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SCIENTIFIC ARTICLE

Can effusion-synovitis measured on ultrasound or MRI predict response to intra-articular steroid injection in hip osteoarthritis?

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Abstract

Objectives Intra-articular steroid injection (IASI) is an effective therapy for hip osteoarthritis (OA), but carries risks and provides significant pain relief to only two thirds of patients. We attempted to predict response to IASI in hip OA patients using baseline clinical, ultrasound, and MRI data.

Methods Observational study of 97 subjects with symptomatic hip OA presenting for IASI. At baseline and 8 weeks we obtained hip MRI, grayscale and Doppler ultrasound, clinical range of motion (ROM), timed-up and go test (TUG) scores, and self-reported Western Ontario and McMaster Universities Osteoarthritis (WOMAC) pain, stiffness, and function scores. Bone-capsule distance (BCD) measurements of inflammation on hip ultrasound and MRI were measured at three locations: the proximal-most uncovered portion of the femoral head, the superficial-most (apex) portion of the femoral head, and the largest fluid pocket at the femoral neck.

Results Ultrasound and MRI BCD correlated with each other significantly and strongly at the apex and neck. Power Doppler findings did not correlate significantly with any other imaging indices. Eight weeks post-injection, WOMAC pain, function, and stiffness scores significantly improved and TUG time improved nearly to the level of significance, but there were no significant changes in ultrasound, MRI, or Doppler indices. Baseline variables were not significantly different between responder and nonresponder WOMAC pain or TUG time cohorts.

Conclusion Basic measures of inflammation on ultrasound and MRI are highly related to each other, but provide little insight into patient function and pain after IASI. Other mechanisms to explain improvement in patient status after IASI are likely at work.

Keywords Osteoarthritis · Corticosteroids · Ultrasonography · Magnetic resonance imaging

Introduction

Hip osteoarthritis (OA) is common and debilitating [1], affecting 8.5% of Canadian adults [2]. Because the hip is a deep joint, diagnosis and management of hip OA can be difficult [3, 4], giving an opportunity for imaging to provide patient-specific insights to optimize treatment.

Intra-articular steroid injection (IASI) has been shown to be highly effective for short-term hip OA pain management [5, 6], potentially superior to other treatments [7, 8], but one third of IASI-treated hip OA patients have no significant pain relief [5]. IASI also has adverse effects, including a 2–3% rate of avascular necrosis (AVN) [9], and a probable increased risk of infection in subsequent arthroplasty [10, 11]. Attempts to predict which hip OA patients will respond to IASI have had inconsistent results [8, 12–14].

Ultrasound is emerging as a tool for evaluating hip OA, particularly for visualizing inflammation [15]. Benefits of ultrasound include low cost [16] and detailed visualization of soft-tissue structures [17]. The few studies on ultrasound in hip OA have conflicting results. Some found that ultrasound features correlated significantly with pain [18] and response to IASI [17, 19], whereas others found no significant utility of ultrasound [14]. Challenges include difficulty acquiring images

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in obese patients, inconsistent scoring systems, limited power and sample size, and a lack of a comprehensive approach. Synovitis and effusion on ultrasound are typically scored as bone–capsule distance (BCD) at the anterior femoral neck using a 7-mm threshold [17, 19–21]. Others have attempted different threshold values [18] or qualitative or categorical measurements for effusion-synovitis [14, 17]. However, no studies to our knowledge have attempted to measure at other locations along the hip joint on ultrasound. We found recently that hip BME was much more reliably measured in the femur than in the acetabulum [22]. We suspected that similarly, the physical meaning and reliability of measurement of joint effusions would also depend on the location where these are measured. We predict that measuring at multiple locations would provide a more complete evaluation of both effusion, which pools in the femoral neck region, and synovitis, which is likely better represented along the apex. There are also no studies that have verified the utility of ultrasound against an imaging gold standard, such as magnetic resonance imaging (MRI) for hip OA. Although costly and unsuitable for high-volume screening, MRI provides exquisite soft-tissue visualization. No study to our knowledge has comprehensively evaluated findings in multiple imaging modalities and physical examination maneuvers to predict response to IASI in hip OA.

Therefore, we sought to predict the response of hip OA patients to IASI using a comprehensive baseline clinical and imaging data set, including ultrasound and MRI. We assessed relations between ultrasound/MRI findings of active inflammation, demographic characteristics, self-reported pain/disability, and physical examination findings. We also determined the reliability of each imaging feature.

Materials and methods

Participants

With approval from the University of Alberta Health Research Ethics Board (approval #Pro00039139), patients in the Edmonton region with hip OA who were referred from various health practitioners to the central bookings of a large community radiology group (between 30 September 2013 to 14 December 2015) for IASI were approached to participate in the study. The patients included were aged 18 years or older, met American College of Rheumatology criteria for symptomatic hip OA [1], were on stable analgesic doses for 2 weeks pre-IASI, and provided written informed consent. We excluded patients unable to receive IASI (e.g., because of allergy or prior avascular necrosis), involved in a legal/compensation claim, had undergone IASI of the same hip within the previous 3 months, had known systemic inflammatory arthropathy, or were on oral/IV steroid treatment. Of 120 willing patients, 97 were eligible to participate. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

Data collection

This is an observational cohort study carried out in Edmonton, Canada, comparing clinical and radiographic features of responders and nonresponders pre- and post-IASI. Study participants were assessed at baseline (day of IASI) and 8 weeks post-injection. Baseline measures included patient characteristics, clinical evaluation, diagnostic imaging (X-ray, MRI, ultrasound), self-reported pain/disability using disease-specific questionnaires, and performance-based physical function. All procedures except radiographs were repeated 8 weeks post-injection (Fig. 1). All physical function tests were performed by physiotherapists.

