.8)	1.0
Tophi				
Intraarticular	17 (47)	10 (67)	2.2 (0.64–7.9)	0.23
Subcutaneous	3 (8)	2 (13)	1.7 (0.25–11.3)	0.62
Intratendinous	4 (11)	0 (0)	0.23 (0.01–4.6)	0.31

* Statistically significant. MRI: magnetic resonance imaging.

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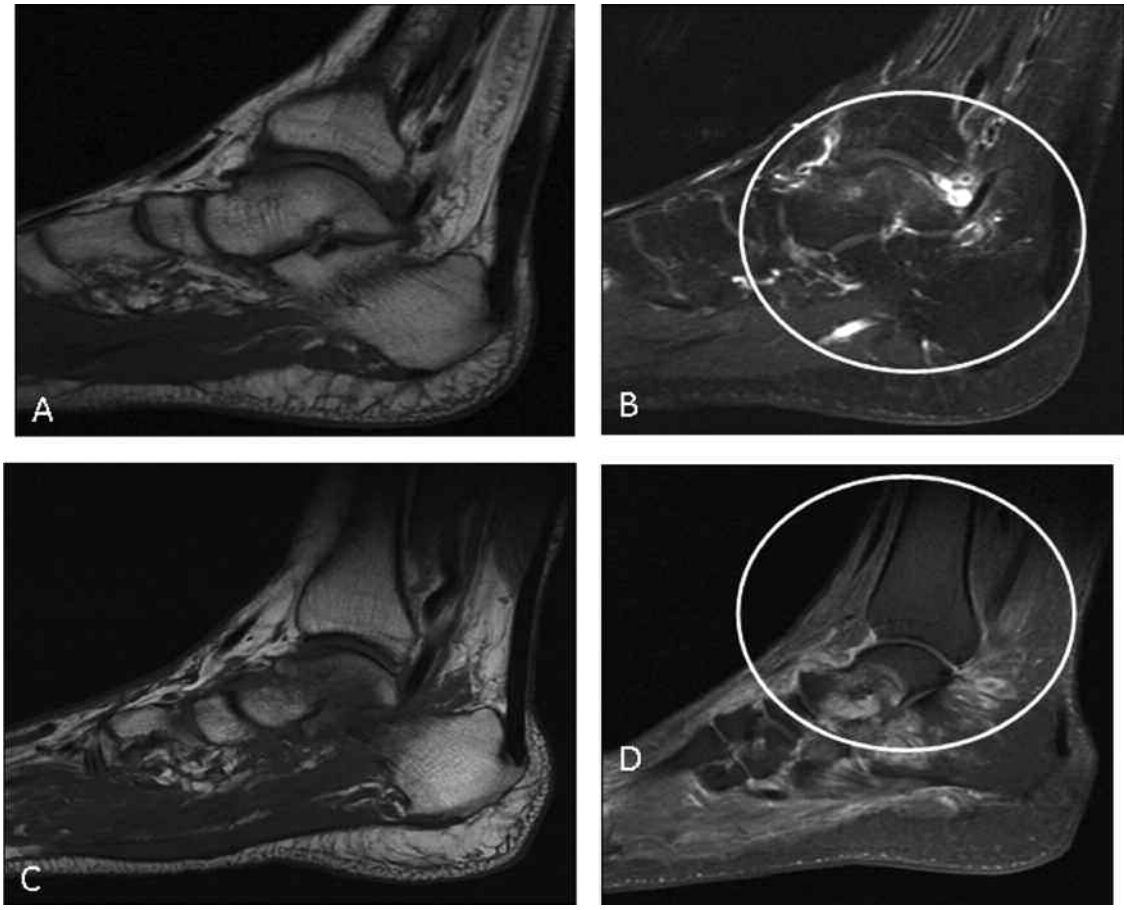

Figure 1. A. Precontrast and B. postcontrast sagittal T1w MRI scans of the ankle in uncomplicated gout (aspirate-proven for crystals but no growth on culture), showing low-grade synovitis at the ankle joint and very minimal bone edema within the talus. C. Precontrast and D. postcontrast scans from a patient with gout complicated by osteomyelitis (*Staphylococcus aureus* from culture and monosodium urate crystals present in synovial fluid) showing florid bone edema at the talus and adjacent soft tissues.