Patient characteristics: included age, sex, weight, height, and body mass index (BMI). We assessed for comorbid conditions at baseline, including the presence of back pain, diabetes, and smoking.

Self-reported pain and physical function: participants completed the visual analogue scale (VAS) version [23] of the Western Ontario and McMaster Universities Arthritis Index (WOMAC) questionnaire at weeks 0 and 8. WOMAC captures information on three domains: pain, stiffness, and physical function [24].

Measures of physical function included the timed-up and go (TUG) test. The TUG test [25] assesses a patient's mobility. It is measured in seconds from the time the participant starts rising from a seat until they complete a walking loop around a cone 3 m away and their bottom touches the seat again.

Active ROM was assessed in the hip about to receive IASI for internal/external rotation (by goniometer), and flexion/extension and adduction/abduction (by inclinometer). Three measurements were taken for each test and averaged.

Imaging

A single weight-bearing AP pelvis radiograph including both hips was obtained at baseline. A fellowship-trained musculoskeletal radiologist with 30 years of experience, RL, rated the Kellgren–Lawrence (K–L) grade of OA severity [26], which focuses on structural damage.

At weeks 0 and 8, patients underwent hip ultrasound performed by a fellowship-trained musculoskeletal radiologist with a 15–6 MHz linear transducer (GE Logiq E9). A frequency of 12 MHz was preferred, but in obese patients it was at times necessary to reduce the frequency to as low as 6 MHz. With the patient laying supine and the probe viewing the hip anteriorly in sagittal plane, we obtained two grayscale and two

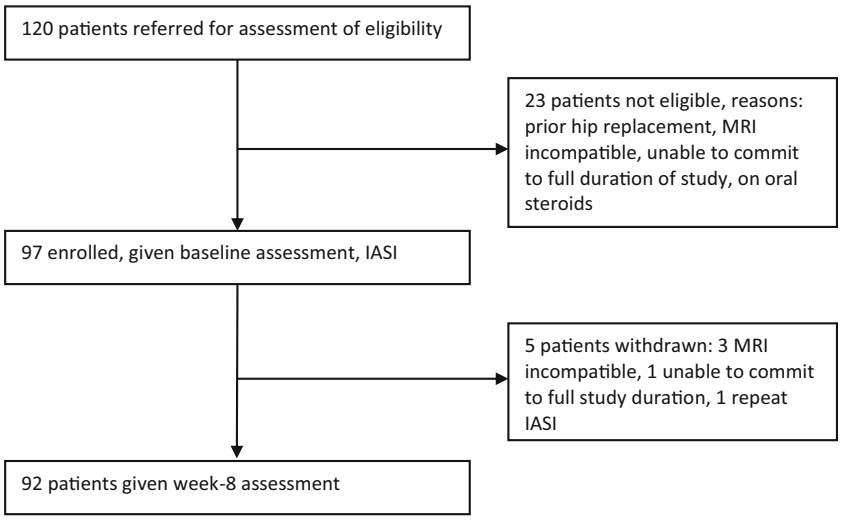

Fig. 1 Flowchart schematic of hip OA patients from referral to the research group for the study to completion of patient follow-up. MRI incompatibility included the presence of a cardiac pacemaker, intolerable pain, and/or claustrophobia from lying in the MRI machine

Doppler images of the femoral head, and two grayscale images of the femoral neck.

On each grayscale ultrasound image, the bone–capsule distance (BCD, cm) was measured from the outer femoral cortex to the outer edge of the synovium. This combines joint fluid and synovium. Although other studies typically measure BCD at the femoral neck, we measured it at three locations: the uppermost (proximal) margin of the uncovered femoral head; the most superficial (apex) point on the head; and the widest fluid pocket along the femoral neck (Fig. 2). To assess inter-reader reliability, two musculoskeletal radiologists (JJ, TN) performed measurements blinded to each other's readings and clinical data. JJ also re-measured a subset of images 7 days later, blinded to the original readings, to assess intra-reader reliability. Readers scored each Doppler image as 0, 1, or 2 to denote no signal, borderline signal, and definite signal respectively.

Magnetic resonance imaging

At baseline and 8 weeks post-IASI, we obtained sagittal hip MRI, including proton density fat-saturated (PDFS) and T2 fat-saturated (T2FS) images, slice thickness 3 mm, field of view FOV 220 × 220, matrix size 384 × 384, repetition time/echo time TR/TE 2,960/40 ms for PDFS, 5,770/100 ms for T2FS. We performed pre- and post-gadolinium sagittal T1FS sequences at FOV and slice thickness matching the PD sequences, TR/TE 522/13 ms. We also obtained post-gadolinium coronal 3D T1-weighted spoiled gradient echo volumetric interpolated breath-hold examination (VIBE) images, TR/TE 7.1/2.4 ms, flip angle 8°, matrix size 512 × 512, slice thickness 1.3 mm, and performed workstation reconstruction into sagittal images of each hip. All MRI were performed on the same 1.5-T Siemens Symphony magnet using a consistent protocol applied by

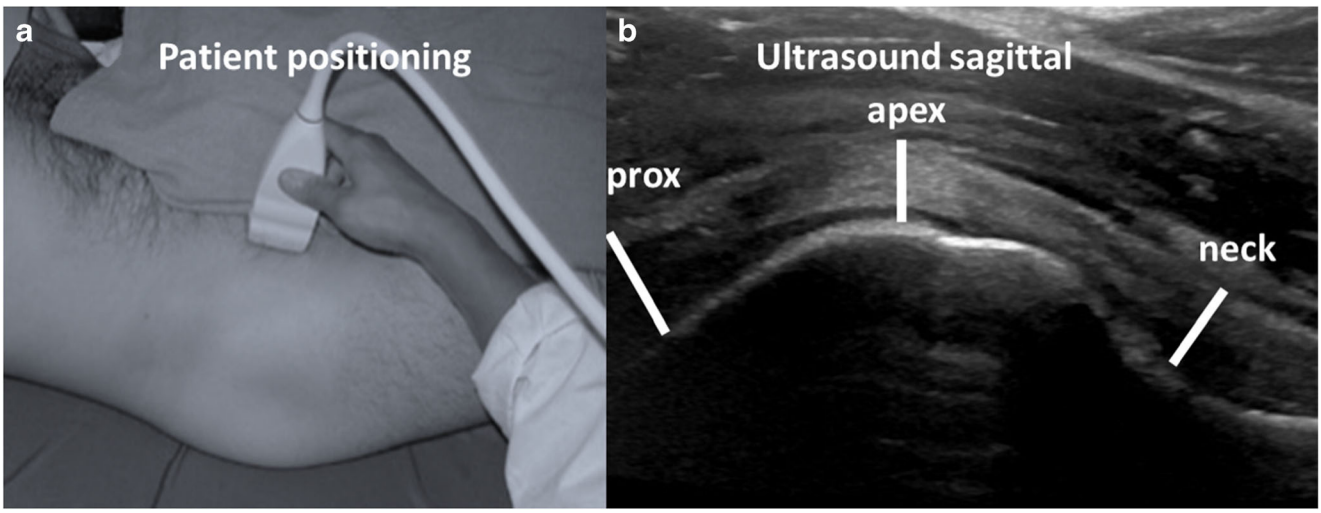

Fig. 2 **a** Patient and probe positioning for ultrasound. **b** Bone-to-capsule distance (BCD) measurement of effusion synovitis on ultrasound. *prox* proximal

one of two senior technologists specifically trained in performing this study. PDFS was optimized for overall anatomical detail, T2FS emphasized fluid signal to directly visualize effusion, and post-gadolinium VIBE enhanced visualization of hyperemic areas, such as in synovitis.

We assessed inflammation on MRI by methods as similar as possible to those used for ultrasound. Two fellowship trained musculoskeletal radiologists (AS and AL) separately measured effusion-synovitis as BCD on each of the three sequences, in the same three locations as on ultrasound (Fig. 3).

Treatment - intra-articular steroid injection

After all the other tests were performed, IASI of 40 mg triamcinolone acetonide was performed under fluoroscopic guidance, after injection of contrast material confirming intra-articular placement, as per standard clinical protocol.

Outcome measures

Improvements in WOMAC scores and TUG time post-IASI were used to stratify patients into responders and non-responders. Minimum clinically important difference (MCID) in WOMAC scores was defined as a threshold of ≥20% improvement, based on expert consensus and previous literature [27].

Statistical evaluation

Using IBM SPSS (v.24; IBM, Armonk, NY, USA), descriptive statistics were calculated for all data and bivariate Pearson correlation coefficients (r) computed between all continuous variables. To detect differences between groups, if tests for normality and homogeneity of variance tests were satisfied, we used single variable analysis-of-variance (ANOVA) tests; otherwise we used nonparametric Mann–Whitney U test. Paired t tests examined response to injection between weeks 0 and 8. To assess reliability, we used intra-class correlation coefficients (ICC, two-way mixed model for consistency) and kappa scores for continuous and categorical variables respectively. Differences for all statistics were deemed significant at $p \leq 0.05$. Patients with missing data were excluded for analysis between weeks 0 and 8, but included for analysis at the time point for which there are data.

Results

Characteristics of participants at baseline

Subjects were 54% male, average age 59 years (range: 28–87), and average BMI 30 (range 18.8–44.39). Although 74.7% of the cohort were overweight/obese (BMI > 25), only 5/ out of 97 reported comorbid diabetes, and 9 out of 97 were current smokers. Subjects showed a high burden of OA on radiographs, with 77 out of 96 patients (80%) having KL grade 2–4.