About half the MRI scans in this dataset were performed without intravenous gadolinium-based contrast. Subgroup analysis of those patients without contrast-enhanced scans showed findings similar to the analysis of the entire group; the OR for the presence of "any bone edema" was 31 (95% CI 1.3–747.6, p = 0.015) and for the presence of "severe bone edema" it was 259 (95% CI 4.4–15,380, p = 0.008).

DISCUSSION

Imaging is becoming increasingly important in rheumatology, with applications in inflammatory arthritis ranging from assisting diagnosis to monitoring disease activity and damage and to predicting prognosis. Advanced imaging in gout remains in its infancy, with most textbooks documenting only the typical changes visible on plain radiography. These occur late and are an insensitive measure of joint pathology. Newer imaging modalities such as CT, dual-energy CT, and MRI are far more sensitive than radiographs, partly because of their tomographic capacity and partly because they have the potential to provide new insight into the pathological processes underlying this condition. Recent studies from our group using CT scanning have confirmed the strong association between tophi and erosions[3,17] and allowed volumetric measurements of tophi to be developed[4]. Tophi have clinical relevance as longterm control of serum urate levels (< 0.36 mmol/l) reduces tophus size and recurrent gouty flares[18]. Hence, measurement of tophus size is likely to be an important outcome measure in trials of urate-lowering therapy. A recent literature review summarized 8 methods of tophus measurement used in clinical trials and reported that physical measurement techniques and ultrasound fulfill the major aspects of the OMERACT filter[19].

MRI is widely used as an imaging modality in other autoimmune inflammatory arthropathies. A well-validated quantitative MRI scoring system, OMERACT-RAMRIS[8], has been developed for RA. However, there is much less literature regarding the MRI characteristics of gout or their clinical utility. MRI reveals important information about joint inflammation in gout as it can demonstrate synovitis, tenosynovitis, and bone edema, none of which can be visualized on CT scans or radiographs. In addition, joint destruction including bone erosion[11,12] and loss of cartilage can be visualized. MRI allows a

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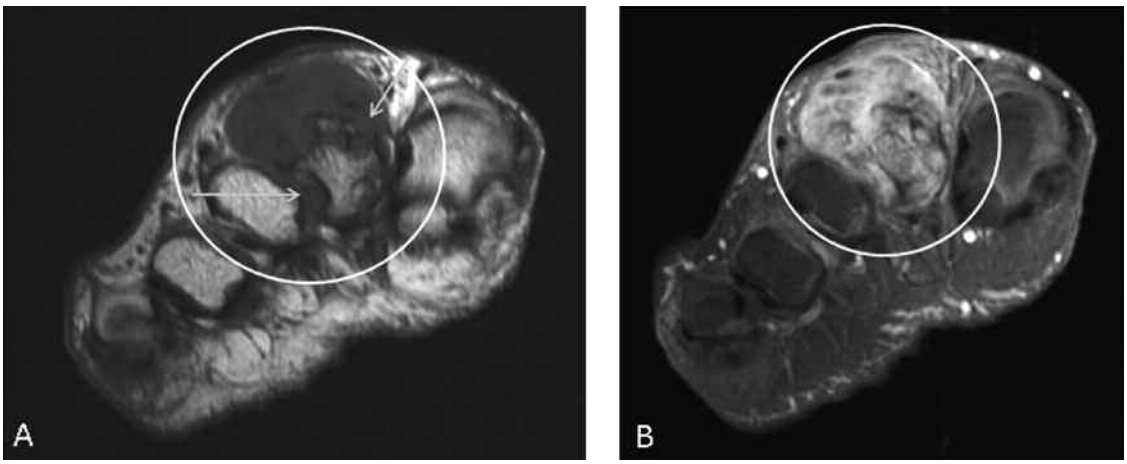

Figure 2. A. Precontrast and B. postcontrast axial T1w MRI scans of the forefoot in uncomplicated gout (aspirate-proven for monosodium urate crystals), showing a large tophus involving the head of the 2nd metatarsal. The tophus enhances with contrast and there are associated erosions (arrows) directly adjacent.