Reliability and baseline imaging findings

Reliability of imaging measurements is shown in Supplementary Table 1. BCD measured on grayscale ultrasound images and MRI

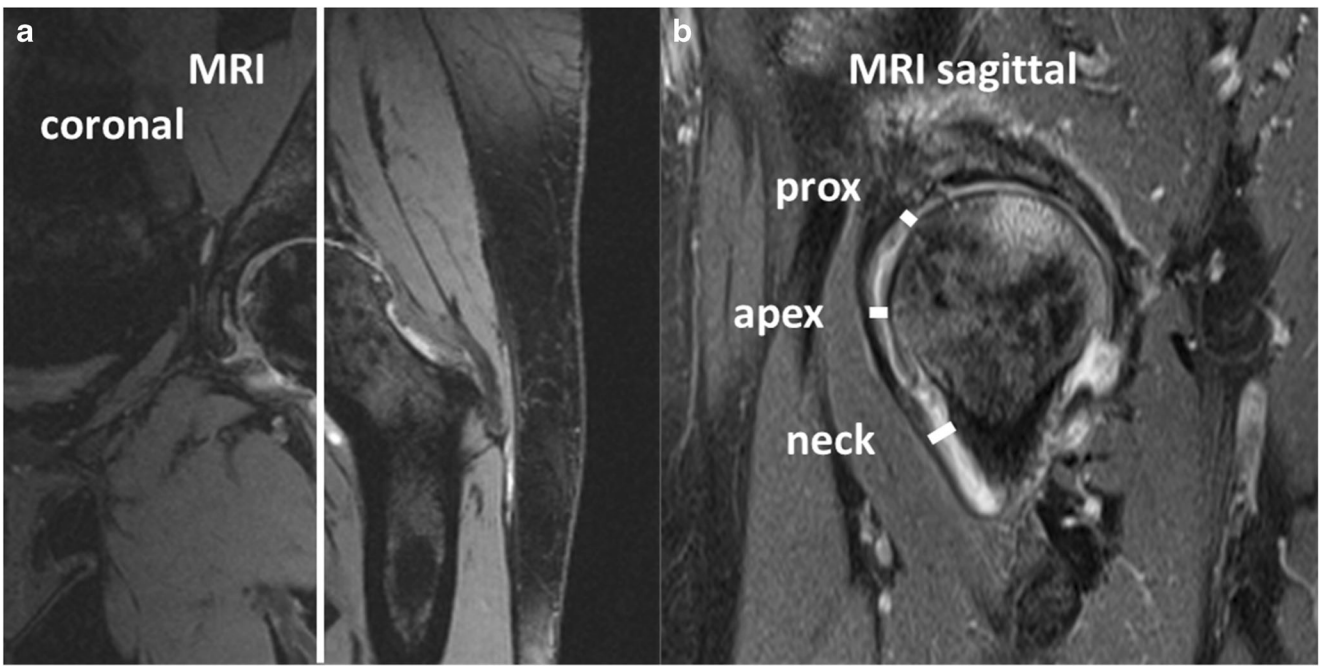

Fig. 3 **a** Coronal MRI view with line for sagittal cross section. **b** BCD measurement of effusion-synovitis on MRI at proximal, apex, and neck locations

showed moderate to high reliability, whereas power Doppler assessment of synovitis had fair inter-observer reliability.

Baseline BCD values for ultrasound and MRI are listed in Table 1 (only significant week 8 changes are shown). Baseline ultrasound and MRI both showed the neck as the widest point of effusion and the apex as the narrowest. BCD was generally slightly smaller on MRI than on ultrasound.

Comparison of variables at baseline

Ultrasound and MRI BCD correlated significantly with each other, especially at the apex and neck, but less so at the proximal location (Tables 2, 3). Power Doppler findings did not correlate significantly with any other imaging indices.

Imaging findings correlated with range of motion (ROM) and with pain and function measures at baseline (Table 4). With ultrasound, only the apex BCD correlated significantly with internal rotation and extension. All MRI measures correlated with internal rotation ROM, again less strongly at the neck than at the apex.

The proximal and apex BCD, on both ultrasound and MRI, correlated significantly and moderately with TUG. The post-gadolinium VIBE sequences correlated more strongly with TUG than other MRI sequences.

Table 1 Baseline (week 0) imaging, physical, and subjective scores for hip osteoarthritis (OA) patients. There were no significant changes in imaging and ROM scores. Only significant week 8–0 change scores were shown