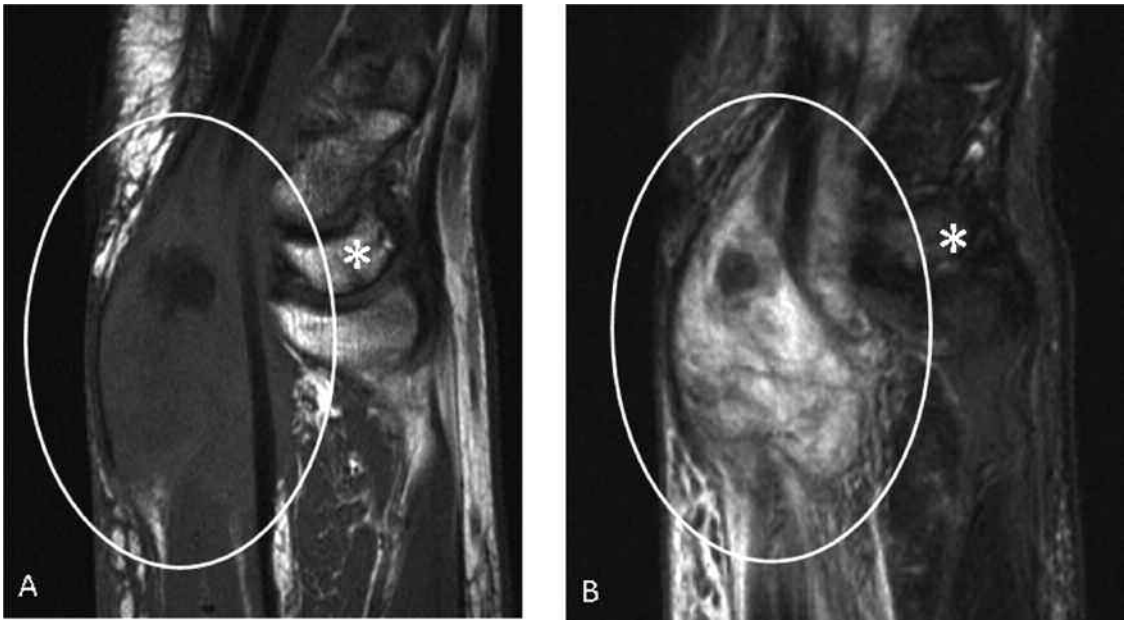

Figure 3. A. Precontrast and B. postcontrast sagittal T1w MRI scans of the wrist in uncomplicated gout (asterisk defines the scaphoid as a point of reference). There is a large tophus involving the flexor tendons that enhances postcontrast. There is a central nonenhancing area that may represent a region of calcification.

different view of tophi, revealing signal change and contrast-enhancement that reflect the inflammatory status of granulomatous tissue within and surrounding these crystalline lesions[9,10]. MRI has been evaluated for measurement of tophus volume, and good intrareader reliability was reported[14].

We report the largest review to date of the MRI features of gout, gathered over the past 10 years from 2 major tertiary rheumatology centers in the Auckland area of New Zealand. As there is a high prevalence of severe erosive and tophaceous gout in Maori and Pacific New Zealanders, these groups were overrepresented in the population studied. This raises the question of whether ethnicity might influence MRI findings. Bone density, for example, has been shown to be higher in Pacific people[20], but there are no reports of MRI features of inflammatory joint disease varying according to ethnicity. Subgroup analysis of different ethnic groups did not alter our major findings, suggesting that ethnicity does not have a significant effect.