		n	Mean	Standard deviation	Percentage change	Minimum	Maximum	*p* value
Ultrasound BCD (mm)								
Proximal	Week 0	89	9.411	8.9		3.8	14.7	
	Week 8	82	8.988	2.436	−4.36%	3.9	17.8	0.529
Apex	Week 0	90	5.888	2.0147		2.7	13.6	
	Week 8	86	5.808	2.713	−1.11%	1.7	19.3	0.822
Neck	Week 0	18	9.078	2.6989		4.3	14.1	
	Week 8	26	9.293	2.621	2.71%	4.8	14.6	0.198
MRI BCD (mm)								
Proximal PDFS	Week 0	93	5.6726	2.20363		2.85	15	
	Week 8	89	5.423	2.044	−4.40%	2.1	12.9	0.429
Apex PDFS	Week 0	93	3.907	1.858		1.6	12.5	
	Week 8	89	3.6961	1.918	−5.40%	1.45	12.9	0.382
Neck PDFS	Week 0	93	7.5392	3.26654		1.95	17.9	
	Week 8	89	7.541	3.332	0.00%	2.75	19.1	0.364
ROM (°)								
Flexion	Week 0	73	93.85	14.59		31	130	
Internal rotation	Week 0	74	18.45	10.066		0	40	
External rotation	Week 0	74	21.74	7.862		0	41	
Extension	Week 0	69	1.68	5.614		−22	15	
	Week 8–0	63	1.25	4.711	74.4%	−10	15	0.038653
TUG time (s)								
	Week 0	96	9.55	4.725		4.6	34.5	
	Week 8–0	89	−0.539	2.877	−5.6%	−22.3	3.4	0.081
WOMAC pain								
	Week 0	96	223.35	99.02		21	458	
	Week 8–0	90	−31.63	89.272	−14.2%	−304	192	0.001
WOMAC stiffness								
	Week 0	96	111.94	45.633		0	196	
	Week 8–0	91	−23.12	45.283	−20.7%	−163	105	<0.001
WOMAC function								
	Week 0	96	714.79	291.362		116	1296	
	Week 8–0	91	−92.54	286.134	−12.9%	−914	664	0.003

BCD bone-capsule distance, *PDFS* proton-density fat-saturated, *ROM* range of motion, *TUG* timed-up and go test, *WOMAC* Western Ontario and McMaster Universities Osteoarthritis Index

Table 2 Pearson's correlation (r) between ultrasound and MRI scores at baseline and week 8–0 change

			Ultrasound week 0		
			Proximal	Apex	Neck
MRI week 0	PD FS	Proximal	0.178	0.450**	0.660**
		Apex	0.176	0.487**	0.563*
		Neck	−0.016	0.254*	0.810**
	T1 FS	Proximal	0.268*	0.539**	0.755**
		Apex	0.206	0.557**	0.673**
		Neck	−0.019	0.256*	0.777**
	VIBE	Proximal	0.132	0.353**	0.745**
		Apex	0.217*	0.468**	0.723**
		Neck	−0.067	0.133	0.627**
	T2 FS	Proximal	0.157	0.454**	0.615**
		Apex	0.124	0.412**	0.566*
		Neck	−0.063	0.204	0.795**

VIBE volumetric interpolated breath-hold examination

*$p < 0.05$, **$p < 0.01$

Correlations with self-reported WOMAC scores were also tested. On ultrasound and MRI, the BCD at the apex showed a mild, consistently significant correlation with all three WOMAC subscales. ROM of flexion had mild correlations with WOMAC pain ($r = -0.294$, $p < 0.05$), ROM of internal rotation had mild correlations with WOMAC stiffness ($r = -0.280$, $p < 0.05$), and function ($r = -0.297$, $p < 0.05$). Of note, of the three WOMAC subscores the pain score showed the least relation to any baseline indices.

Response to intra-articular steroid injection

Changes in imaging findings by 8 weeks after IASI were small. There were no significant changes in BCD measured on ultrasound or MRI, or in Doppler indices.

In contrast, changes in objective findings were substantial. The TUG time improved nearly to the level of significance, and ROM extension and all three WOMAC subscores were significantly improved at week 8 (Table 1).

Baseline variables versus change in outcome measures

Baseline measures were compared with change in outcome variables 8–0 weeks post-IASI. Only on MRI did proximal and apex BCD at baseline show a statistically significant inverse correlation with change in TUG time (Table 5). Change in WOMAC scores had no relation to any imaging measures or ROM.

Differences in all baseline measures were also investigated between responder and nonresponder cohorts. Responders were defined as those with ≥1.4-s improvement in TUG time ($n = 19$), or ≥ 20% improvement in WOMAC pain ($n = 40$), stiffness ($n = 52$), or function ($n = 38$) [27]. Baseline variables were not significantly different between responder and nonresponder cohorts in any of these analyses (Table 6, Supplementary Table 2).

Discussion

We compared hip OA effusion-synovitis measurements on ultrasound and MRI to stratify and predict clinical re-

Table 3 Pearson's correlation (r) between ultrasound and MRI scores at baseline and week 8–0 change

			Ultrasound week 8–0 change		
			Proximal	Apex	Neck
MRI week 8–0 change	PD FS	Proximal	−0.292*	−0.125	−0.788
		Apex	−0.332**	−0.136	0.118
		Neck	−0.150	−0.026	−0.890
	T1 FS	Proximal	−0.385**	−0.201	−0.424
		Apex	−0.384**	−0.056	0.232
		Neck	0.016	0.236*	−0.660
	VIBE	Proximal	0.072	0.178	0.958
		Apex	−0.259*	−0.230	0.110
		Neck	−0.020	−0.125	0.381
	T2 FS	Proximal	−0.119	−0.144	−0.090
		Apex	−0.165	−0.260*	−0.325
		Neck	−0.094	−0.207	−0.092

*$p < 0.05$, **$p < 0.01$

Table 4 Pearson's correlation between imaging scores and ROM, TUG time, and WOMAC pain at baseline