As would be expected in a group with severe and often longstanding gout, we found 71% to have tophi and 69% to have erosive disease. The tophi varied in terms of T2w signal intensity and postcontrast enhancement, as described by others[9,10]. The majority were intraarticular or subcutaneous, but 4 examples of intratendinous tophi were documented, one of which led to presentation with tendon rupture, as depicted in Figure 4C. Intratendinous tophi are rare and predominantly

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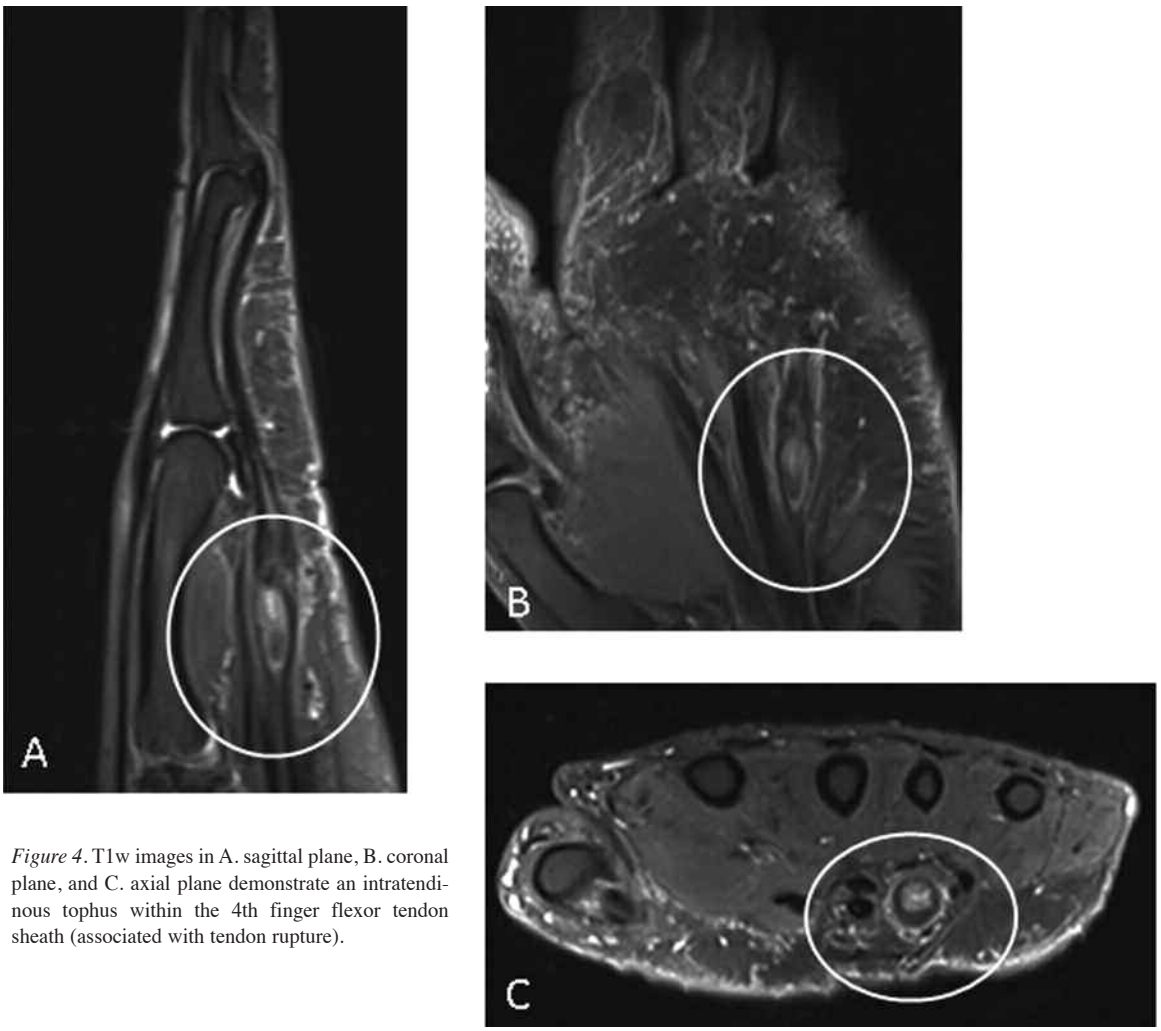

Figure 4. T1w images in A. sagittal plane, B. coronal plane, and C. axial plane demonstrate an intratendinous tophus within the 4th finger flexor tendon sheath (associated with tendon rupture).