			ROM flexion	ROM internal rotation	ROM extension	ROM external rotation	ROM abduction	TUG (s)	WOMAC pain
Ultrasound week 0		Proximal	−0.063	−0.141	0.113	−0.206	−0.103	0.380**	0.184
		Apex	−0.228	−0.347**	0.020	−0.371**	−0.232	0.393**	0.228*
		Neck	−0.121	−0.071	−0.308	−0.322	−0.220	0.252	0.025
MRI week 0	PD FS	Proximal	−0.452**	−0.359**	−0.268*	−0.219	−0.219	0.274**	0.226*
		Apex	−0.531**	−0.392**	−0.233	−0.241	−0.308*	0.294**	0.275**
		Neck	−0.203	−0.281*	−0.104	−0.141	−0.112	0.128	0.100
	T1 FS	Proximal	−0.406**	−0.371**	−0.166	−0.140	−0.211	0.215*	0.232*
		Apex	−0.480**	−0.328**	−0.236*	−0.184	−0.252*	0.182	0.266**
		Neck	−0.215	−0.267*	−0.059	−0.121	−0.148	0.107	0.098
	VIBE	Proximal	−0.400**	−0.409**	−0.179	−0.189	−0.249	0.282**	0.133
		Apex	−0.439**	−0.403**	−0.241*	−0.167	−0.320*	0.298**	0.187
		Neck	−0.189	−0.256*	−0.117	−0.082	−0.129	0.111	0.123
	T2 FS	Proximal	−0.323**	−0.135	−0.166	−0.124	−0.203	0.365**	0.169
		Apex	−0.301*	−0.128	−0.224	−0.136	−0.268*	0.401**	0.167
		Neck	−0.222	−0.161	−0.136	−0.108	−0.110	0.126	0.168

*$p < 0.05$, **$p < 0.01$

sponse to IASI in 97 patients with moderate-to-severe symptomatic hip OA. Baseline imaging findings and hip ROM correlated well with each other, but bore little relation to outcome measures. At 8 weeks after IASI, subjects overall showed a significant response to IASI according to several clinical criteria. Despite this, there was no significant change in any imaging findings of effusion-synovitis. There was some correlation with baseline MRI BCD and with improvement in TUG time, but no difference in imaging findings or ROM between responder and nonresponder WOMAC and TUG time cohorts. We were unable to determine which patients will respond to IASI

Table 5 Pearson's correlation between baseline imaging scores and ROM, and change between weeks 8 and 0 in WOMAC scores and TUG time

			TUG time (week 8–0)	WOMAC pain (week 8–0)	WOMAC stiffness (week 8–0)	WOMAC function (week 8–0)
Ultrasound week 0		Proximal	−0.206	−0.136	0.090	−0.163
		Apex	−0.098	−0.129	0.006	−0.094
		Neck	−0.022	−0.187	−0.070	0.115
MRI week 0	PD FS	Proximal	−0.202	−0.040	0.005	0.080
		Apex	−0.188	−0.025	0.060	0.123
		Neck	−0.066	−0.021	0.048	0.051
	T1 FS	Proximal	−0.239*	0.052	−0.014	0.065
		Apex	−0.228*	0.034	−0.057	0.017
		Neck	−0.099	0.110	−0.046	0.035
	VIBE	Proximal	−0.304**	0.027	−0.033	0.002
		Apex	−0.214*	−0.034	0.026	0.020
		Neck	−0.119	0.115	0.005	0.005
	T2 FS	Proximal	−0.025	−0.005	−0.034	0.032
		Apex	−0.094	0.015	−0.060	0.018
		Neck	−0.013	0.063	0.006	0.053
ROM week 0		Flexion	0.168	−0.027	−0.068	−0.230
		Internal rotation	0.118	0.150	0.126	0.142
		External rotation	−0.088	−0.007	−0.005	−0.118
		Extend	−0.072	0.115	0.107	0.121
		Abduction	−0.108	0.019	0.071	−0.006

*$p < 0.05$, **$p < 0.01$

Table 6 Baseline (week 0) imaging and physical examination values with a 95% confidence interval stratified by WOMAC pain and TUG time responders (>20%, >1.4-s improvement respectively) and nonresponders (<20%, <1.4-s improvement respectively) between weeks 8 and 0 after intra-articular steroid injection. No values reached statistical significance