Table 4. Sensitivity and specificity analysis of bone marrow edema for concomitant osteomyelitis.

	Severe Bone Marrow Edema (95% CI)	Any Bone Marrow Edema (95% CI)
Sensitivity	0.93 (0.68–1.0)	0.93 (0.68–1.0)
Specificity	0.92 (0.78–0.98)	0.64 (0.46–0.79)
Positive predictive value	0.82 (0.57–0.96)	0.52 (0.32–0.712233)
Negative predictive value	0.97 (0.85–1.0)	0.96 (0.79–1.0)
Likelihood ratio	11.2	2.585

affect the extensor tendons of the fingers and flexor tendons of the wrist[21].

We found MRI evidence of all the described features of inflammatory arthritis, with bone marrow edema occurring in half of the MRI scans, synovitis in about one-third, tenosynovitis in 16%, and tendinosis in 2 MRI scans. This contrasts with findings in RA, where synovitis has been reported to occur in 90%[22], suggesting that this feature may be considerably less common in chronic tophaceous gout. However, our data were obtained retrospectively, so we were unable to analyze the relationship between MRI synovitis and clinical evidence of joint inflammation. Moreover, while the majority were scanned during acute episodes (of gout and/or osteomyelitis), 2 patients were scanned during the intercritical period. Thus, further prospective studies would be needed to determine whether MRI synovitis is indeed less frequent in gout than in RA. Also, almost half the MRI scans in our series were performed without intravenous gadolinium, potentially contributing to the lower frequency of synovitis detected.

The MRI bone edema findings presented here are of particular interest. Clearly, bone edema is common in bone and joint infection and it was scored as "severe" in 93% of those with concomitant osteomyelitis, compared to 8% in those with uncomplicated gout. Our group was enriched for patients with concomitant osteomyelitis, as the indication for many of the MRI scans was to investigate for superimposed infection. Finding florid MRI bone edema could have swayed the clinician toward a diagnosis of osteomyelitis when culture results were negative or unavailable. To investigate this possibility, we reanalyzed data from the group in which there was bacteriological confirmation of osteomyelitis, and our major find-

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ings did not change. Thus, our results suggest that florid MRI bone edema is more consistent with a diagnosis of gout with osteomyelitis than that of uncomplicated gout.

Bone edema was surprisingly uncommon in those with uncomplicated gout, with 23/36 (64%) having none at all and the remainder being scored as "mild" only. This suggests that bone edema may be a much less important feature of gout than, for example, of RA, where it occurs in around 60% of patients and has been shown to be a pre-erosive change[22,23]. The histopathological correlate of bone edema has been investigated in RA, where it represents an infiltrate of lymphocytes, plasma cells, macrophages, and osteoclasts[24]. In osteoarthritis, sites of bone edema on MRI scans have been shown to contain foci of necrotic material as well as fibrosis and areas of vascularization extending into overlying cartilage[25]. The histopathology of bone edema in gout remains unknown, although the presence of increased signal on T2w images implies the presence of H+ ions usually contained within cells or vessels. However, the interesting aspect of our findings is that while erosions and tophi were common and severe in these patients, bone edema was disproportionately uncommon and mild. Thus, the link between bone edema and erosion proven in RA seems unlikely to hold in gout, suggesting a very different mechanism of bone damage in the 2 conditions.

The MRI features described here could represent a platform for future development of a quantitative MRI scoring system in gout. Our analysis has illustrated that bone marrow edema is relatively uncommon in uncomplicated gout, and much more common and severe in those with concomitant osteomyelitis. Thus, MRI scanning has an important role in the investigation of patients with gout and in particular in helping diagnose superadded bone infection.

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