			WOMAC pain 20% improvement					TUG time 1.4-s improvement				
			Nonresponders		Responders			Nonresponders		Responders		
			Mean	95% CI	Mean	95% CI	*p* value	Mean	95% CI	Mean	95% CI	*p* value
Ultrasound BCD (mm)		Proximal	9.36	(8.68, 10.04)	9.19	(8.62, 9.77)	0.88	9.18	(8.70, 9.65)	10.05	(8.85, 11.25)	0.12
		Apex	5.90	(5.30, 6.49)	5.72	(5.20, 6.23)	0.67	5.74	(5.31, 6.17)	6.16	(5.08, 7.23)	0.41
		Neck	8.89	(7.53, 10.25)	9.56	(6.54, 12.58)	0.65	9.31	(7.85, 10.77)	8.50	(8.50, 8.50)	0.70
MRI BCD (mm)	PD FS	Proximal	5.75	(5.08, 6.42)	5.56	(4.96, 6.15)	0.68	5.83	(5.32, 6.34)	5.33	(4.23, 6.44)	0.40
		Apex	4.11	(3.53, 4.69)	3.67	(3.18, 4.15)	0.26	4.01	(3.55, 4.46)	3.70	(2.92, 4.47)	0.53
		Neck	7.82	(6.85, 8.79)	7.43	(6.50, 8.36)	0.58	7.82	(7.04, 8.61)	6.98	(5.66, 8.30)	0.32
	T1 FS	Proximal	4.40	(3.70, 5.10)	4.02	(3.49, 4.55)	0.41	4.23	(3.74, 4.72)	4.27	(3.09, 5.45)	0.94
		Apex	3.09	(2.56, 3.62)	2.87	(2.45, 3.29)	0.53	2.96	(2.61, 3.31)	3.07	(2.07, 4.07)	0.80
		Neck	6.55	(5.55, 7.56)	6.16	(5.16, 7.17)	0.60	6.39	(5.55, 7.24)	6.07	(4.66, 7.48)	0.72
	VIBE	Proximal	5.68	(5.01, 6.35)	5.27	(4.68, 5.87)	0.38	5.48	(4.97, 5.98)	5.46	(4.33, 6.58)	0.97
		Apex	4.73	(4.09, 5.37)	4.19	(3.78, 4.59)	0.18	4.53	(4.06, 5.00)	4.28	(3.49, 5.06)	0.61
		Neck	6.80	(5.79, 7.80)	6.23	(5.30, 7.16)	0.43	6.69	(5.85, 7.53)	5.81	(4.67, 6.95)	0.31
	T2 FS	Proximal	3.13	(2.51, 3.76)	2.93	(2.36, 3.49)	0.64	3.17	(2.66, 3.68)	2.81	(2.01, 3.60)	0.50
		Apex	2.22	(1.74, 2.70)	2.06	(1.55, 2.58)	0.66	2.26	(1.84, 2.68)	1.87	(1.24, 2.51)	0.38
		Neck	5.81	(4.81, 6.80)	5.42	(4.51, 6.32)	0.58	5.80	(4.99, 6.62)	4.69	(3.56, 5.82)	0.19
ROM (°)		Flexion	89.97	(84.78, 95.16)	96.48	(92.55,100.41)	0.06	92.69	(89.05, 96.33)	94.36	(85.29, 103.43)	0.70
		Internal rotation	18.50	(15.27, 21.73)	17.74	(14.26, 21.22)	0.75	17.76	(15.16, 20.36)	18.64	(12.86, 24.42)	0.77
		External rotation	21.83	(19.47, 24.19)	20.97	(18.14, 23.80)	0.65	20.96	(19.05, 22.87)	21.64	(16.77, 26.51)	0.77
		Extend	2.09	(0.44, 3.74)	1.47	(0.00, 2.94)	0.58	1.83	(0.62, 3.04)	1.73	(−1.55, 5.01)	0.95
		Abduction	30.55	(26.48, 34.62)	31.19	(27.20, 35.18)	0.83	30.43	(27.43, 33.43)	33.00	(25.01, 40.99)	0.51

from baseline features of effusion-synovitis, despite our novel use of both ultrasound and MRI data.

Although our study population was composed of volunteers referred for IASI and not randomized, our subjects were quite representative of a typical hip OA population, with features similar to the 978-patient Framingham hip OA study [28], in terms of age, BMI, sex distribution, and KL grade (80% ≥2). The high prevalence of effusion-synovitis in our subjects, as defined by ultrasound femoral neck BCD ≥7 mm, was in line with findings in another study of significantly inflamed hip joints [20].

Overall, our imaging features had moderate to high intra- and inter-reader reliability. Although we measured BCD at more locations than others have done, our reliability was similarly high (e.g., ICC = 0.891 vs 0.982) [14]. Other studies included ultrasound-based measures of osteophytes [17], which we did not score because these are more reliably assessed on radiographs. MRI BCD was highly reliable, although post-gadolinium VIBE images, focused on synovitis, were less reliable for the measurement of effusion, likely because of lower spatial and contrast resolution.

No study to our knowledge has directly assessed the inter-observer reliability of Doppler synovitis measurement in hip OA, which was poor in our study. Especially since Doppler ultrasound also has substantial inter-scan variability, not measured here, we conclude that Doppler ultrasound of synovitis at the hip is challenging and not adequately reliable for clinical use. This poor performance compared with the established utility of Doppler ultrasound at other joints, such as in the hands [29], is likely due to the deep location of the hip, which limits Doppler sensitivity to the low flow typically seen, even in hyperemic joints. Another reason for difficulty detecting hyperemia in hip synovitis may be the requirement to image the joint in extension. In this position, the anterior soft tissues are relatively stretched/compressed, which may reduce vascularity.

Effusion-synovitis size correlated well when measured by ultrasound versus MRI, presumably because readers measured BCD at the same three locations (proximal, apex, and femoral neck) using similar techniques. The variation between ultrasound and MRI measurements could be due to different image resolutions between modalities. MRI has lower spatial resolution, increasing the contribution of errors from pixel volume averaging. However, MRIs have more crisply defined edges of synovium and bone from which to measure, in addition to offering more complete visualization of the joint to better define the widest point of the apex and neck. On ultrasound, the contrast resolution between joint fluid and hypoechoic synovium was often low, making it difficult to accurately define the borders to be measured.

Of note, there was a drop in correlation between ultrasound and MRI week 8–0 change. Because there was little change in the effusion sizes at 8 weeks post-IASI, the effect of minor variation in effusion reader measurement would have had a proportionately larger influence on the values of the changes detected, reducing the reliability of the measurements of interval change compared with the baseline measurements.

Ultrasound BCD at the apex, and MRI BCD at the proximal and apex locations, correlated well with ROM (internal rotation and flexion), but measurements at the femoral neck correlated with ROM to a much lesser extent.

There were overall mild correlations between baseline imaging/physical examination and functional status. Inflammatory imaging findings showed consistent, but weak correlations with TUG time. Imaging findings on post-gadolinium VIBE sequences had stronger relations with functional measures than other sequences, possibly because active synovitis affected gross motor function. ROM, notably in flexion/extension, was more closely correlated with TUG than imaging findings, but only moderately. The complexity and nonlinearity of the relationship between simple functional measures, such as ROM, and measures of broader function, such as capacity for gait, in hip OA, has been documented in the literature [30].

Baseline imaging and physical examination measures related only weakly to WOMAC scores. BCD at the apex on ultrasound and on nearly all MRI sequences correlated positively, but weakly, with WOMAC stiffness and function. No ultrasound BCD measures, MRI BCD only on PDFS and T2FS MRI, and no measures of ROM correlated significantly with WOMAC pain. The notable lack of correlation between WOMAC pain and MRI BCD on post-gadolinium VIBE implies that active synovitis might contribute more to hip joint stiffness than joint pain.

These data, especially with MRI confirmation of ultrasound findings, suggest that the traditional location of the measurement of effusion-synovitis at the femoral neck [19, 20, 31–33] may not be the most effective place for measurement. It may be that joint effusions pool at the femoral neck, whereas the apex, a region of stretched/compressed tissue, provides a purer measure of synovial thickening, which seems to be a larger contributor to reduced function in patients than effusion. Further larger studies would be needed to refine these conclusions.

Most relationships among imaging, physical examination, and functional indices at baseline disappeared when comparing baseline status with change in outcome at 8 weeks post-IASI. No baseline findings correlated with changes in WOMAC scores. Patients with higher baseline BCD on MRI did have a mild but statistically significantly larger decrease in TUG time at 8 weeks, indicating greater improvement post-IASI. Overall, outcomes including TUG and WOMAC all showed significant improvements 8 weeks post-IASI, but widespread changes in ultrasound, MRI, or ROM did not occur between 0 and 8 weeks to account for this.

This was an observational study in volunteers, who had to donate 3 h of their time twice in 8 weeks and respond to multiple phone calls, introducing possible recruitment bias. However, our population characteristics were similar to those seen in other hip OA studies, arguing against substantial volunteer bias. We had a relatively small sample size for a clinical study, mainly because of the cost requirements for MRI. It is important to note that despite having many statistically significant findings, some correlations may have been lost given the limited power of our statistics due to sample size. For this reason, we have provided the data for the section Baseline variables versus change in outcome measures, although none of the data reached statistical significance. Given the large amount of data acquired, we also have instances of incomplete data that led to differences in sample size, making some comparisons less reliable, notably ultrasound femoral neck versus apex BCD. However, MRI effusion data were complete and comprehensive, allowing confident verification. We did not score MRI bone marrow lesion (BMLs); accurate measurement is technically challenging and there was little change in BMLs post-IASI in a recent study [22]. There are also various doses of IASI used in practice, in particular 40 mg and 80 mg for triamcinolone acetonide. Although these two doses may have had different outcomes, we used 40 mg as per our regional clinic practice, also consistent with the study by Lambert et al., which showed significant effect at week 8 follow-up [27]. Finally, it is important to note that the comparison of responders and nonresponders was exploratory and limited to univariate comparisons. Although there were no statistically significant findings with univariate relationships between outcome and predictors, we conducted a multivariate analysis to further explore potential relationships. Despite using a liberal variable inclusion criterion ($p < 0.20$), there were no variables found to independently relate to the outcomes (data not shown).

Despite these limitations, we found that imaging and physical examination findings at baseline only mildly related to the pain and disability experienced by patients with hip OA. Substantial improvements in pain and disability 8 weeks post-IASI were seen as expected, but could not be convincingly explained by any baseline features on a comprehensive assessment. There may be a relationship between BCD measured on MRI and improvement in TUG time, which should be explored in further studies. However, basic measures on ultrasound, MRI, and physical examination do not consistently predict response to IASI. Other, unmeasured factors are likely contributing to steroid effects.

Conclusion

Effusion-synovitis reflecting inflammation can be reliably measured at the hip on ultrasound and MRI, but showed little clinical utility for predicting response to steroid treatment, nor any consistent insight into patient functional status. MRI findings may be related to change in function after IASI, which should be explored further. Unmeasured additional phenomena are likely at work.

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Compliance with ethical standards

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